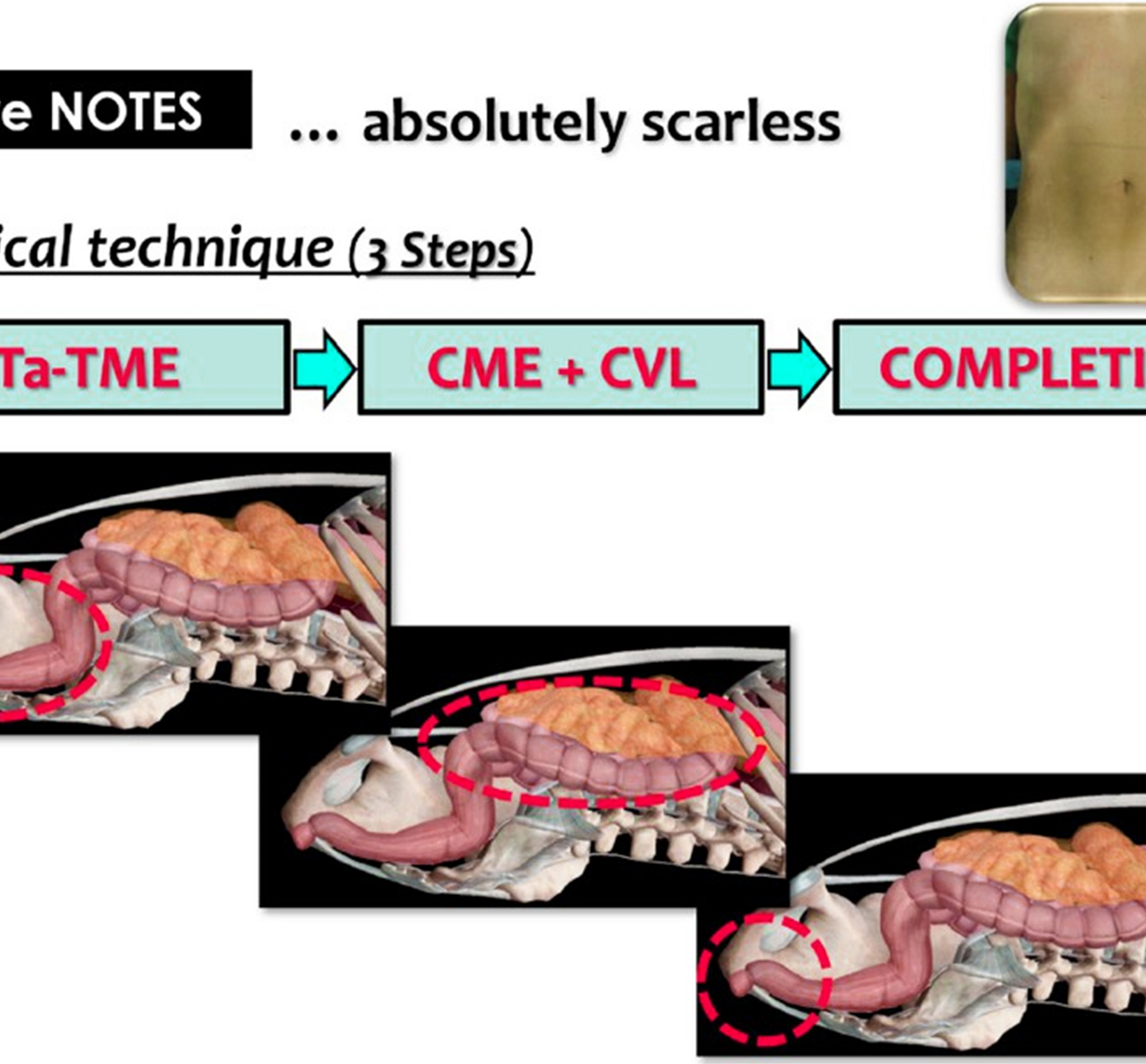
ISSN 2574-1225 (Online)
Volume 3 | 2019

Mini-invasive Surgery



www.misjournal.net
OAE Publishing Inc.

EDITORIAL BOARD

GENERAL INFORMATION

About the Journal

Mini-invasive Surgery (MIS), ISSN 2574-1225 (Online), is a peer-reviewed and continuously published online journal with print on demand compilation of articles published. The journal's full text is available online at www.misjournal.net. The journal allows free access (Open Access) to its contents and permits authors to self-archive final accepted version of the articles on any OAI-compliant institutional/subject-based repository. The journal aims to promote the greater exchange and dissemination of ideas, findings, novel techniques, and the utilization of new instruments and materials among experts in this discipline around the world. Our journal also aims to document specific clinical findings that may indicate new or alternative understanding of existing surgical techniques. The journal provides a global platform that deals with all extensive works and research related to all areas of minimally invasive surgery, endoscopy, treatment, and diagnosis. The journal is indexed by Google Scholar, J-Gate, CNKI, Chaoxing "Domain" Publishing Platform and ResearchBib.

Information for Authors

Manuscripts should be prepared in accordance with Author Instructions.
Please check www.misjournal.net/pages/view/author_instructions for details.
All manuscripts should be submitted online at https://www.oaemesas.com/mis.

Copyright

Permissions

For information on how to request permissions to reproduce articles/information from this journal, please visit www.misjournal.net.

Disclaimer

The information and opinions presented in the journal reflect the views of the authors and not of the journal or its Editorial Board or the Publisher. Publication does not constitute endorsement by the journal. Neither the MIS nor its publishers nor anyone else involved in creating, producing or delivering the MIS or the materials contained therein, assumes any liability or responsibility for the accuracy, completeness, or usefulness of any information provided in the MIS, nor shall they be liable for any direct, indirect, incidental, special, consequential or punitive damages arising out of the use of the MIS. The MIS, nor its publishers, nor any other party involved in the preparation of material contained in the MIS represents or warrants that the information contained herein is in every respect accurate or complete, and they are not responsible for any errors or omissions or for the results obtained from the use of such material. Readers are encouraged to confirm the information contained herein with other sources.

Publisher

OAE Publishing Inc.
245 E Main Street ste122, Alhambra, CA 91801, USA
Website: www.oaepublish.com

Contacts

E-mail: editorialoffice@misjournal.net
Website: www.misjournal.net

Mini-invasive Surgery

CONTENTS

Mini-invasive Surgery

Review

Open Access

Check for updates

Minimally-invasive liver resection for liver tumors in children: a snapshot of the current landscape

Miriam Cortes-Cerisuelo[1], Michael Berger[2]

[1]Liver Transplantation, Institute of Liver Studies, Liver Transplant Surgery, King's College Hospital, National Health Service Foundation Trust, London SE5 9RS, UK.
[2]Department of Pediatric Surgery, Research Laboratories, Dr. von Hauner Children's Hospital, Ludwig-Maximilians-University, Munich 80337, Germany.

Correspondence to: Dr. Michael Berger, Department of Pediatric Surgery, Dr. von Hauner Children's Hospital, Ludwig-Maximilians-University, Lindwurmstrasse 4, Munich 80337, Germany. E-mail: michael.fabian.berger@gmail.com

How to cite this article: Cortes-Cerisuelo M, Berger M. Minimally-invasive liver resection for liver tumors in children: a snapshot of the current landscape. *Mini-invasive Surg* 2019;3:1. http://dx.doi.org/10.20517/2574-1225.2018.60

Received: 29 Aug 2018 **First Decision:** 8 Nov 2018 **Revised:** 28 Nov 2018 **Accepted:** 11 Dec 2018 **Published:** 8 Jan 2019

Science Editor: Fernando Andrés Alvarez **Copy Editor:** Cui Yu **Production Editor:** Huan-Liang Wu

Abstract

Minimally-invasive liver resection (MILR) is a promising approach and has become a standard therapy option for a variety of indications, including liver tumors, in adults. Although minimally-invasive techniques are common practices in children, the usage and literature regarding MILR in children is scarce. In this article, we give an update on the current literature, share some of our own experience and give a future outlook of the potential benefits and shortcomings regarding MILR in children.

Keywords: Minimally-invasive liver resection, pediatric cancer, hepatoblastoma, laparoscopy, liver tumor

INTRODUCTION

Minimally-invasive liver resection (MILR) has been successfully integrated as a valuable surgical tool in adult patients both for cancer resections as well as donor hepatectomies for liver transplantation[1-3]. Although minimally-invasive surgical techniques are an essential component in the treatment of pediatric patients with hepatobiliary disease, literature on MILR hepatic tumors in children is scarce. This understanding is explained at least partially by the immense rarity of these tumors in the pediatric age group. In order to better standardize the invasive and complex treatment of hepatic malignancies in children and to obtain more reliable research data regarding their treatment, corresponding study groups from different parts of the world have put in place a global interdisciplinary initiative called The Children's Hepatic Tumors

International Collaboration (CHIC)[4]. One of the tasks in this collaboration is the standardization of the surgical resection involved, by whatever means. In this article, we focus on reviewing the existing literature on MILR in children and try to give an outlook of the possibilities and limitations of applying MILR in children with cancer and how it could fit into current, standardized treatment strategies.

MILR IN ADULTS

MILR is now considered an established treatment option in adult liver tumor surgery with a curative intent of both benign and malignant disease[1-3]. This advancement has been the result of increased surgical experience, high-quality imaging laparoscopes with better visualization of the operative field and the availability of specialized laparoscopic instruments for transecting the liver parenchyma[3,5,6]. In large centers, outcomes and complication rates are similar to those of open resection, notwithstanding the known benefits of a minimally-invasive surgical approach[2,7]. Currently, there is an international multicenter randomized controlled trial in Europe (ORANGE PLUS-II) comparing open *vs.* laparoscopic right or left hemihepatectomies for malignancies with the main outcome being time to functional recovery (https://clinicaltrials.gov/ct2/show/NCT01441856).

The knowledge acquired from minimally-invasive liver surgery (MILS) for liver tumors in adults has opened the horizon for a variety of additional indications for MILS in the adult population. For example, in addition to tumor resections, MILR has now gained acceptance as a means for resections carried out for live donor liver transplant, especially in the setting where the recipient is a child and the intended graft is that of a left lateral segment[8-13]. The first laparoscopic donor hepatectomies (left lateral section grafts) were reported in 2002 and were performed for living donor liver transplantation (LDLT) in children[14]. A recent large series of 220 consecutive donations in pediatric live donor liver transplants showed similar recipient outcomes including graft survival with better perioperative outcomes of the donors[15]. The data on full lobe resection for live donor liver transplant in the adult setting, especially concerning the right lobe, appear to be less clear and are currently being discussed. However, at this time, many centers see encouraging results with this approach[16,17]. It is likely that full laparoscopic right lobe hepatectomy, as is the case for the left lateral segments, will become an accepted approach for adult live donor liver transplant as expertise with MILR continues to grow. This approach has become the standard method in some large LDLT centers with exceptionally high volume[18,19].

CURRENT TREATMENT OF PEDIATRIC LIVER TUMORS

Pediatric liver tumors are uniquely different from adult liver tumors[20]. While adult liver tumors typically develop as carcinomas in cirrhotic or otherwise diseased livers, this type of growth is the exception in the pediatric population. Rather, pediatric liver tumors are of embryonic origin and arise in otherwise healthy livers, surrounded by healthy liver parenchyma. As will be explored later on, this understanding has important implications for the resection of liver tumors in children, especially when considering a minimally-invasive approach.

A wide variety of different tumors can arise in the pediatric liver. These include benign tumors such as the infantile hepatic hemangioma as the most common benign liver tumor in children as well as the mesenchymal harmatoma and the focal nodular hyperplasia[21,22]. Hepatoblastoma is not only the most common malignant liver tumor in children, but also the most common liver tumor in children in general[21,22]. Others, but considerably less common malignant liver tumors in the pediatric populations are the undifferentiated embryonal sarcoma of the liver, the rhabdomyosarcoma of the biliary tree and the hepatocellular carcinoma (HCC) of childhood[21,22]. It is of utmost importance that any surgeon treating such tumors is intimately familiar with the details of the clinical development, their growth pattern, their prognosis, as well as the up to date concerted interdisciplinary treatment algorithms of the large pediatric tumor study groups. The current treatment approach of pediatric liver tumors is perhaps best exemplified with the treatment algorithm of hepatoblastoma[23,24], the most common pediatric liver tumor[21,22]. Hepatoblastoma typically arises before or right around 3 years of age[25,26]. Hepatoblastoma shares this important feature with essentially all other pediatric liver tumors, with the exception of HCC of childhood[21,22]. While the latter is found mostly in adolescence, the large majority of all other childhood tumors arise at very young age. As it is easily understandable, this insight has significant impact when selecting the operative approach.

Traditionally, knowledge regarding hepatoblastoma has been extracted from the four major cooperative study groups: the International Childhood Liver Tumors Strategy Group (SIOPEL), Children's Oncology Group (COG), the German Society for Pediatric Oncology and Hematology, and the Japanese Study Group for Pediatric Liver Tumors. Because the numbers of patients in these individual groups were low due to the rarity of the disease and all groups used fundamentally different staging and stratification systems, the comparability of the data obtained was limited[23,24]. For this reason, with the involvement of the four groups, a worldwide coalition for the study of hepatoblastomas was formed[4,24]. As one of its first tasks, CHIC has recently generated a novel risk stratification based on data from more than 1,600 children treated for 25 years for hepatoblastoma. This risk stratification is based on the stage classification according to PRETEXT (pre-treatment extension), the initial AFP value at diagnosis, the presence of metastases, the presence of vascular invasión and the age of the child, and characterizes the four risk levels: very low, low, intermediate and high[24]. Because this stratification system will be used in a new global research study on hepatoblastoma (PHITT) starting in 2018, all other risk stratifications regarding hepatoblastoma have become obsolete. In the PHITT trial, the PRETEXT (pre-treatment extension) grouping system of SIOPEL is used for childhood liver tumors[27]. This system is based exclusively on pretherapeutic imaging and is thus independent of the surgical or therapeutic intervention. It describes the extent of the tumor across the 4 surgical sectors of the liver and additionally contains defined PRETEXT risk factors. PRETEXT risk factors include invasion of the tumor into one or more hepatic veins (abbreviated by the letter V) or portal vein (P) and extrahepatic tumor invasion (E), tumor rupture (R) or multifocality of the tumor (F). Because a high prognostic relevance for this classification has been proven, it has gained international acceptance[24]. In the studies of the US COG, until recently, the traditional staging system, which relies on tumor size in terms of resectability, was used at the same time[21,22]. Because of its primarily surgical perspective, this system has above all relevance in HCC[21]. However, the COG-staging system is not part of the PHITT trial[24].

Since most childhood liver tumors are either benign and partly regress spontaneously (infantile hepatic hemangioma) or respond well to chemotherapy (hepatoblastoma), primary resection is usually not indicated as a primary therapeutic approach[21,22]. This understanding is especially true in infants, toddlers and schoolchildren. Primary resection in benign tumors is indicated when they grow in size, when there are radiological changes suspicious of malignancy and/or if they become symptomatic[22]. As part of the PHITT trial, the surgical treatment decision is clearly regulated and represents a separate study branch within the trial. According to the trial, an initial resection is indicated in children only if there is a stage PRETEXT I or II liver tumor and the tumor is safely removable via a simple lobectomy (trial details at https://clinicaltrials.gov/ct2/show/NCT03017326). All other children undergo a biopsy first and then, if the diagnosis of a hepatoblastoma is confirmed, two cycles of chemotherapy are initiated. After reimaging, the resection will be performed as long as it can be carried out as a simple lobectomy and only if the tumor can be removed safely and completely with this approach. If this is not possible, there will be two more chemotherapy blocks, blocks 3 and 4. During the administration of blocks 3 and 4, the child is evaluated for liver transplantation, which can then be carried out without further delay after completion of block 4. In individual cases, the improvement after the end of block 4 may instead of the liver transplantation call for a complex or extended resection, always on the premise that the tumor can be completely removed. In cases where there is doubt of resectability, the surgery can be performed when an organ becomes available and with another recipient ready as a backup in case the tumor can be successfully resected. Reviewing the results of this study section of the PHITT trial will hopefully clarify which patients will benefit more from extended resection *vs.* transplantation and vice versa. For children who undergo resection, the study does not distinguish between an open and a laparoscopic approach. However, it is clear that any innovative surgical technique such as MILR must be properly integrated in a way that respects these surgical parameters.

MINIMALLY-INVASIVE HEPATOBILIARY SURGERY IN THE PEDIATRIC POPULATION

Minimally-invasive hepatobiliary surgery has long been established in the pediatric population. As is the case for adults, one of the most commonly performed minimally-invasive hepatobiliary surgeries carried out in children is cholecystectomy. This surgery can be safely performed by single-incision laparoscopic surgery (SILS)[28]. More complex operations of reconstructive nature are similarly standard of care in pediatric surgery. Resection of a choledochal cyst and reconstruction of bile flow with hepaticojejunostomy is routinely carried out in pediatric surgery, although some centers report higher complication rate compared to open surgery[29,30]. This operation has been carried out successfully with a SILS approach[31]. One of the major long-term complications of choledochal cyst resection is, independent of the surgical approach, stenosis of the hepaticojejunal anastomosis requiring dilation by the interventional radiologist or surgical revision. Redo hepaticojejunostomy for children with choledochal cyst can - in experienced hands - be carried out safely as a minimally-invasive approach[32,33]. Other indication in which laparoscopic hepatobiliary surgery has been advocated in the pediatric population is the resection of hepatic cysts, even in the neonates[34,35]. Although these cysts rarely require intervention, if they do they usually do not require formal liver resections but simple cyst resection.

While the above-mentioned indications have withheld the test of time and are widely accepted amongst pediatric surgeons around the world, one indication remains controversial. The excitement for the early success of laparoscopic hepatobiliary surgery in children, especially that of choledochal cyst resection, has lead to the laparoscopic reconstruction of biliary atresia over open reconstruction, which was until then the mainstay therapy of this disease as a bridge to liver transplant. Despite the initial enthusiasm, increasing evidence shows inferior outcomes for the laparoscopic approach of this sophisticated procedure[36-38], which is currently not considered standard of care. Nevertheless, a recent study with a large sample size has shown, for the first time, an equal outcome for the laparoscopic approach when looking at 3 and 5-year native liver survival, confusing the interpretation of current data[39]. At our center, we perform the Kasai procedure open for all cases of biliary atresia unless primary liver transplant is necessary.

Laparoscopic correction of extra-hepatic congenital portosystemic shunts (CPS) in children has also been described[40]. CPS is a rare entity and may lead to the development of jaundice, encephalopathy and pulmonary hypertension[41]. Obliteration of the shunt by the interventional radiologist by coiling or with a vascular plug is not always an option, especially in large shunts or in those with flow directed to the inferior vena cava with risk of migration of the foreign body into the heart. While the laparoscopic approach could be an option, open laparotomy is generally required in these cases.

MILR FOR PEDIATRIC LIVER TUMORS

Although laparoscopic hepatobiliary surgery is commonplace in pediatric surgery, anatomical liver resection in the pediatric population remains one of the last ambitions in the evolution of laparoscopic surgery. This understanding is explained partially by the low frequency of liver tumors in children, which makes it difficult for surgeons to accumulate experience with this technique.

Thus far, most laparosocopic hepatectomies reported in children are case reports and small case series of non-anatomical resections for small, peripheral and isolated lesions[34,42-46]. Tabrizian and Midulla[34] and

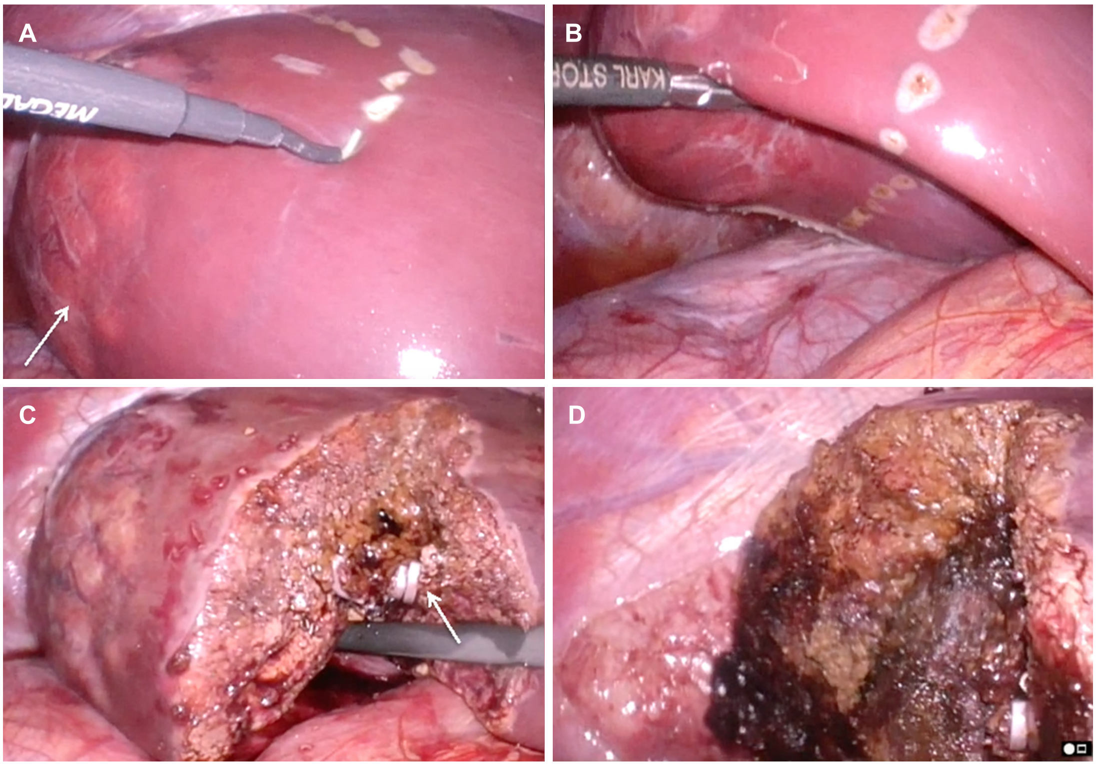


Figure 1. Intraoperative view of an anatomical segment 7 resection of a 12-year-old girl with a large adenoma. A: The resection line is being mapped out with the electrocautery, the tumor in segment 7 is shown (white arrow); B: the mobilized right lobe is shown with the resection line completely mapped out; C: the corresponding Glisson bundle of segment 7 with its portal vein branch, arterial branch and bile duct is divided between clips (white arrow); D: the completed resection. There was only minimal blood loss in the case

Oh *et al.*[43] used a full laparoscopic approach to excise hepatic cysts. Interesting about these two particular case reports is the fact that both children had large cysts and were rather young, one being a newborn and the other being only 2-month-old. Dutta *et al.*[42] reported a case of successful non-anatomical laparoscopic hepatic resection of a large mesenchymal hamartoma. This operation took place in a 2-year-old boy. Yoon *et al.*[44] performed a total laparoscopic left lateral sectionectomy in a 5-year-old girl who suffered from the same tumor. The operative time in their case was 150 min and the estimated blood loss was 100 mL. There were no complications and the length of stay (LOS) was 11 days. The postoperative pathology showed a disease-free resection margin and confirmed the diagnosis of mesenchymal hamartoma of the liver. Kim *et al.*[45] in 2011 reported on 38 children with confirmed diagnosis of hepatoblastoma treated between 1991 and 2009 at the Asan Medical Center Children's Hospital in Seoul, Korea[45,46]. In their retrospective review, of the 38 children with hepatoblastoma, a total of two resections were carried out as total laparoscopic resections and both cases were partial hepatectomies. There were no complications and both children were free of disease at follow up after 8.1 and 19.3 months, respectively. In Figure 1 we present a case of our own unpublished cohort. This 12-year-old girl suffered from a large hepatic adenoma and underwent laparoscopic resection of segment 7. There were no complications and the tumor was removed with negative margins.

Besides these anecdotal case reports, there is only one larger study on the subject in the current English literature. Michaelle Veenstra and Alan Koffron published in 2015 this first comprehensive review of MILR in children[47]. In their retrospective review, they included 36 children who underwent MILR for benign and malignant disease. For these children, the data analyzed included patient demographics, operative technique, pathology, complications, recurrence, and outcome. From a technical point of view, MILR was carried out as one of the following three approaches: pure laparoscopic, hand-assisted laparoscopy, and a hybrid laparoscopic assisted method. In the latter approach, the initial parts of the resection were carried out laparoscopically and finished as an open resection, overall allowing for a smaller incision than typically necessary for an open resection. Of all patients on the case series, 19 were females and the mean age was 2.7 years (9 months to 17 years). While three of these patients were adolescents between 12-16 years undergoing liver resection for benign tumors, two were under the age of 2 years undergoing liver resection for hepatoblastoma[47]. Of all resections carried out, 15 were for benign tumors and 21 were for malignant tumors. Of the 21 children with malignant tumors, 20 had hepatoblastoma and the remaining one was an adolescent of 17 years with a fibrolamellar HCC. All were unifocal lesions with a size ranging from 2-16 cm in the benign tumor group and from 2-9 cm in the malignant tumor group. Of the 36 children, 31 (86%) surgeries were performed as pure laparoscopic resections and 5 (14%) were carried out either as hand-assisted or hybrid procedures. Of the 31 purely laparoscopically performed resections, 10 were segmentectomies, 5 were sectionectomies, and 16 were hemihepatectomies. Of the 5 hand-assisted or hybrid procedures, one was a segmentectomy, and 4 were hemihepatectomies. The operative time correlated with the amount of liver resected and was 74 (50-110) min for the segmentectomy group, 120 (48-200) min for the sectionectomies and 195 (55-450) min for the hemihepatectomies. Five patients required blood transfusion, 4 of which underwent hemihepatectomy as hand-assist or hybrid procedure. Five patients suffered postoperative complications. There was one seroma, one port site infection, one-line infection, one port dehiscence, and one hypertrophic scar. The LOS was 3 days (2-6) for the segmentectomies, 4 days (2-5) for the sectionectomies, and 5 days (2-9) for the hemihepatectomies. This LOS is shorter compared of what is published for open resection of malignant tumors in children[48]. All malignant tumors were removed with R0 margins. Follow-up for children with malignant disease was 12-36 months and there were no local recurrences. One child had pulmonary metastasis prior to resection, which had resolved on radioimaging following neoadjuvant chemotherapy, however, this child had recurrence of the pulmonary lesions during the follow-up period after the resection. In this same study, patients not considered for MILR were those that would not tolerate laparoscopy, malignant lesions that could not be safely removed with adequate margins laparoscopically and those with lesions too close to major vascular or biliary structures on imaging to allow safe laparoscopic resection[47]. Taken together, although their review does not include comparisons to contemporaneous open controls, this comprehensive report for the first time shows that with appropriate patient selection and the necessary expertise, MILR can safely be carried out in children with both benign and malignant liver disease with excellent outcomes and minimal morbidity. Additionally, it clarifies that patients bearing malignant tumors with PRETEXT III or above (three sections are involved, and no two adjoining sections are free), with macrovascular invasion that require reconstruction of the vena cava or the portal vein, or with doubts of resectability in whom liver transplantation is the next treatment option, may be poor candidates for MILR.

OUTLOOK INTO THE FUTURE

Minimally-invasive hepatobiliary surgery in children requires not only specialized equipment but also particular expertise in order to confine precision work in the enclosed space of the child's abdominal cavity. This is especially important for the consideration of MILR for pediatric tumors, because they typically arise before the age of 3 years, when the entire abdominal cavity has the average size of an adult man's liver. Therefore, a hand-assisted approach, which is wide spread in adult MILR, is more difficult to perform in the child due to the enclosed working space. Also, the incision required for the hand-port nearly confines the incision necessary for open surgery, especially in a small child, therefore reducing the effect of "minimally-invasive" surgery. However, it is important to note that the incision for a hand-port is usually vertical in the midline of the upper abdomen and does not transect the rectus muscle, usually the main driver of postoperative pain following typical open surgery. Nevertheless, unless operating on a large child or an adolescent, hand-assisted MILR is unlikely to represent a breakthrough in pediatric oncological liver surgery. On the contrary, other techniques widely spread in the pediatric population may be of great benefit when considering MILR in this particular population. Perhaps its biggest value can be found in cases that are elaborate and may otherwise not be completed safely without full conversion. Foremost, this includes SILS.

SILS allows operating through one access site, eliminating the multiple sites traditionally used, even in small children[28]. When performing complex hepatobiliary cases laparoscopically in a child, including MILR, we advocate using a hybrid approach in which the SILS-port is used in addition to traditional trocar sites. This allows introducing more instruments from various angles without making additional incisions and hence gives more flexibility for the intracorporal work. In such an approach, the incision for the SILS-port can safely be extended up to 5 cm or more depending on the type of port used, an ideal length for either extraction of bowel for an extracorporal anastomosis or for the extraction of a resected tumor. Importantly, different from traditional laparoscopically-assisted procedures, the SILS-port, after having been taken out the tumor specimen, will remain a seal and can be reinserted unlimited amount of times despite the extension of the original incision. This allows for greater flexibility when performing combined intra- and extracorporeal reconstructive work or when removing more than one tumor specimen at a time. Although complete hepatectomy has been successfully carried out in adults uniquely through SILS[49], the authors have no experience nor know of any experience with performing MILR in children exclusively through a SILS port other than for simple atypical resections of peripheral lesions. However, the enclosed space of the pediatric abdominal cavity in children put aside, theoretically there is no reason that such a procedure is technically not feasible. One wonders though, given the small size of additional trocar sites in children, if it is necessary.

Robotic surgery has been recently introduced in the clinical practice and it has been accepted as an effective option to perform high-demanding procedures including hepatobiliary surgery in adults[50]. A recent review on the application of robotic surgery to liver surgery in adults when compared to open or laparoscopic shows no inferiority, however, randomized control trials are necessary to reach broader conclusions[51]. The role of robotic surgery in pediatric surgery remains controversial partly because of the lack of pediatric-sized robotic instruments and equipment, the elevated cost and the need for robotic-trained pediatric surgeons. In children, similar to adult surgery, robotic surgery has become popular in pediatric urology, being the pyeloplasty and partial nephrectomies the more accepted procedures[52]. Nothing is known about the role and the advantages of robotic procedures in liver surgery in children.

Independent of the technical challenges in MILR in children, the most important task of our field will be to assure that the current recommendations for surgical resection of the corresponding pediatric oncological study groups, especially CHIC, are not compromised by the innovation of MILR. This is especially true for malignant tumors such as hepatoblastoma and HCC, for which there is overwhelming evidence that incomplete resection significantly worsens prognosis, even if followed by liver transplant[23]. As MILR continues to grow within pediatric oncology, more research is needed to evaluate the full impact of MILR in children. The current evidence is summarized in Table 1, representing one article with level III evidence (comprehensive retrospective review) and several articles with level IV evidence (case reports and case series). A large prospective study would be the highest possible level of evidence addressing the question of whether there are significant differences in outcome and morbidity between open and laparoscopic liver resection for pediatric tumors and would certainly be much desired. However, similar to the obstacles found when creating the current PHITT study, due to the rarity of hepatic tumors in children, such a trial would have to be designed as a global effort in order to obtain adequate numbers for reliable statistical analysis. Until then, it would be nevertheless of immense value if more literature were to become available on the subject, whether small prospective studies or comprehensive retrospective reviews.

CONCLUSION

MILR for liver tumors is the last bastion in the evolution of pediatric hepatobiliary surgery. Slowly, accumulating evidence around the world indicates that with experience and careful patient selection, laparoscopic liver resections can be carried out safely and without compromising outcomes. The children operated with this approach appear to benefit from the typical advantages of minimally-invasive surgery.

Table 1. Overview of existing literature for minimally-invasive liver resection in children

Year	Ref.	Article type	Study population	Age	*n*	Type of resection	Level of evidence
2006	Yoon *et al.*[44]	Case report	Mesenchymal hamartoma	5 years	1	Total laparoscopic left lateral sectionectomy	4
2007	Dutta *et al.*[42]	Case report	Mesenchymal hamartoma	2 years	1	Successful non-anatomical resection	4
2010	Tabrizian and Midulla[34]	Case report	Congential hepatic cyst	2 months	1	Complete laparoscopic cyst excision	4
2011	Kim *et al.*[45]	Case series	Hepatoblastoma	9 months, 2 years	2	Totally laparoscopic partial hepatectomy	4
2012	Oh *et al.*[43]	Case report	Congential hepatic cyst	6 weeks premature	1	Complete laparoscopic cyst excision	4
2016	Linden *et al.*[35]	Case series	Congential hepatic cyst	5 days, 7 weeks, 6 years, 14 years	4	Complete laparoscopic cyst excision	4
2016	Veenstra and Koffron[47]	Restrospective review	Benign and malignant liver tumors	9 months to 17 years	36	Segmentectomy, sectionectomy, or hemihepatectomy	3

Nevertheless, evidence regarding the topic remains scarce and of poor quality, and further efforts must take place to evaluate the full impact of MILR in children. Most importantly, applying this surgical innovation should not compromise prognosis of children with hepatic tumors.

DECLARATIONS

Acknowledgement

We thank Khrisna Menon, MD, Liver Transplantation, Institute of Liver Studies, Liver Transplant Surgery, King's College Hospital, National Health Service Foundation Trust, London, United Kingdom for revising the manuscript and for providing the graphical illustration shown in this article.

Authors' contributions

Literature search, analyse and wrote the manuscript: Cortes-Cerisuelo M, Berger M

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Copyright

REFERENCES

1. Wakabayashi G, Cherqui D, Geller DA, Buell JF, Kaneko H, et al. Recommendations for laparoscopic liver resection: a report from the second international consensus conference held in Morioka. Ann Surg 2015;261:619-29.
2. Koffron AJ, Auffenberg G, Kung R, Abecassis M. Evaluation of 300 minimally invasive liver resections at a single institution: less is more. Ann Surg 2007;246:385-92; discussion 392-4.

3. Koffron A, Geller D, Gamblin TC, Abecassis M. Laparoscopic liver surgery: shifting the management of liver tumors. Hepatology 2006;44:1694-700.
4. Czauderna P, Haeberle B, Hiyama E, Rangaswami A, Krailo M, et al. The Children's Hepatic tumors International Collaboration (CHIC): novel global rare tumor database yields new prognostic factors in hepatoblastoma and becomes a research model. Eur J Cancer 2016;52:92-101.
5. Han HS, Cho JY, Yoon YS. Techniques for performing laparoscopic liver resection in various hepatic locations. J Hepatobiliary Pancreat Surg 2009;16:427-32.
6. Guro H, Cho JY, Han HS, Yoon YS, Choi Y, et al. Current status of laparoscopic liver resection for hepatocellular carcinoma. Clin Mol Hepatol 2016;22:212-8.
7. Han HS, Shehta A, Ahn S, Yoon YS, Cho JY, et al. Laparoscopic versus open liver resection for hepatocellular carcinoma: case-matched study with propensity score matching. J Hepatol 2015;63:643-50.
8. Thenappan A, Jha RC, Fishbein T, Matsumoto C, Melancon JK, et al. Liver allograft outcomes after laparoscopic-assisted and minimal access live donor hepatectomy for transplantation. Am J Surg 2011;201:450-5.
9. Troisi R, Debruyne R, Rogiers X. Laparoscopic living donor hepatectomy for pediatric liver transplantation. Acta Chir Belg 2009;109:559-62.
10. Troisi RI, Wojcicki M, Tomassini F, Houtmeyers P, Vanlander A, et al. Pure laparoscopic full-left living donor hepatectomy for calculated small-for-size LDLT in adults: proof of concept. Am J Transplant 2013;13:2472-8.
11. SSoubrane O, de Rougemont O, Kim KH, Samstein B, Mamode N, et al. Laparoscopic living donor left lateral sectionectomy: a new standard practice for donor hepatectomy. Ann Surg 2015;262:757-61; discussion 761-3.
12. Chen KH, Siow TF, Chio UC, Wu JM, Jeng KS. Laparoscopic donor hepatectomy. Asian J Endosc Surg 2018;11:112-7.
13. Han YS, Ha H, Kwon HJ, Chun JM. Pure laparoscopic donor right hepatectomy in a living donor with type 3a biliary variation: a case report. Medicine (Baltimore) 2017;96:e8076.
14. Cherqui D, Soubrane O, Husson E, Barshasz E, Vignaux O, et al. Laparoscopic living donor hepatectomy for liver transplantation in children. Lancet 2002;359:392-6.
15. Broering DC, Elsheikh Y, Shagrani M, Abaalkhail F, Troisi RI. Pure laparoscopic living donor left lateral sectionectomy in pediatric transplantation: a propensity score analysis on 220 consecutive cases. Liver Transpl 2018;24:1019-30.
16. Kim KH, Kang SH, Jung DH, Yoon YI, Kim WJ, et al. Initial outcomes of pure laparoscopic living donor right hepatectomy in an experienced adult living donor liver transplant center. Transplantation 2017;101:1106-10.
17. Lee KW, Hong SK, Suh KS, Kim HS, Ahn SW, et al. One hundred and fifteen cases of pure laparoscopic living donor right hepatectomy at a single center. Transplantation 2018;102:1878-84.
18. Han HS, Cho JY, Kaneko H, Wakabayashi G, Okajima H, et al. Expert panel statement on laparoscopic living donor hepatectomy. Dig Surg 2018;35:284-8.
19. Chen KH, Huang CC, Siow TF, Chio UC, Chen SD, et al. Totally laparoscopic living donor right hepatectomy in a donor with trifurcation of bile duct. Asian J Surg 2016;39:51-5.
20. von Schweinitz D. Hepatoblastoma: recent developments in research and treatment. Semin Pediatr Surg 2012;21:21-30.
21. Zimmermann A, Perilongo G. Pediatric liver tumors. Available from: https://link.springer.com/book/10.1007/978-3-642-14504-9#toc. [Last accessed on 18 Dec 2018]
22. Holcomb GW, Murphy JD, Ostlie DJ. Ashcraft's Pediatric Surgery. 6th ed. Elsevier; 2014.
23. Meyers RL, Czauderna P, Otte JB. Surgical treatment of hepatoblastoma. Pediatr Blood Cancer 2012;59:800-8.
24. Meyers RL, Maibach R, Hiyama E, Häberle B, Krailo M, et al. Risk-stratified staging in paediatric hepatoblastoma: a unified analysis from the Children's Hepatic tumors International Collaboration. Lancet Oncol 2017;18:122-31.
25. Ross JA, Gurney JG. Hepatoblastoma incidence in the United States from 1973 to 1992. Med Pediatr Oncol 1998;30:141-2.
26. Ross JA. Hepatoblastoma and birth weight: too little, too big, or just right? J Pediatr 1997;130:516-7.
27. Roebuck DJ, Aronson D, Clapuyt P, Czauderna P, de Ville de Goyet J, et al. 2005 PRETEXT: a revised staging system for primary malignant liver tumours of childhood developed by the SIOPEL group. Pediatr Radiol 2007;37:123-32.
28. Seims AD, Nice TR, Mortellaro VE, Lacher M, Ba'Ath ME, et al. Routine utilization of single-incision pediatric endosurgery (SIPES): a 5-year institutional experience. J Laparoendosc Adv Surg Tech A 2015;25:252-5.
29. Nederlandse Studiegroep voor Choledochus Cysten/malformaties (NeSCHoC), van den Eijnden MHA, de Kleine RHJ, de Blaauw I, Peeters PGJM, et al. Choledochal malformation in children: lessons learned from a Dutch National study. World J Surg 2017;41:2631-7.
30. Lee H, Hirose S, Bratton B, Farmer D. Initial experience with complex laparoscopic biliary surgery in children: biliary atresia and choledochal cyst. J Pediatr Surg 2004;39:804-7; discussion 804-7.
31. Son TN, Liem NT, Hoan VX. Transumbilical laparoendoscopic single-site surgery with conventional instruments for choledochal cyst in children: early results of 86 cases. J Laparoendosc Adv Surg Tech A 2014;24:907-10.
32. Diao M, Li L, Cheng W. Laparoscopic redo hepaticojejunostomy for children with choledochal cysts. Surg Endosc 2016;30:5513-9.
33. Diao M, Li L, Cheng W. Recurrence of biliary tract obstructions after primary laparoscopic hepaticojejunostomy in children with choledochal cysts. Surg Endosc 2016;30:3910-5.
34. Tabrizian P, Midulla PS. Laparoscopic excision of a large hepatic cyst. JSLS 2010;14:272-4.
35. Linden AF, Pulcrano ME, Duffy BJ, Lange PA, Tsung DY, et al. Laparoscopic excision of congenital hepatic cysts in the pediatric population: a case series and literature review. J Laparoendosc Adv Surg Tech A 2016;26:493-7.
36. Wong KK, Chung PH, Chan KL, Fan ST, Tam PK. Should open Kasai portoenterostomy be performed for biliary atresia in the era of laparoscopy? Pediatr Surg Int 2008;24:931-3.
37. Chan KW, Lee KH, Tsui SY, Wong YS, Pang KY, et al. Laparoscopic versus open Kasai portoenterostomy in infant with biliary atresia: a retrospective review on the 5-year native liver survival. Pediatr Surg Int 2012;28:1109-13.
38. Lishuang M, Zhen C, Guoliang Q, Zhen Z, Chen W, et al. Laparoscopic portoenterostomy versus open portoenterostomy for the

treatment of biliary atresia: a systematic review and meta-analysis of comparative studies. Pediatr Surg Int 2015;31:261-9.
39. Li Y, Xiang B, Wu Y, Wang C, Wang Q, et al. Medium-term outcome of laparoscopic Kasai portoenterostomy for biliary atresia with 49 cases. J Pediatr Gastroenterol Nutr 2018;66:857-60.
40. Kimura T, Soh H, Hasegawa T, Sasaki T, Kuroda S, et al. Laparoscopic correction of congenital portosystemic shunt in children. Surg Laparosc Endosc Percutan Tech 2004;14:285-8.
41. Watanabe A. Portal-systemic encephalopathy in non-cirrhotic patients: classification of clinical types, diagnosis and treatment. J Gastroenterol Hepatol 2000;15:969-79.
42. Dutta S, Nehra D, Woo R, Cohen I. Laparoscopic resection of a benign liver tumor in a child. J Pediatr Surg 2007;42:1141-5.
43. Oh PS, Hirose S, Parakh S, Cowles RA. Laparoscopic excision of an antenatally diagnosed large simple hepatic cyst in the newborn. Pediatr Surg Int 2012;28:719-23.
44. Yoon YS, Han HS, Choi YS, Lee SI, Jang JY, et al. Total laparoscopic left lateral sectionectomy performed in a child with benign liver mass. J Pediatr Surg 2006;41:e25-8.
45. Kim T, Kim DY, Cho MJ, Kim SC, Seo JJ, et al. Surgery for hepatoblastoma: from laparoscopic resection to liver transplantation. Hepatogastroenterology 2011;58:896-9.
46. Kim T, Kim DY, Cho MJ, Kim SC, Seo JJ, et al. Use of laparoscopic surgical resection for pediatric malignant solid tumors: a case series. Surg Endosc 2011;25:1484-8.
47. Veenstra MA, Koffron AJ. Minimally-invasive liver resection in pediatric patients: initial experience and outcomes. HPB (Oxford) 2016;18:518-22.
48. Zwintscher NP, Azarow KS, Horton JD. Morbidity and mortality associated with liver resections for primary malignancies in children. Pediatr Surg Int 2014;30:493-7.
49. Struecker B, Haber P, Öllinger R, Bahra M, Pascher A, et al. Comparison of single-port versus standard multiport left lateral liver sectionectomy. Surg Innov 2018;25:136-41.
50. Araujo RLC, de Castro LA, Fellipe FEC, Burgardt D, Wohnrath DR. Robotic left lateral sectionectomy as stepwise approach for cirrhotic liver. J Robot Surg 2018;12:549-52.
51. Guerra F, Di Marino M, Coratti A. Robotic surgery of the liver and biliary tract. J Laparoendosc Adv Surg Tech A 2018; doi: 10.1089/lap.2017.0628.
52. Howe A, Kozel Z, Palmer L. Robotic surgery in pediatric urology. Asian J Urol 2017;4:55-67.

Zhang *et al.* *Mini-invasive Surg* 2019;3:2
DOI: 10.20517/2574-1225.2018.64

Mini-invasive Surgery

Review

Open Access

Check for updates

Current status of technique for Billroth-I anastomosis in totally laparoscopic distal gastrectomy for gastric cancer

Shun Zhang[1,2], Tetsu Fukunaga[1]

[1]Department of Gastroenterology and Minimally Invasive Surgery, Juntendo University Hospital, Tokyo 113-8421, Japan.
[2]Department of Gastroenterology Surgery, Shanghai East Hospital, Shanghai 200120, China.

Correspondence to: Dr. Tetsu Fukunaga, Department of Gastroenterology and Minimally Invasive Surgery, Juntendo University Hospital, 3-1-3 Hongo, Bunkyo-ku, Tokyo, Japan. E-mail: t2fukunaga@juntendo.cac.jp

How to cite this article: Zhang S, Fukunaga T. Current status of technique for Billroth-I anastomosis in totally laparoscopic distal gastrectomy for gastric cancer. *Mini-invasive Surg* 2019;3:2. http://dx.doi.org/10.20517/2574-1225.2018.64

Received: 2 Oct 2018 **First Decision:** 23 Oct 2018 **Revised:** 19 Dec 2018 **Accepted:** 24 Dec 2018 **Published:** 14 Jan 2019

Science Editor: Tetsu Fukunaga **Copy Editor:** Cui Yu **Production Editor:** Huan-Liang Wu

Abstract
Several reconstruction techniques are possible after totally laparoscopic distal radical gastrectomy. An optimal technique of digestive tract reconstruction after distal gastrectomy has not yet been established. The ideal reconstruction should be not only for doctors but also for patients. Alimentary intake, satisfactory nutritional status and easy performing should be all considered. The aim of the study was to describe the different Billroth-I reconstruction techniques that can be proposed after totally laparoscopic distal radical gastrectomy.

Keywords: Billroth-I anastomosis, totally laparoscopic distal gastrectomy, gastric cancer

INTRODUCTION
In 1994, Kitano firstly reported the technique for laparoscopy assisted Billroth-I (B-I)[1]. Since then, the use of laparoscopic treatments for gastric cancer is increasing due to the advantages of improving patients' quality of life. The new technologies and improved techniques have allowed laparoscopy gastrectomy to expand its indications and also to use this treatment for more complex cases. Japan Society of Endoscopic Surgery (JSES) conducted national survey every 2 years and indicated the percentage of laparoscopic procedures for gastric cancer was increasing. According to the 12th JSES survey, laparoscopic distal gastrectomy (LDG) was the most commonly performed type of laparoscopic gastrectomy[2].

In initial series for LDG, the majority of anastomoses were performed by laparoscopy assisted procedures.

The assisted procedures needed a mini-laparotomy incision of 60-70 mm in length made on the epigastrium[3]. But this procedure was not always easy to do, especially on patients with a small remnant stomach or obese patients with thick abdominal walls[4]. Anastomosis in such restricted space was usually difficult. With the accumulation of laparoscopic surgery experience and the development of laparoscopic devices, the gastrointestinal reconstruction now can be completed laparoscopically. Furthermore, unnecessary manipulations and the incision made on the epigastrium can be avoided.

The ideal reconstruction should be not only for doctors but also for patients. Alimentary intake, satisfactory nutritional status and easy performing should be all considered[5]. The B-I anastomosis is preferred by many doctors. It is said that the B-I anastomosis is simple and can provide a physiological route for food digestion and absorb without the need for an intestinal bypass or blind loop. Until now, various intracorporeal B-I anastomosis techniques were reported. In this article, we will review theses reconstruction methods.

HAND-SEWN ANASTOMOSIS IN INTRACORPOREAL B-I RECONSTRUCTION

After the accumulation of operative experience, some experienced surgeons had also presented intracorporeal hand-sewn techniques.

Takiguchi *et al*.[6] firstly reported B-I intracorporeal hand-sewn anastomosis in 2003. In his study, the Albert-Lembert method was used for the laparoscopic hand-sewing procedure and the anastomosis time was 90 min. Due to the complexity of the procedure and large amount of time required for anastomosis, it seemed that the hand-sewn anastomosis was not widely performed.

After almost 10 years, Matsuo e*t al*.[7] reported another study about hand-sewn B-I anastomosis. They performed hand-sewn gastroduodenal anastomosis in 18 cases. The mean time of B-I anastomosis was 64.6 min. Matsuo *et al*.[7] described that 3-0 absorbing thread was placed in the lesser curvature as a supporting thread. A seromyotomy of the stomach was performed at the posterior wall. Both the remmant stomach and the duodenum's seromuscular layer were discontinuously sutured by extracorporeal knot-typing method. The lumen was opened with the stomach and the duodenum in a fixed status. The thread of the anchor suture was lifted upward to the abdominal wall. After that all layers of the stomach and the duodenum at the posterior wall were continuously sutured. The authors believed that hand-sewn anastomosis had some advantages. Hand-sewn sutures were not affected by the degree of freedom of the duodenum. Because staplers were not used, the anastomosis area was soft and highly flexible. The hand-sewn anastomosis was economical due to that less staplers were used.

CIRCULAR STAPLER USED IN INTRACORPOREAL B-I RECONSTRUCTION

In the open surgery, circular stapler is well applied as a standardized reconstruction method of gastroduodenostomy. However, when it was attempted laparoscopically, the situation was often the opposite.

Uyama *et al*.[8] firstly described intracorporeal B-I reconstruction using a circular stapling device and introduced one case in 1995. The method was defined by the same anatomic parameters as for the open B-I. After that, Moriya *et al*.[9] and Mayers and Orebaugh[10] also reported B-I gastroduodenostomy with a circular stapler device. Both techniques were complicated and difficult to operate, and especially at the left subcostal area where an extended incision was needed. The extra incision spoiled the merit of minimally invasive surgery.

There are 2 major difficulties when circular stapler is applied in laparoscopic gastroduodenostomy: the first is the lack of a safe and fast intracorporeal purse-string suture technique and the second is the difficulty in manipulating the stapler and the stomach in a narrow abdominal cavity. In order to enable the anvil placement into the dudenum, many strategies were applied, such as a triple stapling procedure[8] and the use of the natural pyloric ring with endo-looping of the duodenum[9]. Some techniques usually used in esophagoenteral anastomosis were also reported, such as using specially modified laparoscopic purse-string instrument[11] and opening the lumen and applying manual purse-string suture[12]. However, there are still many difficulties to be overcome.

Kim *et al.*[13] reported a method which seemed to be quick and economical. The atraumatic clamps were used to prevent slippage of the duodenum which was cut with ultrasonic shear instead of linear stapler. After that, a seromuscular suture was done around the duodenal outer layer along the clamp. Omori *el al.*[14] reported a method like reverse puncture technique used in total gastrectomy. The anvil secured with vicryl suture was inserted into the duodenum through semicircumferential duodenotomy. The needle was advanced to the anterior duodenal wall and then the duodenum was staple-transected. Finally, the center rod penetrated the duodenal wall. In this method the need for purse-string suture placement was totally eliminated.

Although the skill inserting anvil head in the duodenal stump can be improved, laparoscopically inserting the circular stapler into the remnant stomach was not always easy. After removing two-thirds to three-quarters of the stomach, the small remnant stomach was usually so small that it was difficult to insert the stapler, even from the epigastric region. Sometime it was very difficult to form a straight line among the duodenum, remnant stomach and the circular stapler from the umbilical wound. Omori *el al.*[15] described a novel method to insert the circular stapler to connect the anvil head. Firstly, the anvil head was passed through the posterior gastric wall with laparoscopic endloop, which can make the duodenum and remnant stomach form a straight line. Secondly anterior gastric suture was used to exteriorize the anvil shaft partly from the gastrotomy. And then the anvil shaft was advanced into the remnant stomach to make the anvil and the stapler join tighter.

LINEAR STAPLER INTRACORPOREAL B-I RECONSTRUCTION

Delta-shaped anastomosis and modified delta-shaped anastomosis

With the development of laparoscopic instruments and the continuous accumulation of surgical experience in recent years, linear stapler intracorporeal gastrointestinal anastomosis techniques have been developed.

Kanaya *et al.*[16] firstly reported a anastomosis method which used only laparoscopic linear staplers in the hope of overcoming the drawbacks of extracorporeal reconstruction. The method named delta-shaped anastomosis (DA) was a modified intracorporeal B-I reconstruction which was soon promoted. The emergence of the DA method made intracorporeal gastroduodenostomy possible, which greatly promoted the development of totally laparoscopic distal gastrectomy (TLDG). Utilization DA method allows gastroduodenal anastomosis with a diameter of at least 30 mm while avoiding stricture. Kanaya *et al.*[17] analyzed the result of initial 100 procedures and showed that the mean time of the anastomosis was 13 min and the rate of anastomosis related complications was rare in 2011.

But some surgeons worry about the blood supply affected during cutting, which would result in leakages ranging from 0.42% to 8.5%[17-20] and anatomical distortion which exist in twisting around the anastomosis[21]. In order to overcome the twisting around the anastomosis, some modified delta-shaped techniques were studied.

Huang *et al.*[22] reported modified DA in 2014. This was different from the conventional DA in closing the common stab incision of stomach and duodenum. In order to avoid the poor blood supply of the duodenum, the duodenal cutting was totally resected. The appearance of the anastomoses was changed from two intersections to only one as an inverted T-shape, which could decrease the anastomotic weak point. They reported comparable postoperative outcomes and showed that modified DA was technically safe and feasible[23] in another study.

After DA, many surgeons develop many other anastomosis methods based on linear stapler.

Triangulating stapling technique

Tanimura *et al*.[24] described the triangulating stapling technique based on a linear stapling device in 2008. The mean anastomotic time was 35 min. In this method, the duodenum can be transected in any direction, and by forming a triangle, the anastomosis lumen is made wide with no ischemic areas. Both stumps of duodenum and remnant stomach were opened fitting their caliber, the gastroduodenostomy linear stapler in the posterior wall and 2 everted sutures in the anterior wall with linear staplers. Before each direction anastomosis, both duodenum and remnant stomach were elevated ventrally with 3 stay sutures. But there are still some problems about this method. There were some differences between the stomach and duodenum in terms of lumen size, wall thickness, and wall extensibility. The first introverted anastomosis, which forms the base of the triangle, was cumbersome once all of the staple lines on the stomach and duodenum had been cut off.

Book-binding technique

Ikeda *el al*.[25] described the book-binding technique using linear stapler in 2012. The mean anastomotic time was 34 min. In their method, the duodenum was transected form the greater curvature side to the lesser curvature side. Small openings are made in the remnant stomach and duodenal stumps just wide enough to insert one of the jaws of the linear stapler. After the first stapling, there were three staple lines including those from the transection of the stomach and duodenum, which ran in parallel to the anterior wall. To prevent the formation of ischemic areas, a large opening was created on the anterior wall by transecting the entire duodenal stump and one-third of the gastric stump together with the anterior wall of the first anastomosis line. The anterior hole was then fired by linear stapler twice to close the large opening. Because a large opening was created on the anterior wall by transecting tissue and anastomosis line, maybe some tension was generated after the anterior hole was closed by the linear stapler. Further studies need to be done.

Linear-shaped gastroduodenostomy

Byun *et al*.[26] developed a linear-shaper gastroduodenostomy method by which the appearance of anastomosis was completed inverted T-shaped in 2009. Duodenum was transected from the greater curvature side to less side. One incision was done in the greater curvature of remnant stomach at the point 60 mm apart from the resected line. The other incision was done on the superior edge of the duodenal transection line. After creating the c anastomosis lumen, the common entry incision was closed by laparoscopic linear staplers. Finally, the greater curvature of stomach and the antero-superior of duodenum were perpendicular. By using this method, the rotation duodenum and remnant stomach was not needed which can reduce the risk of poor vascular supply. In their study, there were less bile reflux, gastritis degree and residual food grade compared to DA anastomosis in 6 months after surgery.

Augmented rectangle technique

In our group, we developed a method named augmented rectangle technique (ART) anastomosis. Three automatic laparoscopic linear staplers were used to create the gastroduodenostomy and the anastomotic opening was wide and less likely to become stenosed or twisted[27]. This method was easy and time-saving. We performed 160 LDG operations using this technique from December 2013 to August 2017. There were no postoperative complications associated with the reconstruction, such as anastomotic leakage, hemorrhage or stenosis. In the ART method, the duodenum was transected form the greater curvature side to less side. Small incisions were made in duodenal stumps and the greater curvature of remnant stomach in order to insert the jaws of the linear stapler. After inserting the stapler, the lesser curvature

Table 1. Summary of different methods applied in intracorporeal Billroth-I reconstruction

Year	Author	No.	Age	Method	Anastomotic time (min)	Operative time (min)	Blood loss	Postoperative stay (d)	Anastomosis-related complations
				Hand-sewn anastomosis in intracorporeal B-I reconstruction					
2003	Takiguchi *et al.*[6]	1	50	Hand-sewn	90	420	NS	7	0
2012	Matsuo *et al.*[7]	18	NS	Hand-sewn	64.6	NS	53.1 ± 91	21.7	0
				Circular stapler used in intracorporeal B-I reconstruction					
1995	Uyama *et al.*[8]	1	56	CS	NS	318	NS	14	0
2012	Kim *et al.*[13]	23	60.3 ± 11.3	CS	43.3 ± 15.4	209.7 ± 49.9	72.6 ± 47.9	7.7 ± 2.3	0
2012	Omori *et al.*[15]	20	NS	CS	NS	279	NS	9	0
				Linear stapler intracorporeal B-I reconstruction					
2011	Kanaya *et al.*[17]	100	65.5 ± 9.3	DA	13.0 ± 3.9	239.2 ± 53.2	92.6 ± 89.7	16.7 ± 13.8	1 (anastomotic leak)
2014	Okabe *et al.*[20]	185	NS	DA	NS	283	NS	NS	5 (anastomotic leak) 3 (delayed gastric emptying)
2011	Noshiro *et al.*[19]	71	70 ± 10	DA	NS	260 ± 56	63 ± 79	NS	6 (anastomotic leak)
2014	Huang *et al.*[22]	102	60 ± 12	Modified DA	12.2 ± 4.2	150.6 ± 30.2	48.2 ± 33.2	12.0 ± 6.5	2 (anastomotic leak)
2008	Tanimura *et al.*[24]	196	NS	TST	28 ± 4	249 ± 38	NS	NS	1 (anastomotic leak)
2013	Ikeda *et al.*[25]	9	59.3	BBT	34 ± 7	255 ± 13	50 ± 66	14.2 ± 2.3	0
2016	Byun *et al.*[26]	190	57.2 ± 12.5	LSGD	NS	147.9 ± 49.4	97.3 ± 95.7	6.8 ± 3.1	2 (anastomotic stenosis)
2018	Fukunaga *et al.*[27]	160	69.5 ± 10	ART	NS	227 ± 75	47.3 ± 50	12 ± 5	0

CS: Circular stapler; DA: delta-shaped anastomosis; TST: triangulating stapling technique; BBT: book-binding technique; LGSD: linear-shaped gastroduodenostomy; ART: augmented rectangle technique; NS: not stated

end of the duodenal stump was rotated externally by 90°. After the initial suturing between the remnant stomach and the duodenum, the two sides (posterior wall and cranial wall), the posterior wall and caudal wall, form a V-shape. A 30 mm linear stapler was applied to close the insertion holes up to the closest side of the duodenal resection margin. After gastric and duodenal resection margins were ensured to be close together, the 60 mm laparoscopic linear stapler was used to transect the duodenal resection margin to create the margin. After the above steps, all the previous linear staplers were removed from duodenal resection margin.

Thanks to the elimination of the stay sutures in the anastomosis site, the risk of leakage of the intestinal contents into the peritoneal cavity can be reduced with a result of reduced incidence of peritoneal abscess[28,29]. Removing the staple line of the duodenal stump without creating a T-shaped anastomotic region can avoid postoperative stenosis. The ART can create larger 4-sided anastomosis diameters than 3-sided ones, without worrying about whether the width of the opening will be reduced by the final stapling.

APPLICATION OF BARBED SUTURE IN INTRACORPOREAL ANASTOMOSES

Intracorporeal suturing and knot typing in some B-I anastomosis were time-consuming and tedious and especially these procedures were the last steps to do in LDG. But various devices have been developed to simplify the placement of intracorporeal sutures, and barbed suture is one such device. Using the barber suture could reduce the number of knot typing, the suturing efficiency and reduce the cost of intracorporeal reconstruction with staplers[30]. Lee *et al.*[30] used barber sutures to close entry hole in 354 patients instead of staplers with a result of minimizing the suturing time. There were no patients who needed to be converted to usual sutures or mechanical closure with staplers and only one patient presented with postoperative anastomotic bleeding.

CONCLUSION

Several reconstruction techniques are possible after TLDG [Table 1]. The best reconstruction is the one, that simplifies the technique, maintains satisfactory nutritional status and quality of life while keeping postoperative morbidity as low as possible. We believe that the new technologies and improved techniques will bring more benefits to patients and doctors.

DECLARATIONS

Authors' contributions

Study's conception and design: Zhang S, Fukunaga T
Writing the paper: Zhang S
Provided administrative, technical, and material support: Fukunaga T

Availability of data and materials

Not applicable.

Financial support and sponsorship

The study was supported part by Japan China Sasakawa Medical Fellowship.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Kitano S, Iso Y, Moriyama M, Sugimachi K. Laparoscopy-assisted Billroth I gastrectomy. Surg Laparosc Endosc 1994;4:146-8.
2. Bandoh T, Shiraishi N, Yamashita Y, Terachi T, Hashizume M, et al. Endoscopic surgery in Japan: the 12th national survey(2012-2013) by the Japan Society for Endoscopic Surgery. Asian J Endosc Surg 2017;10:345-53.
3. Zhang DT, Yan D, Jiang X, Song C. A modified uncut roux-en-y anastomosis in laparoscopic-assisted distal gastrectomy: balance of the cost and minimally invasion. Trans Surg 2018;3:1-5.
4. Kim MG, Kim KC, Kim BS, Kim TH, Kim HS, et al. A totally laparoscopic distal gastrectomy can be an effective way of performing laparoscopic gastrectomy in obese patients (body mass index ≥ 30). World J Surg 2011;35:1327-32.
5. Piessen G, Triboulet JP, Mariette C. Reconstruction after gastrectomy: which technique is best? J Visc Surg 2010;147:e273-83.
6. Takiguchi S, Sekimoto M, Miyake Y, Fujiwara Y, Yasuda T, et al. Totally laparoscopic distal gastrectomy using the hand-sewn Billroth-I anastomotic technique: report of a case. Surg Today 2003;33:371-4.
7. Matsuo K, Shimura H, Tanaka S, Nakano M, Hashimoto T, et al. Laparoscopic distal gastrectomy with intracorporeal handsewn Billroth-I anastomosis (ICHSA). Surg Endosc 2012;26:2981-7.
8. Uyama I, Ogiwara H, Takahara T, Kato Y, Kikuchi K, et al. Laparoscopic Billroth I gastrectomy for gastric ulcer: technique and case report. Surg Laparosc Endosc 1995;5:209-13.
9. Moriya H, Shimizu S, Okano T, Yamaguchi S. Experimental study of laparoscopic gastrectomy: intracorporeal Billroth I gastroduodenostomy. Surg Laparosc Endosc 1997;7:32-7.
10. Mayers TM, Orebaugh MG. Totally laparoscopic Billroth I gastrectomy. J Am Coll Surg 1998;186:100-3.
11. Usui S, Nagai K, Hiranuma S, Takiguchi N, Matsumoto A, et al. Laparoscopy-assisted esophagoenteral anastomosis using endoscopic purse-string suture instrument "Endo-PSI (II)" and circular stapler. Gastric Cancer 2008;11:233-7.
12. Kinoshita T, Oshiro T, Ito K, Shibasaki H, Okazumi S, et al. Intracorporeal circular-stapled esophagojejunostomy using hand-sewn purse-string suture after laparoscopic total gastrectomy. Surg Endosc 2010;24:2908-12.
13. Kim HI, Woo Y, Hyung WJ. Laparoscopic distal gastrectomy with an intracorporeal gastroduodenostomy using a circular stapler. J Am Coll Surg 2012;214:e7-13.
14. Omori T, Nakajima K, Nishida T, Uchikoshi F, Kitagawa T, et al. A simple technique for circular-stapled Billroth I reconstruction in laparoscopic gastrectomy. Surg Endosc 2005;19:734-6.
15. Omori T, Tanaka K, Tori M, Ueshima S, Akamatsu H, et al. Intracorporeal circular-stapled Billroth I anastomosis in single-incision laparoscopic distal gastrectomy. Surg Endosc 2012;26:1490-4.
16. Kanaya S, Gomi T, Momoi H, Tamaki N, Isobe H, et al. Delta-shaped anastomosis in totally laparoscopic Billroth I gastrectomy: new

technique of intraabdominal gastroduodenostomy. J Am Coll Surg 2002;195:284-7.
17. Kanaya S, Kawamura Y, Kawada H, Iwasaki H, Gomi T, et al. The delta-shaped anastomosis in laparoscopic distal gastrectomy: analysis of the initial 100 consecutive procedures of intracorporeal gastroduodenostomy. Gastric Cancer 2011;14:365-71.
18. Kim BS, Yook JH, Choi YB, Kim KC, Kim MG, et al. Comparison of early outcomes of intracorporeal and extracorporeal gastroduodenostomy after laparoscopic distal gastrectomy for gastric cancer. J Laparoendosc Adv Surg Tech A 2011;21:387-91.
19. Noshiro H, Iwasaki H, Miyasaka Y, Kobayashi K, Masatsugu T, et al. An additional suture secures against pitfalls in delta-shaped gastroduodenostomy after laparoscopic distal gastrectomy. Gastric Cancer 2011;14:385-9.
20. Okabe H, Obama K, Tsunoda S, Tanaka E, Sakai Y. Advantage of completely laparoscopic gastrectomy with linear stapled reconstruction: a long-term follow-up study. Ann Surg 2014;259:109-16.
21. Lee Y, Tan CH, Park DJ. Current status of intracorporeal gastroduodenostomy and modified delta-shape anastomosis after distal gastrectomy for gastric cancer. J Vis Surg 2016;2:158.
22. Huang C, Lin M, Chen Q, Lin J, Zheng C, et al. A modified delta-shaped gastroduodenostomy in totally laparoscopic distal gastrectomy for gastric cancer: a safe and feasible technique. PLoS One 2014;9:e102736.
23. Huang CM, Lin M, Lin JX, Zheng CH, Li P, et al. Comparision of modified and conventional delta-shaped gastroduodenostomy in totally laparoscopic surgery. World J Gastroenterol 2014;20:10478-85.
24. Tanimura S, Higashino M, Fukunaga Y, Takemura M, Nishikawa T, et al. Intracorporeal Billroth 1 reconstruction by triangulating stapling technique after laparoscopic distal gastrectomy for gastric cancer. Surg Laparosc Endosc Percutan Tech 2008;18:54-8.
25. Ikeda T, Kawano H, Hisamatsu Y, Ando K, Saeki H, et al. Progression from laparoscopic-assisted to totally laparoscopic distal gastrectomy: comparison of circular stapler (i-DST) and linear stapler (BBT) for intracorporeal anastomosis. Surg Endosc 2013;27:325-32.
26. Byun C, Cui LH, Son SY, Hur H, Cho YK, et al. Linear-shaped gastroduodenostomy (LSGD): safe and feasible technique of intracorporeal Billroth I anastomosis. Surg Endosc 2016;30:4505-14.
27. Fukunaga T, Ishibashi Y, Oka S, Kanda S, Yube Y, et al. Augmented rectangle technique for Billroth I anastomosis in totally laparoscopic distal gastrectomy for gastric cancer. Surg Endosc 2018; doi: 10.1007/s00464-018-6266-1.
28. Jeong O, Jung MR, Park YK, Ryu SY. Safety and feasibility during the initial learning process of intracorporeal Billroth I (delta-shaped) anastomosis for laparoscopic distal gastrectomy. Surg Endosc 2015;29:1522-9.
29. Lin M, Zheng CH, Huang CM, Li P, Xie JW, et al. Totally laparoscopic versus laparoscopy-assisted Billroth-I anastomosis for gastric cancer: a case-control and case-matched study. Surg Endosc 2016;30:5245-54.
30. Lee SW, Kawai M, Tashiro K, Bouras G, Kawashima S, et al. Laparoscopic distal gastrectomy with D2 lymphadenectomy followed by intracorporeal gastroduodenostomy for advanced gastric cancer: technical guide and tips. Transl Gastroenterol Hepatol 2017;2:84.

Yap *et al. Mini-invasive Surg* 2019;3:3
DOI: 10.20517/2574-1225.2018.57

Mini-invasive Surgery

Review

Open Access

Check for updates

Transanal total mesorectal excision: current updates

Raymond Yap, John Monson

Center for Colon & Rectal Surgery, Florida Hospital, Orlando, FL 32804, USA.

Correspondence to: Dr. John Monson, Center for Colon& Rectal Surgery, Florida Hospital, 2415 North Orange Avenue, Suite 300 Orlando, Orlando, FL 32804, USA. E-mail: john.monson.md@flhosp.org

How to cite this article: Yap R, Monson J. Transanal total mesorectal excision: current updates. *Mini-invasive Surg* 2019;3:3. http://dx.doi.org/10.20517/2574-1225.2018.57

Received: 14 Aug 2018 **First Decision:** 12 Nov 2018 **Revised:** 7 Jan 2019 **Accepted:** 14 Jan 2019 **Published:** 13 Feb 2019

Science Editor: Gordon N. Buchanan **Copy Editor:** Cui Yu **Production Editor:** Huan-Liang Wu

Abstract
Transanal total mesorectal excision (TaTME) is the latest in a long list of developments in the surgical treatment of low rectal cancer. This article describes the evolution of the technique, a brief summation of the technical procedure, the current literature into its results, and the possible future direction that it might take. It is the authors' opinion that TaTME will form another technique within the modern colorectal surgeon's armament.

Keywords: Transanal total mesorectal excision, transanal, rectal cancer

INTRODUCTION

The evolution of dedicated surgical techniques in the treatment of rectal cancer over the past century is one of fascinating progress. The concept of the total removal of the mesocolon as described by Miles[1] is the foundation of one of the most important principles in rectal cancer surgery today; that is the complete removal of both the primary cancer and any associated lymph nodes. Heald *et al.*[2] then emphasized the idea of the "holy plane", when he described total mesorectal excision as sharp dissection along a definable avascular tissue plane to remove the rectum and the mesorectum in an intact envelope.

The achievement of this goal in rectal surgery is often not straightforward. Obtaining adequate trans-abdominal access to the deep pelvis for cases of mid to low rectal cancer continues to challenge even the most experienced of colorectal surgeons. This is made more difficult in a subset of patients, namely those who are obese, male, and with a narrow pelvis. Numerous techniques over the years have been developed to try and combat these challenges, although usually without overwhelming success or widespread adoption.

Transanal total mesorectal excision (TaTME) is the latest innovation that aims to overcome these significant limitations in rectal cancer surgery. It has its roots in 1984, when Buess *et al.*[3] described transanal endoscopic microsurgery (TEMs) using a fixed rectoscope platform that improved both visibility and extended the extent of the surgical field. Although expensive, this technique resulted in more negative margins and less fragmentation of the specimen when compared to conventional transanal excision. Further development of minimally invasive and advanced endoscopic platforms such as transanal minimally invasive surgery (TAMIS)[4] and the ability to create and maintain pneumorectum led finally to the development of the TaTME for en-bloc resection of rectal cancers as first described by Sylla *et al.*[5] in 2009. Indeed, it is the development of CO_2 insufflation for the rectum using the AirSeal device (CONMED Corp., Utica, NY) with sufficient smoke evaluation that brings the most significant progression from TEMs/TAMIS to TaTME.

The implementation of novel technical and technologic innovations in surgery has often been fraught with unintended consequences. With an emphasis on safety and acceptability of clinical outcomes, the lessons learned from missteps arising throughout the implementation of minimally invasive surgery in other fields (e.g., laparoscopic cholecystectomy and bile duct injury) have justifiably led the surgical community to heed the cautionary tales of early adopters. The technical complexity of TaTME, in addition to the identification of new or rarely-seen anatomic landmarks and planes have led to the occurrence of otherwise rare complications such as urethral injury. This has led to reflection and delay in the dissemination in the technique.

This paper aims to provide a summary of the indications, considerations, surgical technique and evidence for TaTME. It will assume a certain amount of prior knowledge in the treatment of rectal cancer, where areas such as pre-operative staging and standard treatment modalities will be only briefly mentioned.

PREOPERATIVE EVALUATION

A thorough evaluation of the recently diagnosed rectal cancer patient is of the utmost importance to determine an appropriate treatment plan. This evaluation includes a complete history and physical examination, including digital rectal exam and rigid proctoscopy. Preoperative work-up should include a full colonoscopy to rule out any synchronous lesions. A baseline carcinoembryonic antigen level should be obtained prior to treatment as a prognostic tool and for post-treatment surveillance. A variety and combination of radiographic studies can be performed preoperatively with a different associated benefit profile for each study. Computed tomography (CT), magnetic resonance imaging (MRI), endoanal ultrasound (EUS), positron emission tomography (PET) and PET-CT may be used depending on the clinical situation.

Of these, pelvic MRI is of most interest when considering cases for TaTME. These should be done with the use of a pelvic-specific coil and thin-sectioned, multiplanar T2-weighted images[6-8]. MRI is the best current modality for determining the extent of locally advanced tumors, identifying the mesorectal fascia/the circumferential resection margin (CRM), and is at least equal to EUS for the staging of mesorectal lymph nodes[9-11]. However, the breath of anatomical information provided by MRI also allows for preoperative planning in TaTME cases. Careful study of the pre-operative MRI can help the surgeon consider how to proceed at difficult points in the operation. Attention should be taken to path of the mesorectal fascia which is clearly delineated on MRI. As orientation can be challenging intra-operatively, identifying the angle by which the mesorectum first dives posteriorly and then curves anteriorly may help the surgeon stay within the correct plane. Further attention should be drawn to where the CRM may be threatened by tumor during the operation.

TaTME was developed to aid in the challenging mid to low rectal cancer cases, although precise definition of its indications has not been fully evaluated. A recent consensus statement was published which listed the following indications for TaTME: (1) male gender; (2) narrow and/or deep pelvis; (3) visceral obesity and/or a body mass index (BMI) > 30 kg/m^2; (4) prostatic hypertrophy; (5) a tumor height < 12 cm from the anal verge; (6) a tumor diameter > 4 cm; (7) distortion of tissue planes secondary to neoadjuvant radiotherapy; and (8) an impalpable, low primary tumor requiring accurate placement of the distal resection margin[12]. They listed their contradictions as obstructing rectal tumours, emergency presentations and T4 tumors. It is noted that many surgeons have used thinner female patients who have not undergone neoadjuvant chemoradiotherapy as part of their learning curve. This is likely due to the fact that planes may be easier to identify, the risk of urethral injury is possibly lower, and salvage from a conventional top-down approach is more straightforward.

SURGICAL APPROACH

A brief description of the surgical technique will be listed below.

Equipment

It is assumed that equipment required for an open and laparoscopic low anterior resection is readily available. Specialized equipment for this technique which the authors use include: (1) GelPoint Path Transanal Access Platform (Applied Medical, Inc., Rancho Santa Maragarita, CA); (2) AirSeal Access Port (CONMED Corp., Utica, NY); (3) Articulating hook diathermy (SILS hook, Medtronic, Minneapolis, MN).

We acknowledge that other platforms do exist and are also currently in development.

Preparation

All patients are given full mechanical bowel preparation. Standard pre-operative procedures such as antibiotics, urinary catheter and deep vein thrombosis prevention are assumed. The patient is placed in stirrups in the modified Lloyd-Davies position. Preparation of the abdomen and perineum should include washing out of the vagina and rectum with betadine.

Technique

The operation may begin trans-anally, transabdominally or simultaneously from both approaches with two surgical teams. The benefit of a simultaneous approach is that it is associated with significantly reduced operating duration. If a simultaneous approach is embarked upon, there must be two separate scrub setups and two laparoscopic towers/insufflators. Even in the single surgeon situation, two separate setups and laparoscopic towers is recommended to aid transition between the two. The TaTME dissection can be performed with the surgeon standing or sitting. However, if the surgeon stands, better ergonomic access is afforded to the assistant as they try to fit under the patient's right leg.

We routinely set the patient up as if having a laparoscopic total mesorectal excision. This includes some kind of strapping to the chest, and use of gelfoam mat to ensuring the patient does not slide during the operation. We do not routinely use a bean-bag.

Firstly, a purse-string suture (2/0 prolene) is placed with sufficient margin distal to the tumor. This can be achieved transanally with the aid of a Lone-Star and anal retractors if the tumor is low enough [Figure 1]. If the tumor is higher, this can be done by inserting the GelPoint port, and establishing pneumorectum to facilitate suturing through the TAMIS platform. A secure and airtight purse-string suture is mandatory as any defect will allow leakage of tumor content from above, and air into the colon from below. A second lavage with betadine is then performed and the GelPoint port channel inserted if it has not been already. Three ports are inserted into the GelPoint cap at 10 o'clock (Airseal, 8 mm port), 2 and 6 o'clock (10 mm working ports). The cap is then secured and pneumorectum is established with the AirSeal device at 10-12 mmHg.

Next, dissection is commenced. A 5 or 10 mm 30-degree rigid or flexible laparoscope is used for visualization and inserted into the 6 o'clock port. The circumferential intraluminal line is marked out and

 Yap *et al*. *Mini-invasive Surg* 2019;3:3 I http://dx.doi.org/10.20517/2574-1225.2018.57

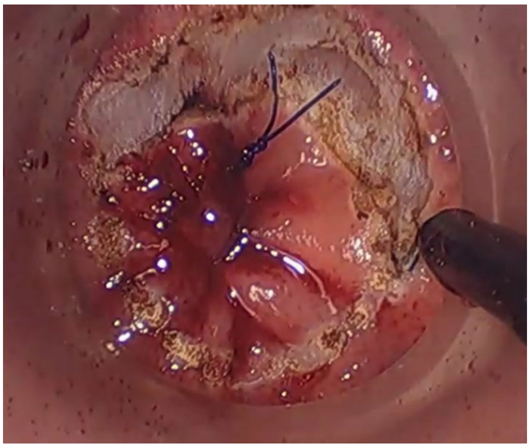


Figure 1. Transanal total mesorectal excision purse-string and proctectomy

full-thickness rectal wall incision performed with hook diathermy. Usually, the dissection is commenced posteriorly as the plane between the presacral fascia and TME envelope is easiest to identify. An important tip is that the rectum is usually pushed away to create more operating space, as opposed to laparoscopically where the colon is usually pulled towards the operator. From this starting point, the dissection is then performed circumferentially, with care taken not to continue in only one or two quadrants which would lead to asymmetrical rectal retraction. Laterally, remaining close to the mesorectal fascia will reduce injury to the pelvic sidewall and the nervi erigentes. Anteriorly, the dissection is in the rectovaginal plane or posterior to Denonvilliers' fascia in males. This dissection may be tailored depending on the position of the invasive portion of the tumor, intentionally proceeding anterior to Denonvilliers' fascia if necessary to secure a clear margin. Another important note is that sometimes an "O" sign appears during dissection in the fatty tissue [Figure 2]; this is an indication that an incorrect plane that is too lateral has been entered[13].

This dissection is then continued up towards the peritoneal reflection. Care must be taken to try and breach the peritoneal cavity as late as possible, as once there is a connection between the two spaces, dissection becomes more difficult due to the bellowing movement of mesorectum as pressures attempt to equalize.

The intraperitoneal dissection is completed either simultaneously or sequentially in the usual fashion with splenic flexure mobilization and high ligation of the inferior mesenteric artery. The colon is either exteriorized and transected through an abdominal incision, or if so desired, the specimen can be delivered trans-anally with the assistance of a wound retractor by transecting the proximal margin laparoscopically with a stapler. Care must be taken if a transanal extraction is attempted; the mesentery of the colon must be divided to ensure that the marginal artery is torn.

A second purse-string is then placed with a 0 or 2/0 prolene in the distal cut end, while an anvil of a circular stapler is secured to the proximal colon. A 19F Blakes drain is then cut to approximately 10 cm and placed on the end of the anvil to facilitate transanal retrieval. Once this is accomplished, the purse-string then being secured around the anvil. The stapler is then engaged and fired in the standard fashion. Other techniques for a stapled end-to-end anastomosis have been described as well as techniques for other types of anastomoses including: hand-sewn coloanal anastomosis and side-to-end stapled anastomosis[14,15].

Although urethral injury is an oft-commented point raised in regards to TaTME, it mainly a concern where the starting point of the dissection is intersphincteric or extremely close to the anorectal ring. Here, as discussed in simulation by Kneist *et al*.[16], the perineal body is the only structure that protects this area and separates these structures from the rectum. This is due to the fact that the prostate must be mobilized from

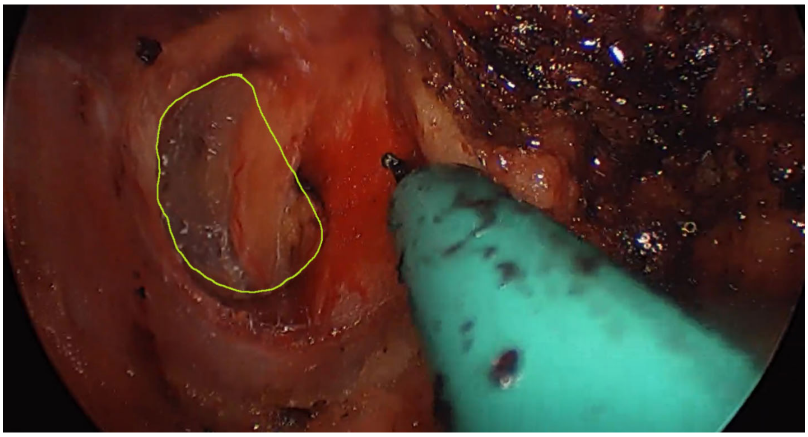


Figure 2. "O" sign. Marked in yellow

Table 1. Steps of the transanal total mesorectal excision

Bottom (transanal total mesorectal excision)	Top (intraperitoneal)
1. Placement of purse-string suture distal to the tumor.	1. Complete mobilization of the descending and sigmoid colon.
2. Introduce advanced endoscopic platform transanally.	2. Splenic flexure mobilization.
3. Circumferential full-thickness proctotomy.	3. Inferior mesenteric artery high ligation.
4. Distal to proximal dissection within the avascular mesorectal plane.	4. Proximal rectal dissection.
Joint	
5. Transection of proximal colon.	
6. Securing of proximal anvil and insertion of transanal distal purse string.	
7. Passing down of anvil from intraperitoneal to transanal space.	
8. Securing of transanal distal purse string.	
9. Firing of stapler.	
10. Concluding steps (e.g., Leak test, drains, closure) as per conventional technique.	

the anterior pelvis for urethral injury to occur. Methods to avoid this in these low dissections are to continue the inter-sphincteric dissection as high as possible in an open fashion, to clearly identify the prostate either endoscopically or in an open fashion, and finally when entering the plane anteriorly, to allow for pneumodissection as this plane will open up once it has been entered. Extreme anterior angles of the port should also be avoided to lessen the risk of this devastating injury.

A brief summary of the steps required for TaTME are demostrated in Table 1.

TRAINING AND DEVELOPMENT

As mentioned previously, the technical complexity of TaTME and the occurrence of otherwise rare complications should bring pause to any surgeon considering the technique. Proponents of the technique have attempted to set a framework had through which TaTME could be widely adopted in a responsible manner. This was published by the International TaTME Educational Collaborative in 2013[17].

Surgeons seeking to develop this technique should have experience with TAMIS or TEMs, as well as open and laparoscopic rectal dissection. It has been suggested a minimum of ten TAMIS or TEMs cases and at least twenty rectal dissections have been completed before embarking on this journey, although these are guidelines only.

Currently, surgeons are encouraged to participate in one or more multi-day courses that are run at expert centers. These involve a structured learning curriculum combining theory sessions, observation of live cases and technical simulation with human cadaveric models. Further education is performed through a number of proctored cases where an expert comes to supervise the operating surgeon. Operating room nursing staff have also been encouraged to attend courses to help assist with the implantation of this new technique. Concurrently, there is ongoing collection of data via voluntary registries where surgeons self-report their own experience. This has led to further education through the presentation of this data, alongside cautionary operative videos both at scientific conferences as well as using high quality video streaming.

Although the development of this structured process is to be commended, there are still numerous limitations that surgeons should be aware of. Firstly, this model of education has scant evidence to prove its efficacy in teaching surgical technique. Secondly, participation in the registries is voluntary without stringent audit processes, meaning that the data may not be completely reliable. Thirdly, in the advent of a complication, the use of proctoring in a legal setting is unknown. Although a few papers have proposed possible training models and conducted preliminary evaluations, these have not had the case volume nor full educational assessment or evaluation to make any conclusions on the success or failure of these training models[18-20].

The authors would recommend that the adoption of this technique by any colorectal surgeon should be implemented within units of colorectal surgeons. No surgeon should look to develop this on their own. Two experienced surgeons should be present to form a sounding board for introductory cases. Development of local accreditation processes, audit and a willingness to participate in the current registry are seen as mandatory.

A paper published from our institution suggested that the learning curve on CU-SUM using quality of TME, negative distal resection margin and circumferential resection margin suggested that the learning curve of the case would be approximately 45-51 cases[21].

RESULTS AND DISCUSSION

As transanal TME is an emerging technique, long-term oncologic outcomes are not yet available. A variety of series have been published in the literature, using surrogate histopathological parameters such as resection margins and completeness of TME specimen as well as commenting on safety and feasibility.

Numerous papers on oncological outcomes have been released. Perdawood and Al Khefagie[22] compared a cohort of twenty-five patients who underwent TaTME and compared them to a case-matched cohort of patients who had previously undergone laparoscopic TME. All patients in the TaTME group had specimens graded as complete (80%) or nearly complete (20%), whereas 16% of the laparoscopic TME specimens were incomplete[22]. Similarly, the rate of positive CRM was higher in the laparoscopic TME group (16%) than the TaTME group (4%). There were no differences between the two cohorts in length of circumferential resection margin, distal resection margin, number of harvested lymph nodes, tumor status and lymph node status. Another comparison between laparoscopic TME and TaTME found a higher quality mesorectum specimen grade quality in TaTME (96%) *vs*. laparoscopic TME (72%)[23]. A meta-analysis of the available data by Ma *et al*.[24] showed that TaTME had a decreased rate of a CRM positivity and a higher rate of complete TME grade specimens compared to TaTME[24].

Short-term outcomes for TaTME have been thoroughly examined and reported in several case reports, case studies and systematic reviews[24-26]. Although data is limited to observational studies, this newly developed technique would appear to be safe and feasible based on these early outcomes. A recent systematic review of the published case series posited that the complication rate between TaTME and open or laparoscopic TME are similar[24]. Most concerning, however, is the rate of otherwise rare complications such as urethral injury. A recent publication from the TaTME registry using a total of 720 cases were analysed comprising 634 patients with rectal cancer and 86 patients with benign pathology[26]. Five urethral injuries were reported at a rate of 0.7%, although this is not a reflection of all TaTME cases done in the world to date. Main risk factors appear to be high BMI and a previously irradiated pelvic field. In females, there is also a risk of vaginal injury during the anterior dissection with the subsequent development of a rectovaginal fistula. The same registry study reported a 0.3% rate of vaginal perforation.

Long-term functional data is not yet readily available, although some short-term studies have been published. Koedam *et al*.[27] published a prospective quality of life study on thirty patients that showed that at 6 months, TaTME and laparoscopic TME had similar postoperative functional outcomes. It must be noted that TaTME patients in this study had initial (1 month) significant decrease in quality of life, physical and social functioning, fatigue, general experienced pain, anal pain, low anterior resection syndrome and male sexual interest which appeared to recover. A second study by Pontallier *et al*.[28] also showed no functional difference in bowel habits or urologic function when TaTME was compared to laparoscopic TME.

FUTURE DIRECTIONS

The most pertinent piece of missing literature is a randomized control trial. The COLOR III trial is designed to fill this gap as a multicenter randomised clinical trial comparing TaTME *vs.* laparoscopic TME for mid and low rectal cancer. Initially, the CRM rate was chosen as primary endpoint within a superiority design[29]; however, the trial was subsequently changed to a non-inferiority design with a clinically relevant primary endpoint of local recurrence rate. This trial is currently in the recruitment phase. However, publication of the recent ALaCaRT (Australasian Laparoscopic Cancer of the Rectum Trial) and ACOSOG (American College of Surgeons Oncology Group) Z6051 trials which examined successful achievement of TME both failed to show non-inferiority of laparoscopy compared to open surgery place some doubt to the use of laparoscopic TME as a gold standard[30,31]. The authors anticipate that due to this, the publication of COLOR III will not settle the oncological questions surrounding low rectal cancer surgical technique. Continuing information will come from the registry data and other case series, including 5-year oncological data.

Developments in surgical equipment and in technology may fill the gap. Surgeons have started to attempt a hybrid between TaTME with a robotics platform either for the transanal or intraperitoneal dissection[32]. Of most interest is the use of a flexible TEMs platform which may alleviate the many ergonomic and access issues that a single port system such as TAMIS introduces. There have been unpublished reports that surgeons have started experimenting with this system in TaTME.

Further research is needed to define whether TaTME will provide the perioperative, oncological and functional outcomes in low rectal cancer surgery. In addition, further development in the education of both surgeons and trainees is needed to spread this technique if it does prove valuable. It is likely that rather than prove to be a “silver bullet” solution, TaTME will prove another weapon in the armament of the modern colorectal surgeon in dealing with low rectal cancer.

DECLARATIONS

Authors’ contributions

Concept and design, drafting the manuscript: Yap R, Monson J

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Copyright

REFERENCES

1. Miles WE. A method of performing abdomino-perineal excision for carcinoma of the rectum and of the terminal portion of the pelvic colon (1908). CA Cancer J Clin 1971;21:361-4.
2. Heald RJ, Husband EM, Ryall RD. The mesorectum in rectal cancer surgery--the clue to pelvic recurrence? Br J Surg 1982;69:613-6.
3. Buess G, Kipfmüller K, Hack D, Grüssner R, Heintz A, et al. Technique of transanal endoscopic microsurgery. Surg Endosc 1988;2:71-5.
4. Atallah S, Albert M, Larach S. Transanal minimally invasive surgery: a giant leap forward. Surg Endosc 2010;24:2200-5.
5. Sylla P, Rattner DW, Delgado S, Lacy AM. NOTES transanal rectal cancer resection using transanal endoscopic microsurgery and laparoscopic assistance. Surg Endosc 2010;24:1205-10.
6. Department of Work and Pensions. Differences in life expectancy between those aged 20, 50 and 80 - in 2011 and at birth. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/223114/diffs_life_expectancy_20_50_80.pdf. [Last accessed on 23 Jan 2019]
7. Nougaret S, Reinhold C, Mikhael HW, Rouanet P, Bibeau F, et al. The use of MR imaging in treatment planning for patients with rectal carcinoma: have you checked the "DISTANCE"? Radiology 2013;268:330-44.
8. Beets-Tan RG, Lambregts DM, Maas M, Bipat S, Barbaro B, et al. Magnetic resonance imaging for the clinical management of rectal cancer patients: recommendations from the 2012 European Society of Gastrointestinal and Abdominal Radiology (ESGAR) consensus meeting. Eur Radiol 2013;23:2522-31.
9. Al-Sukhni E, Milot L, Fruitman M, Beyene J, Victor JC, et al. Diagnostic accuracy of MRI for assessment of T category, lymph node metastases, and circumferential resection margin involvement in patients with rectal cancer: a systematic review and meta-analysis. Ann Surg Oncol 2012;19:2212-23.
10. Cerny M, Dunet V, Prior JO, Hahnloser D, Wagner AD, et al. Initial staging of locally advanced rectal cancer and regional lymph nodes: comparison of diffusion-weighted MRI with 18F-FDG-PET/CT. Clin Nucl Med 2016;41:289-95.
11. Memon S, Lynch AC, Bressel M, Wise AG, Heriot AG. Systematic review and meta-analysis of the accuracy of MRI and endorectal ultrasound in the restaging and response assessment of rectal cancer following neoadjuvant therapy. Colorectal Dis 2015;17:748-61.
12. Motson RW, Whiteford MH, Hompes R, Albert M, Miles WF, et al. Current status of trans-anal total mesorectal excision (TaTME) following the Second International Consensus Conference. Colorectal Dis 2016;18:13-8.
13. Bernardi MP, Bloemendaal AL, Albert M, Whiteford M, Stevenson AR, et al. Transanal total mesorectal excision: dissection tips using 'O's and 'triangles'. Tech Coloproctol 2016;20:775-8.
14. Bracey E, Knol J, Buchs N, Jones O, Cunningham C, et al. Technique for a stapled anastomosis following transanal total mesorectal excision for rectal cancer. Colorectal Dis 2015;17:O208-12.
15. Hompes R, Guy R, Jones O, Lindsey I, Mortensen N, et al. Transanal total mesorectal excision with a side-to-end stapled anastomosis - a video vignette. Colorectal Dis 2014;16:567.
16. Kneist W, Stelzner S, Aigner F, Fürst A, Wedel T. Urethral injury in body donor TaTME training. Coloproctology 2017;39:179-83.
17. Francis N, Penna M, Mackenzie H, Carter F, Hompes R, et al. Consensus on structured training curriculum for transanal total mesorectal excision (TaTME). Surg Endosc 2017;31:2711-9.
18. Atallah SB, DuBose AC, Burke JP, Nassif G, deBeche-Adams T, et al. Uptake of transanal total mesorectal excision in North America: initial assessment of a structured training program and the experience of delegate surgeons. Dis Colon Rectum 2017;60:1023-31.
19. McLemore EC, Harnsberger CR, Broderick RC, Leland H, Sylla P, et al. Transanal total mesorectal excision (taTME) for rectal cancer: a training pathway. Surg Endosc 2016;30:4130-5.
20. Abbott SC, Stevenson ARL, Bell SW, Clark D, Merrie A, et al. An assessment of an Australasian pathway for the introduction of transanal total mesorectal excision (taTME). Colorectal Dis 2018;20:O1-6.
21. Lee L, Kelly J, Nassif GJ, deBeche-Adams TC, Albert MR, et al. Defining the learning curve for transanal total mesorectal excision for rectal adenocarcinoma. Surg Endosc 2018; doi: 10.1007/s00464-018-6360-4.
22. Perdawood SK, Al Khefagie GA. Transanal vs laparoscopic total mesorectal excision for rectal cancer: initial experience from Denmark. Colorectal Dis 2016;18:51-8.
23. Velthuis S, Nieuwenhuis DH, Ruijter TE, Cuesta MA, Bonjer HJ, et al. Transanal versus traditional laparoscopic total mesorectal excision for rectal carcinoma. Surg Endosc 2014;28:3494-9.
24. Ma B, Gao P, Song Y, Zhang C, Zhang C, et al. Transanal total mesorectal excision (taTME) for rectal cancer: a systematic review and meta-analysis of oncological and perioperative outcomes compared with laparoscopic total mesorectal excision. BMC Cancer 2016;16:380.
25. Atallah S, Martin-Perez B, Albert M, deBeche-Adams T, Nassif G, et al. Transanal minimally invasive surgery for total mesorectal excision (TAMIS-TME): results and experience with the first 20 patients undergoing curative-intent rectal cancer surgery at a single

institution. Tech Coloproctol 2014;18:473-80.
26. Penna M, Hompes R, Arnold S, Wynn G, Austin R, et al. Transanal total mesorectal excision: international registry results of the first 720 cases. Ann Surg 2017;266:111-7.
27. Koedam TW, van Ramshorst GH, Deijen CL, Elfrink AK, Meijerink WJ, et al. Transanal total mesorectal excision (TaTME) for rectal cancer: effects on patient-reported quality of life and functional outcome. Tech Coloproctol 2017;21:25-33.
28. Pontallier A, Denost Q, Van Geluwe B, Adam JP, Celerier B, et al. Potential sexual function improvement by using transanal mesorectal approach for laparoscopic low rectal cancer excision. Surg Endosc 2016;30:4924-33.
29. Deijen CL, Velthuis S, Tsai A, Mavroveli S, de Lange-de Klerk ES, et al. COLOR III: a multicentre randomised clinical trial comparing transanal TME versus laparoscopic TME for mid and low rectal cancer. Surg Endosc 2016;30:3210-5.
30. Stevenson AR, Solomon MJ, Lumley JW, Hewett P, Clouston AD, et al. Effect of laparoscopic-assisted resection vs open resection on pathological outcomes in rectal cancer: the ALaCaRT randomized clinical trial. JAMA 2015;314:1356-63.
31. Fleshman J, Branda M, Sargent DJ, Boller AM, George V, et al. Effect of laparoscopic-assisted resection vs open resection of stage II or III rectal cancer on pathologic outcomes: the ACOSOG Z6051 randomized clinical trial. JAMA 2015;314:1346-55.
32. Kuo LJ, Ngu JC, Tong YS, Chen CC. Combined robotic transanal total mesorectal excision (R-taTME) and single-site plus one-port (R-SSPO) technique for ultra-low rectal surgery-initial experience with a new operation approach. Int J Colorectal Dis 2017;32:249-54.

Ohmura *et al. Mini-invasive Surg* 2019;3:4
DOI: 10.20517/2574-1225.2018.69

Mini-invasive Surgery

Original Article

Open Access

Intracorporeal hemi-hand-sewn technique for Billroth-I gastroduodenostomy after laparoscopic distal gastrectomy: comparative analysis with laparoscopy-assisted distal gastrectomy

Yasushi Ohmura[1,2], Hiromitsu Suzuki[2,3], Kazutoshi Kotani[2,4], Atsushi Teramoto[2,3]

[1]Department of Cancer Treatment Support Center, Okayama City Hospital, Okayama 700-8557, Japan.
[2]Department of Surgery, Okayama City Hospital, Okayama 700-8557, Japan.
[3]Department of Surgery, Yakage Hospital, Okayama 714-1201, Japan.
[4]Department of Surgery, Kasaoka Daiichi Hospital, Okayama 714-0043, Japan.

Correspondence to: Dr. Yasushi Ohmura, Department of Cancer Treatment Support Center, Okayama City Hospital. 1-20-3 Kitanagase-omotemachi, Kita-ku, Okayama 700-8557, Japan. E-mail: yohmura826@yahoo.co.jp

How to cite this article: Ohmura Y, Suzuki H, Kotani K, Teramoto A. Intracorporeal hemi-hand-sewn technique for Billroth-I gastroduodenostomy after laparoscopic distal gastrectomy: comparative analysis with laparoscopy-assisted distal gastrectomy. *Mini-invasive Surg* 2019;3:4. http://dx.doi.org/10.20517/2574-1225.2018.69

Received: 30 Nov 2018 **First Decision:** 30 Nov 2018 **Revised:** 30 Jan 2019 **Accepted:** 1 Feb 2019 **Published:** 27 Feb 2019

Science Editor: Tetsu Fukunaga **Copy Editor:** Cai-Hong Wang **Production Editor:** Huan-Liang Wu

Abstract

Aim: The purpose of this study was to evaluate the clinical feasibility and efficacy of the intracorporeal hemi-hand-sewn (IC-HHS) technique for Billroth-I gastroduodenostomy in comparison with extracorporeal total hand-sewn (EC-THS) anastomosis. We also examined the size of resected specimens in each procedure.

Methods: The number of enrolled cases of EC-THS and IC-HHS anastomosis groups were 85 and 110 cases, respectively. Perioperative data and the measured sizes of resected specimens were analyzed.

Results: Operation time in the IC-HHS group was significantly longer than the EC-THS group (234.8 min *vs.* 275.0 min, $P < 0.01$), whereas intraoperative blood loss was less in the IC-HHS group (48.4 mL *vs.* 25.4 mL, $P = 0.03$). There were no procedure-related complications in the IC-HHS group. The greater curvature of the EC-THS group was significantly shorter than the IC-HHS group (214.6 mm *vs.* 228.7 mm, $P < 0.01$). There was no correlation between body mass index (BMI) and the length of the greater curvature in the IC-HHS group ($r = 0.07$, $P = 0.47$), but in the EC-THS group, the length of the greater curvature tends to shorten as BMI increases ($r = -0.45$, $P < 0.01$).

Conclusion: IC-HHS technique for Billroth-I gastroduodenostomy revealed feasible with acceptable operation time and postoperative outcome. Another advantage of total laparoscopic distal gastrectomy that intracorporeal transection can facilitate is to ensure an adequate proximal margin, especially in obese middle gastric cancer patients.

Keywords: Laparoscopy, gastrectomy, anastomosis, Billroth I procedure, surgical margin

INTRODUCTION

Since the first laparoscopic gastrectomy was described in 1992[1], the safety and feasibility of laparoscopic gastrectomy have already been demonstrated in the treatment of early gastric cancer[2,3] and several advantages of laparoscopic gastrectomy were reported in comparison with open gastrectomy, such as postoperative recovery and shorter hospital stay[4,5]. Due to being less invasive, laparoscopic gastrectomy was successfully performed in elderly patients and obese patients with an acceptable complication rate and prognosis[6-9].

The reconstruction methods after distal gastrectomy are represented by Billroth-I (B-I), Billroth-II, and Roux-en-Y method. Among them, B-I gastroduodenostomy is the most widely practiced procedure in the world. Due to the fact that the procedure is relatively simple and does not require an anatomical replacement of the digestive tract below the transverse colon[10]. Moreover, it provides a physiologic flow of food contents through the duodenum and decreases the possibility of metabolic problems and nutritional deficiency[11] while postoperative observation of the ampulla of Vater can be carried out reliably and easily. When laparoscopic gastrectomies were first introduced, because of the technical challenges of achieving an intracorporeal B-I reconstruction, most surgeons preferred laparoscopy-assisted approach with mini-laparotomy[12,13]. In laparoscopy-assisted distal gastrectomy (LADG), gastroduodenostomy as well as gastric transection was also performed through a small laparotomy. Therefore, especially in obese patients with thick abdominal walls, it was difficult to pull out the stomach enough to secure an appropriate resection range and to perform safe anastomosis through the small laparotomy.

Recently, several techniques of intracorporeal reconstruction have been developed. Currently, many gastric surgeons are attempting to perform total laparoscopic gastrectomy with intracorporal reconstruction because it offers a good operative field regardless of the patient's figure[14]. Furthermore, the transection level of the stomach can be reliably determined by the intraoperative endoscope in a natural anatomical position without deformation.

In our hospital, we have performed LADG with extracorporeal total hand-sewn (EC-THS) gastroduodenostomy through mini-laparotomy until October 2013[15]. Since intracorporeal delta-shaped (IC-DS) gastroduodenostomy was introduced, this method became the most widely implemented intracorporeal anastomotic technique, especially in eastern countries[16-18]. However, several concerns have been reported, such as anatomical twisting, excessive tension caused by side-to-side anastomosis, duodenal ischemia due to duodenal dissection and preservation, and shortened distal surgical margin. In 2013, as the method of total laparoscopic distal gastrectomy, we devised a new reconstruction method to create end-to-end gastroduodenostomy, in which the posterior wall of the anastomosis was constructed with a linear stapler and subsequently, the anterior wall was sutured with an intracorporeal hand-sewn technique, and reported as intracorporeal "hemi-hand-sewn (HHS) technique"[19].

The purpose of this study was to evaluate the feasibility and efficacy of IC-HHS technique for end-to-end B-I gastroduodenostomy after laparoscopic distal gastrectomy in comparison with conventional EC-THS anastomosis in LADG. In addition, we assumed that there was a possibility that the range of resection might be smaller in laparoscopy-assisted approach in obese patients, but the difference of resection range between the extracorporeal transection and intracorporeal procedure were not reported. Therefore, we evaluated the size of resected specimen and analyzed the differences of the resection range between each procedure.

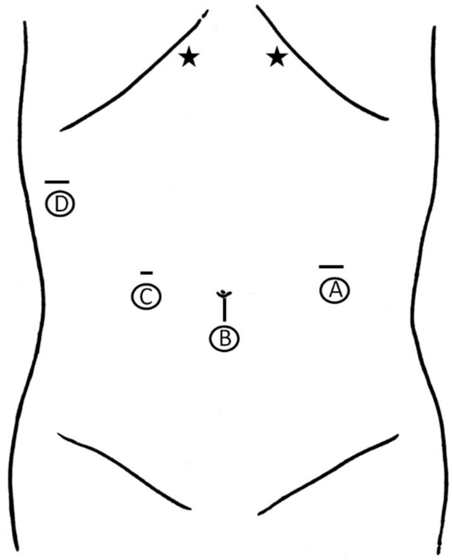


Figure 1. The trocar placement and stomach lifting positions for dual stomach-lifting technique in total laparoscopic distal gastrectomy. All trocars are 12 mm. A and C are used by the operator and D by the assistant. A flexible laparoscope is inserted through B. The nylon threads for stomach lifting are pulled out from the star marks

METHODS

Lymph node dissection

Under general anesthesia, the patient was placed in a modified lithotomy position and subjected to a head-up tilt with the semiboot foot holder: Levitator (Mizuho, Tokyo, Japan). We used a 10-mm, 3D flexible laparoscope; ENDOEYE FLEX 3D® (Olympus Medical, Tokyo, Japan). The operator performed all procedures standing between the patient's legs. We applied a 4 port-laparoscopic distal gastrectomy with dual stomach-lifting technique (DSLT)[15]. The trocar placement and stomach lifting positions are shown in Figure 1. The stomach and duodenum were not transected before completion of the lymph node dissection.

Gastric resection and EC-THS gastroduodenostomy in LADG

Endoscopic clips were preoperatively placed on the proximal site 1 cm from the tumor along the longitudinal axis of the stomach. In the EC-THS group, the mobilized stomach was pulled out via Lap Protector® (Hakko, Nagano, Japan) attached to a 5-cm epigastric mini-laparotomy. After confirmation of clips by palpation, the distal stomach was divided from the greater curvature side by a linear stapler extracorporeally. Then staple line of the remnant stomach was reinforced by continuous seromuscular suturing with 3-0 coated braided synthetic absorbable suture: Vicryl® (Ethicon, Somerville, NJ, USA) from the lesser curvature. Then posterior sero-muscular suturing between the remnant stomach and the duodenum were performed with 3-0 coated braided nylon suture: Bear Braid® (Bear Medic Co., Tokyo, Japan). After ligation, the duodenum was divided by electric scalpel and the distal gastrectomy was completed. When the proximal edge of the tumor was close to the resection margin, frozen-section examination was performed to confirm the absence of any microscopic invasion. Subsequently, whole-layer continuous sutures of the posterior and anterior wall were performed with 3-0 Vicryl. Finally, 2-layer gastroduodenostomy was completed after sero-muscular suture with 3-0 Bear Braid.

Gastric resection and IC-HHS gastroduodenostomy in TLDG

Preoperative endoscopic marking was done with the same maneuver as LADG. Lymph node dissection was also performed with DSLT. Details of surgical procedures and the IC-HHS technique were summarized in the attached video [Video 1].

Endoscopic observation to the duodenum prior to resection made it possible to prevent spillage of gastrointestinal contents during anastomosis. After completion of lymph node dissection, the duodenum was divided with an endoscopic linear stapler: Echelon® 60-3.5 (Ethicon Endo-Surgery, Cincinnati, OH, USA) without duodenal twisting. Transection of the stomach was also performed using endoscopic linear staplers twice under intraoperative gastroscopic navigation (in middle third gastric cancer cases). Then the resected specimen was retrieved via Lap Protector® (Hakko, Nagano, Japan) attached to a 3-cm incision at the umbilical port. After the macroscopic evaluation, a frozen-section examination was performed if needed.

Full-thickness posterior wall anastomosis

After retrieval of the resected stomach, a plate platform: E-Z access® (Hakko) was attached to the wound protector and pneumoperitoneum was restarted, then an intracorporeal anastomosis was performed. First, removal of a small part of the staple using Sonicbeat® (OLYMPUS, Tokyo, Japan) at 5 cm from the greater curvature of the remnant stomach was completed to confirm anastomotic diameter. Then the staple line of the remnant stomach was reinforced by continuous seromuscular suturing with 3-0 Vicryl from the lesser curvature to the defect of the staple. Sero-muscular stay sutures with 3-0 Bear Braid were placed at both the lesser and greater curvatures between the remnant stomach and the duodenum. An entry hole was made by piercing the active blade of Sonicbeat at the greater curvature of the stomach wall, then a tissue pad of Sonicbeat was put into the stomach cavity and the anterior wall was incised toward the staple defect. A similar entry hole was made at the greater curvature of the duodenal wall and the anterior wall of the duodenum was incised toward the lesser curvature side. The assistant grasped two stay sutures ligated at the excessive tissues and lifted them up vertically. Then the posterior wall of the remnant stomach and the duodenum were approximated by Echelon 60-3.5 inserted from the umbilical port. During closure of the stapler forks, it was carefully confirmed that there was no excessive pinching of the anterior wall from left and right lateral abdominal trocars. The endoscopic linear stapler was fired to excise the excessive gastric and duodenal tissues and simultaneously the posterior wall anastomosis was constructed. Then the staple line was observed to confirm that there was no bleeding or pinching of the anterior wall [Figure 2A-G].

Full-thickness anterior wall anastomosis

Subsequently, a full-thickness, continuous suture of the anterior wall was performed with 3-0 Vicryl. The first suture was started at the lower edge of the posterior wall and the first knot was developed inside the lumen involving the staple edge. Next suturing was made from the duodenal mucosa to the serosal side and after 5 over and over suturings, the Vicryl was locked. Using another 20 cm Vicryl, continuous suturing was started from the upper edge of the staple line of the posterior wall anastomosis. Continuous suturing was carried out with an over and over technique and when the two sutures met each other, each end was ligated intracorporeally to finish the full-thickness anterior wall anastomosis [Figure 2H].

Sero-muscular inverting anterior wall anastomosis

Afterwards, interrupted sero-muscular layer suturing of the anterior wall was performed with 3-0 Bear Braid for complete inverting anastomosis [Figure 2I]. The first suture at the lesser curvature involved three points, the anterior and posterior wall of the remnant stomach and the duodenal wall. Approximately 10 sero-muscular sutures were required for inverting gastroduodenostomy. Then, an intracorporeal B-I gastroduodenostomy by HHS technique was completed, which was almost the same shape as a hand-sewn inverting anastomosis by open surgery or EC-THS reconstruction. In the case with intraoperative endoscopy, the anastomotic site was observed after the completion of reconstruction [Figure 3].

Patient evaluation

Total laparoscopic gastrectomy with IC-HHS technique was introduced since November 2013. A total of 452 patients who underwent surgery for gastric cancer in our hospital and related institutions between September 2008 and December 2017 were identified. All patients underwent multi-detector-row computed

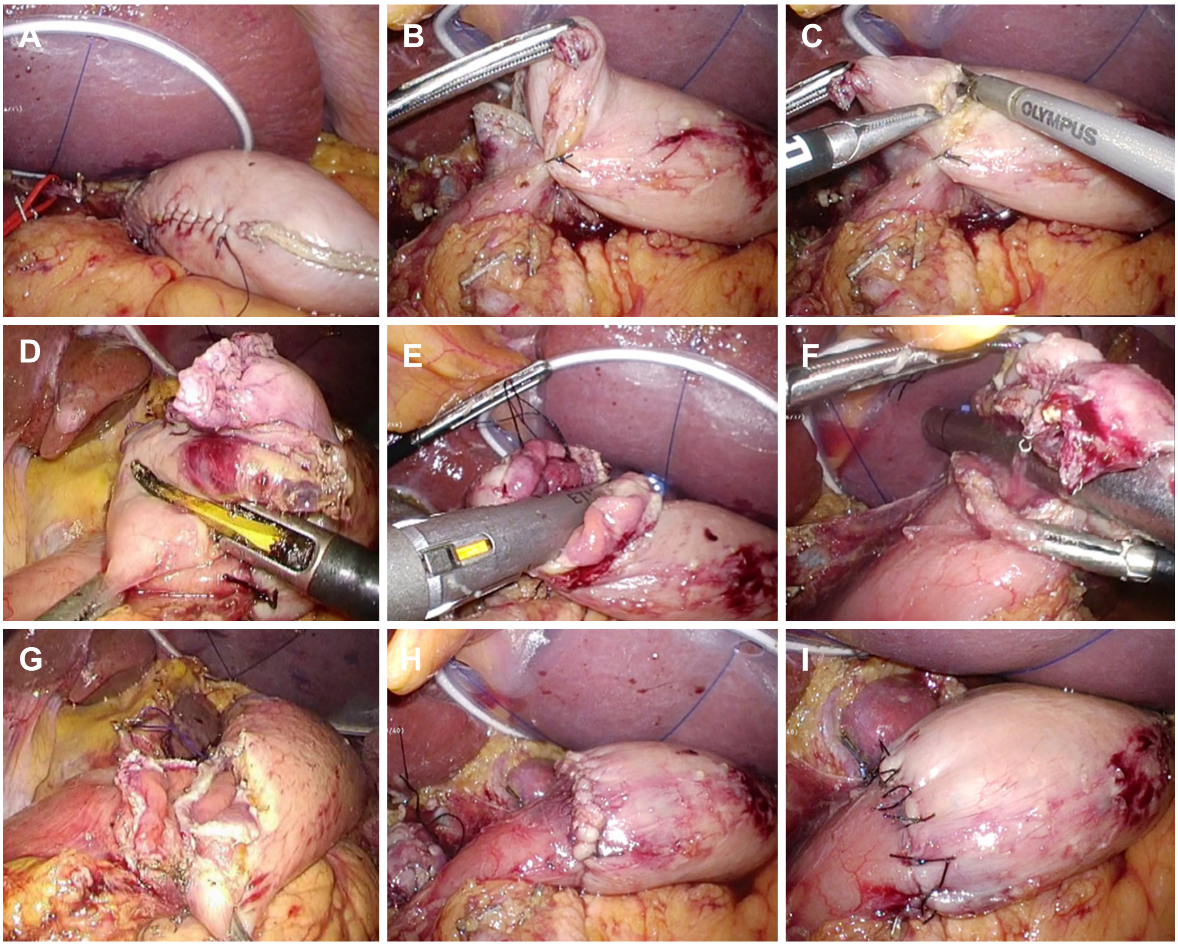


Figure 2. Intracorporeal hemi-hand-sewn Billroth-I anastomosis. After having confirmed approximately 5 cm away from the edge of the greater curvature for anastomosis, the remaining staple line is reinforced by continuous suture (A); sero-muscular stay sutures are placed between the remnant stomach and the duodenum (B); the anterior wall of the remnant stomach is incised (C); subsequently, the anterior wall of the duodenum is also incised (D); the posterior wall of the remnant stomach and the duodenum is brought together with the Echelon 60-3.5 from the umbilical port: laparoscopic view from the stomach side (E) and from the duodenal side (F); full thickness of posterior wall anastomosis is completed (G); then a whole-layer approximation is accomplished by continuous suture with an absorbable thread (H); finally, an anterior sero-muscular suture is completed by interrupted sutures (I)

tomography scans and upper endoscopy to determine the location and clinical stage of gastric cancer. Adenocarcinoma of the stomach was histologically proven for all patients. Open gastrectomy was performed in 229 patients, while 223 patients underwent laparoscopic gastrectomy. In this study, 21 total gastrectomy cases and 3 proximal gastrectomy cases were excluded. Laparoscopic distal gastrectomy was performed in 199 cases. Among them, 3 patients underwent concurrent colectomy and 1 case with concurrent nephrectomy were also excluded. A total of 195 patients were enrolled into the retrospective study [Figure 4]. All patients gave their written informed consent for laparoscopic procedures. This study protocol was approved by the institutional ethics committee. Demographic characteristics such as age, sex, body mass index (BMI), ASA score, site of the lesion, history of abdominal surgery, and anticoagulant use, were retrospectively extracted from the database.

Surgical outcome and postoperative complications

Operation time, blood loss, extent of lymph node dissection, number of harvested lymph nodes, pathological stage, perioperative complications, length of hospital stay after surgery, and type of reconstruction were retrieved from the database. Postoperative complications were graded according to the Clavien-Dindo classification[20]. Delayed gastric emptying was defined as an emptying disturbance

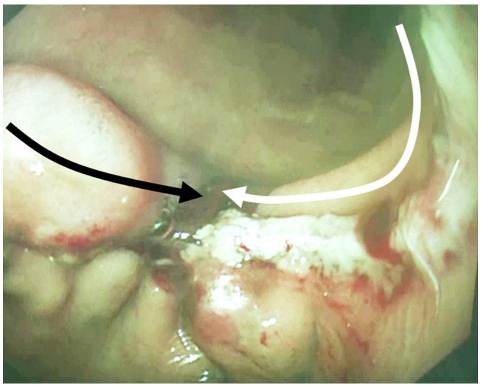


Figure 3. Intraoperative endoscopic finding after completion of gastroduodenostomy by intracorporeal hemi-hand-sewn technique. The suture line of the posterior wall by linear stapler (white arrow) and hand-sewn suture line of the anterior wall (black arrow)

requiring starvation for more than three days, excluding the cases where anastomotic stenosis or mechanical bowel obstruction was confirmed by radiographic or endoscopic examination.

Evaluation of resected specimen

The resected stomach was incised and opened according to the rule of Japanese classification of gastric carcinoma[21] and then was placed on the flat board. After stretching the stomach wall sufficiently, we fixed the edges of the stomach to the board with stainless steel pins. In addition to measuring the size of the tumor, we also measured the length of the greater curvature, lesser curvature, duodenum, proximal margin and distal margin. Where the staple line was removed, a length of 3 mm was added to each as a measured value. Histological data were retrieved from the database based on the 14th version of the staging system of Japanese Gastric Cancer Association[21].

Statistical analysis

Clinicopathological data and perioperative results were statistically compared between the EC-THS group and the IC-HHS group. The length of each part of the resected specimen was also analyzed. Continuous data was analyzed with the Student's *t*-test. The Fisher's exact test or Chi-square test were used for comparison of categorical values. Pearson linear regression analyses were conducted to correlate BMI and the length of the greater curvature of resected stomach. A two-sided P value < 0.05 was considered to be statistically significant.

RESULTS

Patient characteristics

The number of cases of the EC-THS and IC-HHS groups were 85 and 110 cases, respectively. The 195 patients had an average age of 71.0 years (range, 38-93 years). The average BMI was 23.1 (range 17.0-34.0 kg/m^2). As for the location of the tumors, 142 cases were in the middle third of the stomach and 53 cases was in the lower third of the stomach, 5 of them showed duodenal infiltration to the pyloric ring [Table 1].

Surgical outcome

Total laparoscopic or laparoscopy-assisted distal gastrectomies were successfully accomplished in all patients (195 patients). D2 lymph node dissection was performed more frequently in the IC-HHS group (12.7%) compared to the EC-THS group (1.2%) (P < 0.01). The proportion of concurrent cholecystectomy was higher in the IC-HHS group, but there was no significant difference (P = 0.21). Operation time in the IC-HHS group required an average of 275.0 min, which was significantly longer than the 234.8 min in the EC-THS group (P < 0.01). The amount of intraoperative blood loss was less in IC-HHS group (25.4 mL *vs*. 44.0 mL, P = 0.03). The subgroup analysis in D1+ cases revealed similar results; the average operation

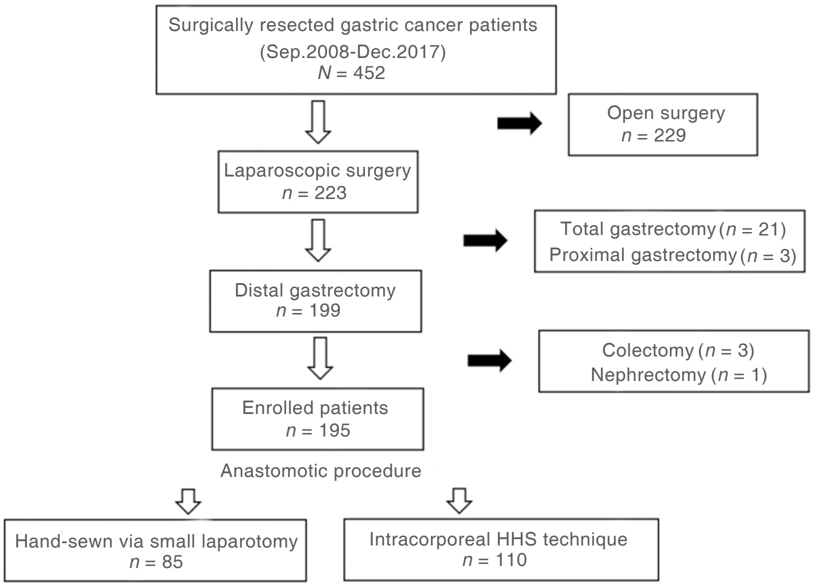


Figure 4. Flow chart for the current study detailing inclusion and exclusion criteria; HHS: hemi-hand-sewn

time was longer in the IC-HHS group (276.4 min) than in the EC-THS group (234.6 min) (P = 0.04) and intraoperative blood loss was smaller in IC-HHS group (26.3 mL) compared to EC-THS group (48.9 mL) (P < 0.01). R0 resection was achieved in all patients with free surgical margin defined by pathological examination.

Postoperative outcome

Surgical site infection was observed at the epigastric wound in the EC-THS group (5 cases) and at the umbilical wound in the IC-HHS group (1 case). Laparoscopic cholecystectomy was required in one case of the IC-HHS group due to necrotic cholecystitis resistant to conservative treatment on day 9 after gastrectomy. One case of delayed gastric emptying was observed in the EC-THS group. The frequency of intra-abdominal abscess or pancreatic fistula development in the EC-THS and IC-HHS group were 3.5% and 1.8%, respectively and they were all cured by administration of antibiotics. One case of postoperative pneumonia in the EC-THS group was also successfully treated by antibiotics.

Evaluation of resected specimen

Table 2 shows the measured length of each part of the resected specimens. The greater curvature of the IC-HHS group was significantly longer than that of EC-THS group (214.6 *vs*. 228.7 mm, P < 0.01). The length of the lesser curvature and the duodenum were not significantly different. There was no correlation between BMI and the length of the greater curvature in the IC-HHS group (r = 0.03, P = 0.47), while in the EC-HS group, the length of the greater curvature weakly correlated with BMI (r = -0.44, P < 0.01). The length of the great curvature of the resected stomach tends to be shorter as BMI increases [Figure 5A and B].

DISCUSSION

This study found that the IC-HHS technique for laparoscopic B-I gastroduodenostomy was successfully accomplished in all 110 cases without any procedure-specific complications, indicating its technical feasibility. The average operation time was about 40 min longer than EC-THS reconstruction. The similar difference in the subgroup analysis in D1+ cases suggested that the extended operation time was due to the difference in the anastomotic procedures. Anastomotic leakage and stricture were not observed in our experiences.

Table 1. Demographic characteristics, perioperative details, and pathological outcome of gastric cancer patients

Variable	EC-THS (*n* = 85)		IC-HHS (*n* = 110)		*P* value
	Mean ± SD	Range	Mean ± SD	Range	
Backgrounds					
Age, mean ± SD (y.o.)	70.7 ± 9.5	44-88	71.2 ± 10.2	38-93	$P = 0.68$
Sex, No. (%)					
Male	58 (68.2%)		77 (70.0%)		$P = 0.79$
Female	27 (31.8%)		33 (30.0%)		
BMI, mean ± SD (kg/m^2)	23.5 ± 3.3	19-31	22.7 ± 3.5	17-34	$P = 0.17$
ASA classification, No. (%)					
I	17 (20.0%)		18 (16.4%)		$P = 0.57$
II	55 (64.7%)		74 (67.3%)		
III	13 (15.3%)		18 (16.4%)		
Location, No. (%)					
Upper stomach	0 (0.0%)		0 (0.0%)		$P = 0.21$
Middle stomach	58 (68.2%)		84 (76.4%)		
Lower stomach	27 (31.8%)		26 (23.6%)		
Lower stomach (D+)	2 (1.8%)		3 (2.7%)		
Prior abdominal surgery, No. (%)					
Yes	23 (27.1%)		20 (18.2%)		$P = 0.14$
No	62 (72.9%)		90 (81.8%)		
Anticoagulant use, No. (%)					
Yes	17 (20.0%)		21 (19.1%)		$P = 0.87$
No	68 (80.0%)		89 (80.9%)		
Perioperative details					
Lymph node dissection, No. (%)					
D1+	84 (98.8%)		96 (87.3%)		$P < 0.01$
D2	1 (1.2%)		14 (12.7%)		
Operation time, mean ± SD (min)	234.8 ± 29.6	175-302	275.0 ± 34.7	230-411	$P < 0.01$
Blood loss, mean ± SD (mL)	48.4 ± 39.6	5-180	25.4 ± 32.6	3-140	$P = 0.03$
Cholecystectomy, No. (%)	8 (9.4%)		17 (15.6%)		$P = 0.21$
Complications, C-D grade No. (%)					
Grade I	5 (5.9%)		1 (0.9%)		
Grade II	4 (4.7%)		2 (1.8%)		
Grade IIIa	0 (0.0%)		0 (0.0%)		
Grade IIIc	0 (0.0%)		1 (0.9%)		
LOHS, mean ± SD (day)	14.6 ± 3.8	5-23	13.3 ± 4.8	7-34	$P = 0.04$
Pathological outcomes					
T stage, No. (%)					
Mucosa	47 (55.3%)		64 (58.2%)		$P = 0.83$
Submucosa	24 (28.2%)		27 (24.5%)		
Muscularis propria	8 (9.4%)		8 (7.3%)		
Subserosa	6 (7.1%)		11 (10.0%)		
N stage, No. (%)					
0	83 (97.6%)		105 (95.5%)		$P = 0.43$
1 (1-3)	2 (2.4%)		5 (4.5%)		
Lymph node yield, mean ± SD (No.)	30.8 ± 10.2	11-59	29.4 ± 9.8	11-59	$P = 0.34$
Pathological stage, No. (%)					
IA	67 (78.8%)		90 (81.8%)		$P = 0.75$
IB	11 (12.9%)		8 (7.3%)		
IIA	6 (7.1%)		6 (5.5%)		
IIB	1 (1.2%)		6 (5.5%)		

EC-THS: extracorporeal-total hand-sewn group; IC-HHS: intracorporeal-hemi-hand-sewn group; SD: standard deviation; BMI: body mass index; ASA score: American Society of Anthologist score; C-D grade: Clavien-Dindo classification grade; LOHS: post-operative length of hospital stay

Though a B-I gastroduodenostomy requires only one anastomosis, it is difficult to perform through a small laparotomy in obese patients. The degree of difficulty is greatly affected by the patient's figure. On the

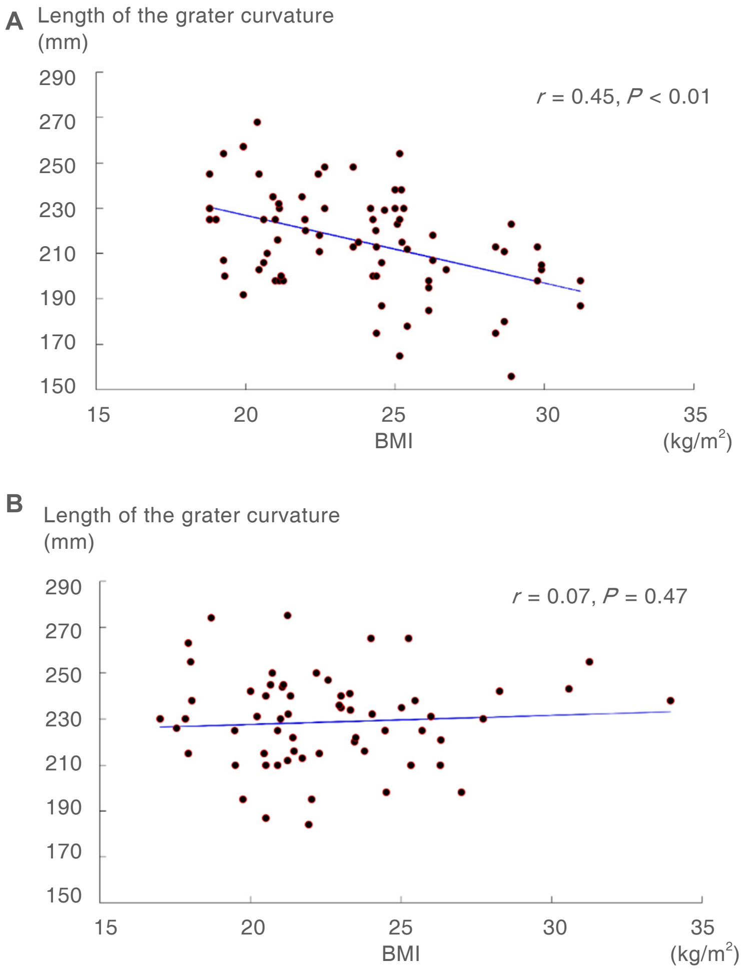


Figure 5. Simple linear regression analyses between BMI and the length of the greater curvature of resected stomach. The length of the greater curvature weakly correlated with BMI in the extracorporeal total hand-sewn group (A); while there was no correlation between BMI and length of the greater curvature in the intracorporeal hemi-hand-sewn group (B)

Table 2. Size of resected specimen

	EC-THS (n = 85)	IC-HHS (n = 110)	P value
Maximum tumor, mean ± SD (mm)	31.6 ± 15.5	35.6 ± 28.1	P = 0.20
Greater curvature, mean ± SD (mm)	214.6 ± 21.7	228.7 ± 19.7	P < 0.01
Lesser curvature, mean ± SD (mm)	148.7 ± 17.6	149.2 ± 18.3	P = 0.50
Duodenum, mean ± SD (mm)	14.7 ± 3.6	14.1 ± 4.0	P = 0.22
Proximal margin, mean ± SD (mm)	53.4 ± 32.4	54.1 ± 32.5	P = 0.88
Distal margin, mean ± SD (mm)	77.1 ± 35.7	78.5 ± 39.8	P = 0.87

SD: standard deviation; EC-THS: extracorporeal-total hand-sewn group; IC-HHS: intracorporeal-hemi-hand-sewn group

other hand, intracorporeal B-I reconstruction by means of open surgery requires considerable advanced technical skill. Therefore, several procedures for B-I intracorporeal gastroduodenostomies specific to laparoscopic surgery have been reported, such as IC-DS gastroduodenostomy[16], triangulation stapling technique[22], book binding technique[23,24], overlap method[25], and double-stapling technique with circular stapler. Sufficient blood supply of digestive tracts, absence of excessive tension, well-apposed tissues at the anastomotic site, and appropriate anastomotic techniques are critically important factors for successful and safe anastomosis. In terms of blood supply and tension between the reconstructing digestive tract, hemi-double stapling technique with circular stapler is the best procedure for gastroduodenostomy[26]. However, it is difficult to keep a sufficient operative field for safe intracorporeal anastomosis. Currently, IC-DS anastomosis has been widely performed in East Asian countries[14,16]. Shorter operation time and superior short-term surgical outcomes were reported in comparison with the other methods[27,28], however, some concerns were reported. First, due to anatomical twisting from the IC-DS method, it is relatively difficult for inexperienced surgeons to understand deviated anatomy. Second, a IC-DS gastroduodenostomy is a functional end-to-end anastomosis, but is an anatomical side-to-side anastomosis, more tension is generated compared to anatomical end-to-end anastomosis[23]. Moreover, additional duodenal dissection and formation of the triangular area of the duodenal wall might be responsible for the ischemic status, which is one of the most significant risk factors of anastomotic failure. Technically, a skillful assistant is desirable for cooperative work when inserting a stapler during IC-DS gastroduodenostomy. Okabe *et al.*[29] reported two cases of duodenal injury during IC-DS gastroduodenostomies and they had to change the reconstruction method.

On the other hand, other anastomotic procedures using intracorporeal hand-sewn techniques were reported[30-32]. Takiguchi *et al.*[30] performed a total laparoscopic method by performing Billroth-I hand-sewn anastomosis and reported excellent postoperative recovery. In attempting to intracorporeal anastomosis, we initially applied total hand-sewn Albert-Leinbert anastomosis which was a promising and stable anastomotic method in open surgery after thorough training and since 2012. Total hand-sewn Albert-Leinbert anastomosis was performed in 19 patients. Although there was no major problem in their postoperative course, it took an average of nearly 100 min longer compared to the EC-THS method. Then, we devised a new reconstruction method to create end-to-end gastroduodenostomy, in which the posterior wall of the anastomosis was constructed with a linear stapler and subsequently, the anterior wall was sutured by an intracorporeal hand-sewn technique. We previously reported this procedure as a “HHS technique” in 2013[19]. Koeda and colleagues reported similar technique as a hybrid technique using linear staplers and manual suturing in 19 pylorus-preserving gastrectomy cases with good postoperative results[33].

There are some reports using a barbed suture in order to facilitate intracorporeal suturing, however, complications following the use of this unique suture have been reported in several other surgeries[34-36]. The most commonly encountered complication with the use of barbed sutures was postoperative bowel obstruction. In terms of its intended shape, a barbed suture develops irreversible tension created during the suturing. Therefore, excessive traction narrows the anastomotic lumen, which can also cause postoperative stricture. Therefore, we used absorbable blade for continuous Albert suturing and nylon blade for interrupted Leinbert suturing, as were adopted to conventional open surgery.

Although single layer continuous anastomosis could simplify the procedure and shorten operation time, we performed two-layer anastomosis. In bariatric surgery, staple-line reinforcement was strongly recommended for laparoscopic sleeve gastrectomy to decrease complications[37]. Also, it was reported that laparoscopic reinforcement with Lembert’s sutures of a duodenal stump could help to avoid duodenal stump leakage in Rou-en Y reconstruction[38,39]. We applied a two-layer technique with interrupted inverting sutures for the intracorporeal gastroduodenostomy. Due to the fact laparoscopic surgery has been developed as a minimally invasive surgery, once postoperative complications arise, the disadvantages incurred by patients are greater than that of conventional laparotomy surgery. Reconstruction can be done without hand suturing by other anastomotic techniques in most cases, however, there are no reports showing the result of delta-shaped anastomosis in open gastrectomy even at medical facility that introduced IC-DS anastomosis as the standard procedure. This does not mean that delta anastomosis is the best anastomotic method but may indicate that it is a complementary procedure during the development of laparoscopic surgery. We believe that acquisition of intracorporeal suturing skills are still important and the ideal reconstruction methods established in the long history of open surgery deserved to be reproduced as much as possible in laparoscopic surgery. IC-HHS anastomosis requires an advanced suturing technique and longer operation time, but we believe it is undesirable to give too much priority to shortening operation time. Completing a straight suture line in gastroduodenostomy at the co-axial position is a great opportunity to acquire basic intracorporeal suturing technique and the acquired technique will be useful in unexpected difficult situations, such as unintended bowel injury.

In LADG, extracorporeal stomach transection with a linear stapler is performed from the greater curvature and it is sometimes difficult to ensure an optimal proximal margin in obese patients with middle third gastric cancer. When the patient has a thick abdominal wall, it is necessary to pull out the stomach with considerable traction however there is an absolute limitation to our ability. At the beginning of the totally laparoscopic distal gastrectomy (TLDG), there were some concerns about the difficulty of locating the tumor and securing the resection margin as a technical limitation. However, with the routine intraoperative endoscopy, it has become possible to decide the transection line more reliably. Although there were some reports analyzing the data of proximal and distal resection margin[40-43], the difference of the resected specimen between extracorporeal and intracorporeal approach had not been discussed. Therefore, we conducted an evaluation of the size of the resected specimen in this study. The result of our study revealed that the length of the greater curvature of the resected stomach was shorter in the EC-THS group compared to the IC-HHS group. In the EC-THS group, the length of the greater curvature tended to shorten as BMI increases. Resectable range of the proximal stomach might be limited in the EC-THS group as the degree of obesity increases. On the other hand, with regard to the transection at the lesser curvature side, it is possible to insert the tip of the linear stapler near the esophago-gastric junction. We supposed that this was the reason why there was no difference in the length of the resected lesser curvature. Despite of the higher proportion of middle third gastric cancer in the IC-HHS group, there was no difference in the proximal margin between the two groups. The intracorporeal procedure was superior not only in terms of intracorporeal reconstruction but also of intracorporeal transection, because it was possible to determine a more reliable transection level of the stomach to secure an optimal surgical margin. As described above, the extracorporeal anastomosis through a small incision sometimes requires excessive traction on the organs and increases intraoperative manipulation, especially in obese patients. The excessive traction of the organs in a narrow operative field sometimes causes unexpected vessel injuries in a blind spot. Additionally, although we carefully confirmed that there was no bleeding before making a small laparotomy, unexpected bleeding due to congestion of the stomach was often experienced at the time when the stomach was pulled out from the small laparotomy. This might cause the difference of intraoperative blood loss. In total laparoscopic gastrectomy, wide and anatomically undeviated surgical field minimizes unintended surgical trauma.

In conclusion, the IC-HHS technique for end-to-end Bi-I gastroduodenostomy revealed feasible with acceptable operation time and postoperative outcome. The DSLT and IC-HHS techniques allowed the operator to perform all procedures from initial skin incision to wound closure at the co-axial position without changing position. Although IC-HHS anastomosis requires an advanced suturing technique, we believe that it is necessary to keep basic training for intracorporeal suturing in addition to using automatic suturing equipment. Resectable range of the stomach was limited as the BMI increases in extracorporeal stomach transection. Intracorporeal stomach transection is desirable especially in obese patients. The advantage of TLDG has been reported providing a safe operative field during the reconstruction regardless of patient’s figure. Additionally, the results of this study demonstrated another advantage of TLDG. It means that intracorporeal gastric resection makes it possible to perform safe gastric transection at a more proximal site in obese middle third gastric cancer patients without unexpected tissue damage.

DECLARATIONS

Authors’ contributions

Conception and design of the study, data analysis, literature research, manuscript writing, manuscript editing, and manuscript revision: Ohmura Y, Suzuki H, Kotani K, Teramoto A

Availability of data and materials
Not applicable.

Financial support and sponsorship
None.

Conflicts of interest
All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate
All patients gave their written informed consent for laparoscopic operative procedures. This study protocol was approved by the institutional ethics committee.

Consent for publication
Not applicable.

REFERENCES

1. Goh P, Tekant Y, Isaac J, Kum CK, Ngoi SS. The technique of laparoscopic Billroth II gastrectomy. Surg Laparosc Endosc 1992;2:258-60.
2. Kim W, Kim HH, Han SU, Kim MC, Hyung WJ, et al. Decreased morbidity of laparoscopic distal gastrectomy compared with open distal gastrectomy for stage I gastric cancer: short-term outcomes from a multicenter randomized controlled trial (KLASS-01). Ann Surg 2016;263:28-35.
3. Katia H, Mizusawa J, Katayama H, Takagi M, Yoshikawa T, et al. Short-term surgical outcomes from a phase III study of laparoscopy-assisted versus open distal gastrectomy with nodal dissection for clinical stage IA/IB gastric cancer: Japan Clinical Oncology Group Study JCOG0912. Gastric Cancer 2017;20:699-708.
4. Bandoh T, Shiraishi N, Yamashita Y, Terachi T, Hashizume M, et al. Endoscopic surgery in Japan: the 12th national survey (2012-2013) by the Japan Society for Endoscopic Surgery. Asian J Endosc Surg 2017;10:345-53.
5. Deng Y, Zhang Y, Guo TK. Laparoscopy-assisted versus open distal gastrectomy for early gastric cancer: a meta-analysis based on seven randomized controlled trials. Surg Oncol 2015;24:71-7.
6. Fujisaki M, Shinohara T, Hanyu N, Kawano S, Tanaka Y, et al. Laparoscopic gastrectomy for gastric cancer in the elderly patients. Surg Endosc 2016;30:1380-7.
7. Yoshida M, Koga S, Ishimaru K, Yamamoto Y, Matsuno Y, et al. Laparoscopy-assisted distal gastrectomy is feasible also for elderly patients aged 80 years and over: effectiveness and long-term prognosis. Surg Endosc 2017;31:4431-7.
8. Sugimoto M, Kinoshita T, Shibasaki H, Kato Y, Gotohda N, et al. Short-term outcome of total laparoscopic distal gastrectomy for overweight and obese patients with gastric cancer. Surg Endosc 2013;27:4291-6.
9. Son SY, Jung DH, Lee CM, Ahn SH, Ahn HS, et al. Laparoscopic gastrectomy versus open gastrectomy for gastric cancer in patients with body mass index of 30 kg/m2 or more. Surg Endosc 2015;29:2126-32.
10. Kim CH, Song KY, Park CH, Seo YJ, Park SM, et al. A comparison of outcomes of three reconstruction methods after laparoscopic distal gastrectomy. J Gastric Cancer 2015;15:46-52.
11. Beyan C, Beyan E, Kaptan K, Ifran A, Uzar AI. Post-gastrectomy anemia: evaluation of 72 cases with post-gastrectomy anemia. Hematology 2007;12:81-4.
12. Kitano S, Iso Y, Moriyama M, Sugimachi K. Laparoscopy-assisted Billroth I gastrectomy. Surg Laparosc Endosc 1994;4:146-8.
13. Hiki N, Fukunaga T, Tokunaga M, Ohyama S, Yamada K, et al. An effective duodenum bulb mobilization for extracorporeal Billroth I anastomosis of laparoscopic gastrectomy. J Gastrointest Surg 2009;13:230-5.
14. Kim JJ, Song KY, Chin HM, Kim W, Jeon HM, et al. Totally laparoscopic gastrectomy with various types of intracorporeal anastomosis using laparoscopic linear staplers: preliminary experience. Surg Endosc 2008;22:436-42.
15. Ohmura Y, Nishi H, Fukuda K, Mano M. Technical modification of laparoscopy-assisted distal gastrectomy. J Jp Soc Endosc Surg 2004;9:191-5. (in Japanese)
16. Kanaya S, Gomi T, Momoi H, Tamaki N, Isobe H, et al. Delta-shaped anastomosis in totally laparoscopic Billroth I gastrectomy: new technique of intraabdominal gastroduodenostomy. J Am Coll Surg 2002;195:284-7.
17. Okabe H, Obama K, Tsunoda S, Tanaka E, Sakai Y. Advantage of completely laparoscopic gastrectomy with linear stapled reconstruction: a long-term follow-up study. Ann Surg 2014:259:109-16.
18. Kim JJ, Song KY, Chin HM, Kim W, Jeon HM, et al. Totally laparoscopic gastrectomy with various types of intracorporeal anastomosis using laparoscopic linear staplers: preliminary experience. Surg Endosc 2008;22:436-42.
19. Ohmura Y, Kumano K, Watanabe S, Mitsuoka N, Watanabe T. A new intracorporeal anastomosis method in laparoscopic distal

gastrectomy. Billroth-I reconstruction by hemi-hand-sewn-technique. J Jp Soc Endosc Surg 2013;18:407. (in Japanese)
20. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-13.
21. Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma: 3rd English edition. Gastric Cancer 2011;14:101-12.
22. Tanimura S, Higashino M, Fukunaga Y, Takemura M, Nishikawa T, et al. Intracorporeal Billroth 1 reconstruction by triangulating stapling technique after laparoscopic distal gastrectomy for gastric cancer. Surg Laparosc Endosc Percutan Tech 2008;18:54-8.
23. Ikeda T, Kawano H, Hisamatsu Y, Ando K, Saeki H, et al. Progression from laparoscopic-assisted to totally laparoscopic distal gastrectomy: comparison of circular stapler (i-DST) and linear stapler (BBT) for intracorporeal anastomosis. Surg Endosc 2013;27:325-32.
24. Nishimura S, Oki E, Tsutsumi S, Tsuda Y, Sugiyama M, et al. Clinical significance of totally laparoscopic distal gastrectomy: a comparison of short-term outcomes relative to open and laparoscopic-assisted distal gastrectomy. Surg Laparosc Endosc Percutan Tech 2016;26:372-6.
25. Byun C, Cui LH, Son SY, Hur H, Cho YK, et al. Linear-shaped gastroduodenostomy (LSGD): safe and feasible technique of intracorporeal Billroth I anastomosis. Surg Endosc 2016;30:4505-14.
26. Schneider C, Cobb W, Scott J, Carbonell A, Myers K, et al. Rapid excess weight loss following laparoscopic gastric bypass leads to increased risk of internal hernia. Surg Endosc 2011;25:1594-8.
27. Kim CH, Song KY, Park CH, Seo YJ, Park SM, et al. A comparison of outcomes of three reconstruction methods after laparoscopic distal gastrectomy. Gastric Cancer 2015;15:46-52.
28. Komatsu S, Ichikawa D, Kubota T, Okamoto K, Shiozaki A, et al. Clinical outcomes and quality of life according to types of reconstruction following laparoscopy-assisted distal gastrectomy for gastric cancer. Surg Laparosc Endosc Percutan Tech 2015;25:69-73.
29. Okabe H, Obama K, Tsunoda S, Tanaka E, Sakai Y. Advantage of completely laparoscopic gastrectomy with linear stapled reconstruction: a long-term follow-up study. Ann Surg 2014;259:109-16.
30. Takiguchi S, Sekimoto M, Miyake Y, Fujiwara Y, Yasuda T, et al. Totally laparoscopic distal gastrectomy using the hand-sewn Billroth-I anastomotic technique: report of a case. Surg Today 2003;33:371-4.
31. Chen K, Wu D, Pan Y, Cai JQ, Yan JF, et al. Totally laparoscopic gastrectomy using intracorporeally stapler or hand-sewn anastomosis for gastric cancer: a single-center experience of 478 consecutive cases and outcomes. World J Surg Oncol 2016;14:115.
32. Matsuo K, Shimura H, Tanaka S, Nakano M, Hashimoto T, et al. Laparoscopic distal gastrectomy with intracorporeal handsewn Billroth-I anastomosis (ICHSA). Surg Endosc 2012;26:2981-7.
33. Koeda K, Chiba T, Noda H, Nishinari Y, Segawa T, et al. Intracorporeal reconstruction after laparoscopic pylorus-preserving gastrectomy for middle-third early gastric cancer: a hybrid technique using linear stapler and manual suturing. Langenbecks Arch Surg 2016;401:397-402.
34. Sakata S, Kabir S, Petersen D, Doudle M, Stevenson AR. Are we burying our heads in the sand? Preventing small bowel obstruction from the V-loc® suture in laparoscopic ventral rectopexy. Colorectal Dis 2015;17:O180-3.
35. Filser J, Reibetanz J, Krajinovic K, Germer CT, Dietz UA, et al. Small bowel volvulus after transabdominal preperitoneal hernia repair due to improper use of V-Loc barbed absorbable wire - do we always "read the instructions first"? Int J Surg Case Rep 2015;8:193-5.
36. Donnellan NM, Mansuria SM. Small bowel obstruction resulting from laparoscopic vaginal cuff closure with a barbed suture. J Minim Invasive Gynecol 2011;18:528-30.
37. Ser KH, Lee WJ, Lee YC, Chen JC, Su YH, et al. Experience in laparoscopic sleeve gastrectomy for morbidly obese Taiwanese: staple-line reinforcement is important for preventing leakage. Surg Endosc 2010;24:2253-9.
38. Inoue K, Michiura T, Fukui J, Mukaide H, Ozaki T, et al. Staple-line reinforcement of the duodenal stump with intracorporeal Lembert's sutures in laparoscopic distal gastrectomy with Roux-en-Y reconstruction for gastric cancer. Surg Laparosc Endosc Percutan Tech 2016;26:338-42.
39. Kim MC, Kim SY, Kim KW. Laparoscopic reinforcement suture (LARS) on staple line of duodenal stump using barbed suture in laparoscopic gastrectomy for gastric cancer: a prospective single arm phase II study. J Gastric Cancer 2017;17:354-62.
40. Kim MG, Kawada H, Kim BS, Kim TH, Kim KC, et al. A totally laparoscopic distal gastrectomy with gastroduodenostomy (TLDG) for improvement of the early surgical outcomes in high BMI patients. Surg Endosc 2011;25:1076-82.
41. Lee HH, Song KY, Lee JS, Park SM, Kim JJ. Delta-shaped anastomosis, a good substitute for conventional Billroth I technique with comparable long-term functional outcome in totally laparoscopic distal gastrectomy. Surg Endosc 2015;29:2545-52.
42. Jeong O, Jung MR, Park YK, Ryu SY. Safety and feasibility during the initial learning process of intracorporeal Billroth I (delta-shaped) anastomosis for laparoscopic distal gastrectomy. Surg Endosc 2015;29:1522-9.
43. Park KB, Kwon OK, Yu W, Jang BC. Body composition changes after totally laparoscopic distal gastrectomy with delta-shaped anastomosis: a comparison with conventional Billroth I anastomosis. Surg Endosc 2016;30:4286-93.

Mini-invasive Surgery

Review

Open Access

Laparoscopic ablative techniques

Tommaso Silvestri, Bernardino de Concilio, Guglielmo Zeccolini, Antonio Celia

Urology Unit, "San Bassiano" Hospital, ULSS7 Pedemontana, Bassano del Grappa, VI 36061, Italy.

Correspondence to: Dr. Tommaso Silvestri, Urology Unit, "San Bassiano" Hospital, ULSS7 Pedemontana, Bassano del Grappa, VI 36061, Italy. E-mail: tommaso.silve@gmail.com

How to cite this article: Silvestri T, de Concilio B, Zeccolini G, Celia A. Laparoscopic ablative techniques. *Mini-invasive Surg* 2019;3:5. http://dx.doi.org/10.20517/2574-1225.2018.67

Received: 30 Nov 2018 **First Decision:** 30 Nov 2018 **Revised:** 28 Jan 2019 **Accepted:** 11 Feb 2019 **Published:** 4 Mar 2019

Science Editor: Richard Lawrence John Naspro **Copy Editor:** Cui Yu **Production Editor:** Huan-Liang Wu

Abstract
Ablative techniques (AT) offer a combination of nephron-sparing and minimally invasive approaches. AT include different options and cryoablation (CA) and radiofrequency ablation (RFA) have been relatively safe and traditionally can be either performed laparoscopically or percutaneously. CA and RFA have emerged as a leading option for renal ablation, and compared with surgical techniques they offer benefits in preserving renal function with fewer complications, shorter hospitalization times, and allow for quicker convalescence. A mature dataset exists at this time, with intermediate and long-term follow up data available. Generally, laparoscopic access was the first technique used in the past, and typically for anterior and lateral mass. Afterwards, with the improvements in imaging and percutaneous techniques, laparoscopic approaches are progressively decreased and currently limited in few lesions and in relation with the surgeon's and center's experience. Nevertheless, laparoscopic CA and RFA could be useful techniques and currently, recommendations as a first-line therapy are made at this time in limited populations, including elderly patients, patients with multiple comorbidities, and those with imperative indications of a nephron sparing surgery. As more data emerge on oncologic efficacy, and technical experience continue to improve, the application of AT will likely be extended in future treatment guidelines and laparoscopic approaches will be a valid option in the era of tailored therapy.

Keywords: Laparoscopic kidney cryoablation, small renal masses, laparoscopic ablative techniques

INTRODUCTION

Although surgery remains the definitive recommended treatment of small renal masses (SRM), ablative techniques (AT) have emerged recently, particularly for tumors < 4 cm, and for those patients who cannot undergo surgery or with imperative indications of nephron sparing surgery (NSS). AT included: cryoablation (CA), radiofrequency ablation (RFA), microwave ablation, laser thermal ablation, and high-intensity focused ultrasound. Historically CA and RFA have been introduced first worldwide, and recently longer-term outcomes for these techniques have become available[1-5]. They can be performed either laparoscopically or percutaneously with good results in spite of higher reported recurrence and retreatment rates when compared to partial nephrectomy (PN)[6,7].

Historically laparoscopic cryoablation (LCA) has been the most popular approach for performing renal CA[8,9]. Conversely, laparoscopic techniques for RFA have been used less in favor of percutaneous RFA, successfully performed under ultrasound, CT, or MRI guidance[10].

Anyway, over the years, also LCA have seen gradual decrease in utilization as image-guided techniques have improved greatly and currently American Urological Association (AUA) guidelines recommend also percutaneous cryoablation (PCA) as the best possible choice[11,12].

In this review, we focused on LCA in relation to its major diffusion and availability worldwide, particularly with SRMs with diameter > 3 cm in comparison to RFA ablation.

CRYOBIOLOGY AND AVAILABLE SYSTEMS

The principles of cryotherapy, including the mechanism of cell injury and cell death, have been well studied[13-15]. The main mechanism of cryo-toxicity is the induction of coagulative necrosis in targeted areas. The key factors involved in freezing injury include direct mechanical shock, osmotic shock, and cellular hypoxia. Mechanism of action includes protein denaturation via dehydration, transfer of water from the intracellular space to the extracellular space, rupture of cell membranes from ice crystal expansion, a toxic concentration of cellular constituents, thermal shock from rapid super-cooling, slow thawing, vascular stasis, and increased apoptosis. The delayed or indirect destructive effects of cryotherapy continue primarily because of vasculature disruption, resulting in tissue hypoxia and vascular thrombosis[16].

Stephenson started the first cases of LCA in a canine model and the transition to the second and the third generation of cryoprobes have permitted the use of ultra-thin probes, leading to rapid diffusion of the technique[17].

Currently, the available cryogenic systems, that use pressurized argon gas as the source of freezing, are: the SeedNet® System, the Visual-ICE® System (Galil Medical Inc., BTG, UK) and the CRYOcare™ System (Endocare Inc., USA). These systems are used to create a conformal freezing pattern up to 25-17 gauge (2.4-1.47 mm) cryoprobe.

ADVANTAGES AND DISADVANTAGES OF LCA

Currently, considerations such as tumor location and complexity as well as patient morbidity must be made when selecting a modality and approach. With initial experience, LCA was utilized primarily for anteriorly and laterally located tumors, and PCA was the method of choice for posterior tumors[18].

The main advantages of LCA are[19]: (1) placement of probes under direct visualization; (2) real-time US-guided placement of probes and monitoring of procedure (freezing and tissue viability); (3) easier treatment of anterior or hilar tumors; (4) major ability to displace colon or other organs or nearby structures whenever necessary for a safer ablation.

However, increasing experience during the last two decades has demonstrated that although technically challenging, also anterior tumors can be successfully treated via the percutaneous route, often with adjunctive displacement maneuvers[20].

Hence, the main disadvantages of LCA are[21]: (1) general anesthesia is required (it is not an outpatient procedure); (2) a higher rate of complication in comparison to PCA; (3) less rate of pain control and worst cosmetic in comparison to PCA; (4) higher cost rate in comparison to PCA.

PATIENT SELECTION AND INDICATION FOR LCA

The indications for LCA procedure are the same of all ablative techniques and limited to patients with contraindications to surgical extirpative therapy for comorbidities, advanced age, imperative indications for NSS or have a strong preference for nonsurgical management[1].

Currently, the 2017 AUA guidelines recommend consideration of ablation as an alternative to PN for cT1a renal lesions less than 3 cm in size[12]. Otherwise, the European Association of Urology guidelines do not recommend an upper limit of diameter[1]. Today there are data supporting CA for cT1b lesions, but in view of higher recurrence rate and complications should be reserved for patients with imperative indications[22].

The location of the mass is a major factor in determining if the mass should be ablated laparoscopically or percutaneously, but the most important factor is the surgeons' experience.

PROCEDURE AND TECHNIQUES

A transperitoneal approach is generally used for anterior and anteromedial tumors, whereas a retroperitoneal approach permits access to posterior and posterolateral tumors[23,24].

Effective cryosurgical tissue injury depends on: (1) excellent monitoring of the process; (2) fast cooling to a lethal temperature; (3) slow thawing; (4) repetition of the freeze-thaw cycle (2 times); (5) freeze cycle length of 8-10 min is commonplace in literature; (6) thaw cycle at least 5-8 min.

Critical factors of the procedure are: (1) placement of the cryoneedles; (2) reach and center a lethal temperature in the central part of the lesion with an ice ball margin of at least 5 mm to avoid a residual or an untreated tumor[25]; (3) iceball imaging as mentioned above.

Key factors to obtain specific success of LCA: (1) take your time to make a better exposure of the renal lesion: the real key is finding the better position for the cryoneedles; (2) triangle disposition of the cryoneedles by putting the different probes at least 10 mm of distance each other; (3) the using of hemostatic agents to prevent or treat bleeding; (4) high experience of the surgeon in NSS: in some rare case, it could be necessary to put sutures.

The number and size of the cryoprobes placed depends on the size and configuration of the mass. Generally, one probe is needed for each centimeter of tumor diameter to be treated. Recently, the use of multiple smaller probe has increased the variety and size of tumors that can be treated. When mobilization of the kidney is feasible, US probes are placed on the contralateral side of the kidney for visualization. Attention should be reserved for relative warming of the ablation zone by large central vessels: the thermal sink effect might be a limit to achieve the lethal temperature.

Laparoscopic cryoablation

Pneumoperitoneum and trocars placement

General anesthesia is required. The patient is placed in a standard flank position. Pneumoperitoneum is usually achieved in two ways: using the open Hasson technique or by placing a Veress needle in the umbilicus of the patient who have not had previous abdominal surgery or in the upper quadrant (left

Figure 1. Ultrasound evaluation of the lesion

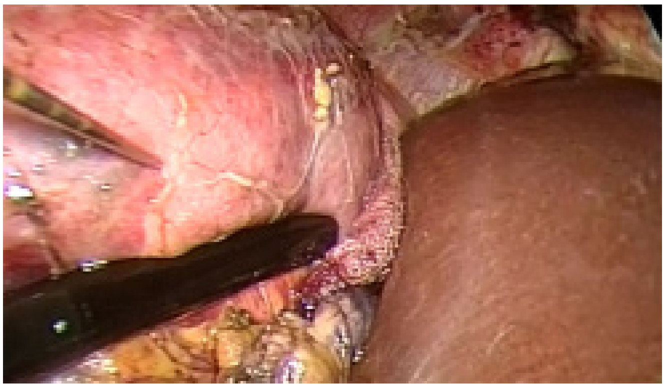


Figure 2. Under ultrasound evaluation a 1.5 cryoprobe is inserted into the mass

or right). Therefore, at least 3 trocars are placed as for laparoscopic nephrectomy. An extra 5 mm port is inserted as per requirement for suction or retraction.

Renal dissection and US

Visceral rotation and reflection of the colon is performed, with a gently kidney mobilization and exposition. Generally, the fat overlying the lesion should be removed, and the tumor region should be carefully dissected. Intraoperative US is performed through the 12-mm trocar. The renal blood vessels are carefully dissected and secured using vessel-loop. Therefore, a Tru-Cut needle biopsy is performed.

Cryoprobes placement

Under US evaluation a 1.5-1.7 mm cryoprobe is inserted into the mass transabdominally through a skin puncture and placed into the lesion. The probe is anchored by freezing the tumor 1-2 mm from the probe [Figures 1 and 2]. Generally, a triangulation of one or two additional probes around the first probe could be performed in relation to the size of the lesion. The "killing zone" temperature must be -20 °C or below.

CA cycles are performed as usual, monitored by the US [Figure 3]. At the end of the second cycles the needles are gently removed [Figure 4] and hemostatic agents such as fibrin glue (FloSeal - Baxter, Illinois, USA) is then applied to the site. The Gerota's fascia is closed and a non-suction drain is put into the peritoneal cavity. All ports are closed in the usual fashion.

DISCUSSION

CA and RFA could be an available treatment option for SRMs in selected patients. Quality of the available data and lack of level I evidence do not allow definitive conclusions regarding morbidity and oncological

Figure 3. First freezing cycle

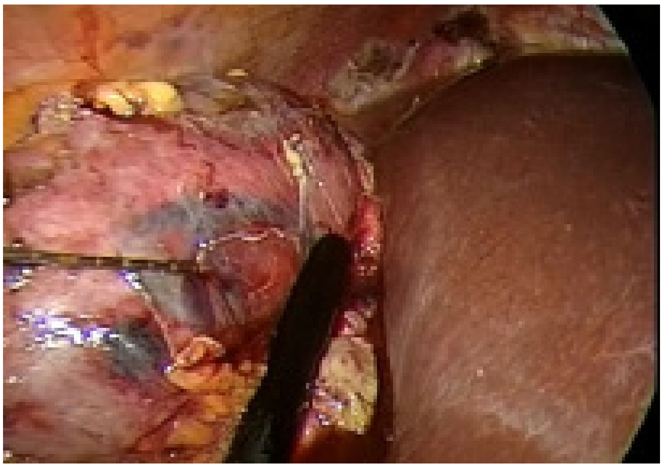


Figure 4. Under ultrasound evaluation the needle is carefully removed

outcomes of CA and RFA. Generally, low-quality studies suggest a higher local recurrence rate for thermal ablation therapies compared to PN. Nevertheless, in currently comparative series no significant differences were reported for OS, CSS, or RFS between RFA and CA[1]. Considering PN as a comparator, recently a meta-analysis reported similar complication rates and postoperative functional outcomes between RFA and PN[26]. The local tumor recurrence rate was higher in the RFA group than in the PN group but there was no difference regarding the occurrence of distant metastasis. Although the majority of series are retrospective and with different follow-ups, recent studies with a long-term follow-up showed that no statistical difference was found in the 5-year OS, CCS, DFS, and local RFS of RCC patients between RFA treatment and PN treatment [Table 1][27]. Johnson *et al.*[28] presented data of SRMs with a diameter less than 3 cm with a median follow up of more than 6 years and a subgroup of patients with a minimum 10-year follow up with imaging. The 6-year disease-free recurrence rate of 89% is consistent with the prior published data. This data could suggest that for lesions less than 3 cm RFA oncologic outcomes were similar to efficacy rates of extirpative surgery[28]. Regarding CA different studies compared open, laparoscopic or robotic PN with PCA or LCA [Table 2]. Oncological outcomes were mixed, not all studies reported all outcomes listed, and some were small and included benign tumors. Globally no study showed an oncological benefit for cryoablation over PN.

Overall, studies comparing renal function before and after CA and PN suggest a degree of functional decline following CA similar to PN. However, in most cases, this is not clinically significant because baseline characteristics of lesions, function and the patient's comorbidities were different. No significant difference

Table 1. Contemporary comparative series comparing radiofrequency with partial nephrectomy and/or radical nephrectomy with oncological outcomes

Author	Year	End point	Therapy	Number of patients	Study design	Follow up (months)	Outcomes
Arnoux *et al*.[43]	2013	Survival, recurrence, complications	RFA PN	36 14	Prospective	22 22	No recurrences in RFA and PN No other oncological outcomes
Bensalah *et al*.[44]	2007	Survival, recurrence, complications	RFA PN	46 56	Retrospective	Mean 15	97% RFS, 100% CSS
Bird *et al*.[45]	2009	Survival, recurrence, complications, renal function	RFA PN	36 33	Retrospective	12 27	No recurrences No deaths
Chang *et al*.[46]	2015	Survival, recurrence, complications, renal function	RFA PN	53 53	Retrospective	68 69	No recurrences No deaths
Chang *et al*.[47]	2015	Survival, recurrence, complications, renal function	RFA PN	64 57	Retrospective	66 70 5-year outcome	85.5%, 92.6%, 81.0% (OS, CSS, DFS) 96.6%, 96.6%, 89.7% (OS, CSS, DFS)
Ji *et al*.[48]	2016	Recurrence, complications	RFA PN	105 74	Retrospective	78 82 5-year outcome	93.3%, 98.0%, 97.1% (OS, CSS, DFS) 94.6%, 98.5%, 97.3% (OS, CSS, DFS)
Kim *et al*.[49]	2015	Survival, recurrence, complications, renal function	RFA PN	27 27	Retrospective	17 11	1 recurrence 2 recurrence
Liu *et al*.[50]	2017	Survival, recurrence, complications, renal function	RFA PN	93 120	Prospective database	78	84.9%, 82.8% (OS, DFS) 88.3%, 88.8% (OS, DFS) Differences > in lesions > 4 cm
Lucas *et al*.[51]	2008	Recurrence, renal function	RFA PN RN	86 85 71	Retrospective	40 44 26	6 recurrence 2 recurrence 0 recurrence
Olweny *et al*.[52]	2012	Recurrence	RFA PN	37 37	Prospective	78 73 5-year	97.2%, 89.2%, 97%, 91.7% (OS, DFS, CSS, local RFS) 100%, 89.2%, 100%, 94.6% (OS, DFS, CSS, local RFS)
Pantelidou *et al*.[53]	2016	Recurrence	RFA PN (robotic)	63 63	Retrospective	48 18	6 Local recurrence, 3 Met 1 Local Recurrence, 1 Met DFS was not significantly different between the two groups (HR = 0.84, 95%CI: 0.19-3.4; *P* = 0.80
Raman *et al*.[54]	2010	Recurrence, renal function	RFA PN	47 42	Retrospective	18 30	5 recurrence 3 recurrence
Stern *et al*.[55]	2007	Recurrence, complications	RFA PN	40 37	Retrospective	-	2 recurrence, 93.4% (DFS) 1 recurrence, 95.8% (DFS)
Sung *et al*.[56]	2012	Recurrence, complications, renal function	RFA PN	40 110	Prospective	37 37 3-year	94.7% (RFS) 98.9% (RFS)
Takaki *et al*.[57]	2010	Recurrence, complications, renal function	RFA PN RN	51 10	Retrospective	34 26 40 5-year	75.0%, 100%, 98.0% (OS, RCC-rS, DFS) 100%, 100%, 75.0% (OS, RCC-rS, DFS) 100%, 100%, 95.0% (OS, RCC-rS, DFS)

RFA: radiofrequency; PN: partial nephrectomy; RN: radical nephrectomy; OS: overall survival; CSS: cancer-specific survival; DFS: disease-free survival; RFS: recurrence-free survival; RCC: renal cell carcinoma; RCC-rS: renal cell carcinoma-related survival

was found between LCA and PCA in renal function outcomes in the two largest comparative studies published so far[29-31].

The reported overall rates of complications for CA procedures range from 7.8% to 20%[30]. The overall published complication rates for PCA (7.8%-12.9%) were lower than the rates for LCA (15%-20%)[30,32].

Table 2. Contemporary comparative series comparing cryoablation with different nephron sparing treatment options with oncological outcomes

Author	Year	End point	Therapy	Number of patients	Study design	Follow up (months)	Outcomes
Kim *et al*.[58]	2014	Survival, recurrence, complications, renal function	PCA LCA	118 145	Prospective evaluation	38 71.4	17%, 86.3%, 86.3% (RR, OS, RFS) 23%, 79.3%, 85.5% (RR, OS, RFS)
El Dib *et al*.[59]	2012	Survival, recurrence, complications	CA RFA	457 426	Retrospective	17.9 18.1	89% CE 90% CE
Atwell *et al*.[60]	2013	Survival, recurrence, complications,	PCA RFA	163 222	Retrospective	1.8 36 (mean)	2.8%, 95.6% (RR, RFS) 3.2%, 97-2% (RR, RFS)
Tanagho *et al*.[61]	2013	Survival, recurrence, complications, renal function	LCA/PCA RPN	267 233	Retrospective	39.8 21.9	12.7%, 83.1%, 96.4%, 77.1% (RR, DFS, CSS, OS) 0%, 100%, 100%, 91.7% (RR, DFS, CSS, OS)
Guillotreau *et al*.[62]	2012	Survival, recurrence, complications, renal function	RPN LCA	210 226	Retrospective	4.8 44.5 (mean)	0% (RR) 11% (RR)
Klatte *et al*.[63] (meta-analysis)	2014	Recurrence, complications	LCA LPN/RPN	-	Retrospective	-	9.4% *vs.* 0.4% Metastasis 4.4% *vs.* 0.4%
Thompson *et al*.[64]	2015	Survival, recurrence, complications, renal function	CA RFA PN	187 180 1,057	Retrospective	1.9 3.6 60	3%, 98%, 100%, 88% (RR, RFS, MSF, OS) 5%, 98%, 93%, 82% (RR, RFS, MSF, OS) 36%, 98%, 99%, 95% (RR, RFS, MSF, OS)

RFA: radiofrequency; PN: partial nephrectomy; RN: radical nephrectomy; LCA: laparoscopic cryoablation; PCA: percutaneous cryoablation; RPN: robotic partial nephrectomy; LPN: laparoscopic partial nephrectomy; CE: cancer extirpation rate; RR: recurrence rate; OS: overall survival; CSS: cancer-specific survival; DFS: disease-free survival; MSF: metastasis-free survival; RFS: recurrence-free survival

RFA seems to be no different in Clavien complication rate in comparison to CA, however, Goel *et al*.[33] founded a lower rate of complication for CA compared with RFA, probably because the freezing-induced injury is less destructive than heat-induced one[33,34]. Generally, the most common complications during the procedure or post-operative are bleeding and rupture of the iceball.

There is no consensus on the definition of recurrence after treatments for SRM and particularly after AT. Local recurrences mostly occur at the site of the primary treatment within the kidney. Conversely, extra-renal local recurrences are rare[35,36]. Today, most analyses have shown lower specific cancer mortality for PN compared to non-surgical treatments. In general, local recurrence rates after CA are higher than after surgery (2%-11% *vs*. 1%-2%)[37,38].

Ideally, histopathological confirmation and re-biopsy of previously treated lesions would improve data of recurrent or residual disease. Conversely, in the literature, the majority of reports relied on radiographic evidence of enhancement to define both residual and recurrent disease. PCA had a higher rate of residual disease/primary treatment failure in comparison to LCA: PCA residual disease seems to be more frequent and to occur earlier than LCA, even if the length of follow-up between groups is difference (approximately 14 months longer for LCA)[29].

Zargar *et al*.[30] found no significant difference in OS or RFS at 5 years between PCA and LCA. Conversely, in other studies seems that a lower rate of patients in the LCA group experienced a local recurrence as compared with the rate of PCA group[30].

Factors that might have contributed to the differences in residual and recurrent disease between PCA and LCA are the size of the lesion, the anatomical location, and the probe size and number (in LCA tendency to use wider probes).

To date, cost issues have not played a major role in driving decisions among treatment options. However, as health care expenses continue to rise, cost concerns are likely to play an ever-increasing role. Different studies have assessed cost, but their results differ based on some key postulated differences such as the period of observation, the definition of success and complication rates, different health-care systems, and also whether those with benign biopsies should be treated or followed up.

Chang *et al*.[39] analyzed the cost-effectiveness of all NSS options for SRMs and concluded that for healthier younger patients (aged 65 years with a < 2 cm lesion or aged 75 years with a 3-4 cm lesion), immediate surgery represents the optimal NSS option with the best incremental cost-effectiveness ratio. Surveillance with possible delayed PCA was a cost-effective option for older patients or those with increased perioperative mortality risk. Observation represented the best strategy for patients who are poor surgical candidates and who had a life expectancy < 3 year. It is worth noting that laparoscopic AT was not cost effective in any scenario regardless of age, comorbidities, and tumor size[39]. Bhan *et al*.[40], comparing RFA, CA, and observation for the treatment of SRMs, established that active surveillance with no initial biopsy and with subsequent PCA in case of disease progression was more cost-effective than immediate CA with or without biopsy and other observation options. They found that in terms of cost-effectiveness, all CA techniques were superior to RFA procedures owing to higher rates of retreatment for RFA[40]. Reporting direct comparative costs of LCA and PCA, LCA was significantly more expensive than PCA (3.5 times on average)[41]. However, these values need to be adjusted for patient and tumor characteristics to better gauge the cost incurred by each approach. Ideally, we have to consider also the cost of readmission, ongoing surveillance, and retreatment into the analysis.

Furthermore, Link *et al*.[42] analyzed the cost-effectiveness of different treatment options, particularly comparative analysis between PCA and laparoscopic treatment options. The PCA was 2.2-2.7 times less costly than the other options and resulted in a cost savings of $3625 to $5155 per case. For Open PN, Laparoscopic PN, and LCA, the operative time and hospitalization accounted for 69%-91% of the cost. The Laparoscopic PN and LCA were cost advantageous over PCA only when more than five cryoprobes were used during the percutaneous procedure[42].

CONCLUSION

AT seems to be a valid treatment option that could reduce complications and general impairment of classical surgical procedures. Finding the perfect candidate for AT is challenging due to the lack of objective criteria in the literature and of standardized techniques. Notably, the percutaneous approach seems to have lower complications rate than laparoscopic approach, especially in CA, and it can offer shorter hospital stay and faster recovery, which can be particularly appealing in an era of cost restriction in healthcare. Afterward, in the era of a multidisciplinary approach and tailored therapy, LCA could be a useful instrument to manage lesions for which PCA might have a failure or could be difficult and unfeasible. Hence, LCA should be collocated in a middle position for the management of SRM between PCA and NSS. Nevertheless, the application of this approach is dictated by the available technology and specific expertise of each center.

DECLARATIONS

Authors' contributions

Made contributions to conception and design of the study/review, performed data analysis and interpretation: Silvestri T, Celia A

Made substantial contributions to conception and design of the study/review, performed an entire revision of data analysis, re-interpretation and the revision for editors: Silvestri T

Performed data acquisition: de Concilio B, Zeccolini G

Availability of data and materials
Not applicable.

Financial support and sponsorship
None.

Conflicts of interest
All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

REFERENCES

1. Ljungberg B, Bensalah K, Canfield S, Dabestani S, Hofmann F, et al. EAU guidelines on renal cell carcinoma: 2014 update. Eur Urol 2015;67:913-24.
2. Klatte T, Shariat SF, Remz M. Systematic review and meta-analysis of perioperative and oncologic outcomes of laparoscopic cryoablation versus laparoscopic partial nephrectomy for the treatment of small renal tumors. J Urol 2014;191:1209-17.
3. Schiffman M, Moshfegh A, Talenfeld A, Del Pizzo JJ. Laparoscopic renal cryoablation. Semin Intervent Radiol 2014;31:64-9.
4. Caputo PA, Ramirez D, Zargar H, Akca O, Andrade HS, et al. Laparoscopic cryoablation for renal cell carcinoma: 100-month oncologic outcomes. J Urol 2015;194:892-6.
5. Larcher A, Fossati N, Mistretta F, Lughezzani G, Lista G, et al. Long-term oncologic outcomes of laparoscopic renal cryoablation as primary treatment for small renal masses. Urol Oncol 2015;33:22.e1-9.
6. Johnson S, Pham KN, See W, Begun FP, Langenstroer P. Laparoscopic cryoablation for clinical stage T1 renal masses: long-term oncologic outcomes at the Medical College of Wisconsin. Urology 2014;84:613-8.
7. Guillotreau J, Haber GP, Autorino R, Miocinovic R, Hillyer S, et al. Robotic partial nephrectomy versus laparoscopic cryoablation for the small renal mass. Eur Urol 2012;61:899-904.
8. Long CJ, Kutikov A, Canter DJ, Egleston BL, Chen DY, et al. Percutaneous vs surgical cryoablation of the small renal mass: is efficacy compromised? BJU Int 2011;107:1376-80.
9. Aron M, Gill IS. Minimally invasive nephron-sparing surgery (MINSS) for renal tumours. Part II: probe ablative therapy. Eur Urol 2007;51:348-57.
10. Mahnken AH, Günther RW, Tacke J. Radiofrequency ablation of renal tumors. Eur Radiol 2004;14:1449-55.
11. Bandi G, Hedican SP, Nakada SY. Current practice patterns in the use of ablation technology for the management of small renal masses at academic centers in the United States. Urology 2008;71:113-7.
12. Campbell S, Uzzo RG, Allaf ME, Bass EB, Cadeddu JA, et al. Renal mass and localized renal cancer: AUA guideline. J Urol 2017;198:520-9.
13. Baust J, Gage AA, Ma H, Zhang CM. Minimally invasive cryosurgery--technological advances. Cryobiology 1997;34:373-84.
14. Gonder MJ, Soanes WA, Smith V. Experimental prostate cryosurgery. Invest Urol 1964;1:610-9.
15. Soanes WA, Gonder MJ, Shulman S. Apparatus and technique for cryosurgery of the prostate. J Urol 1966;96:508-11.
16. Hoffmann NE, Bischof JC. The cryobiology of cryosurgical injury. Urology 2002;60:40-9.
17. Stephenson RA, King DK, Rohr LR. Renal cryoablation in a canine model. Urology 1996;47:772-6.
18. Okhunov Z, Shapiro EY, Moreira DM, Lipsky MJ, Hillelsohn J, et al. R.E.N.A.L. nephrometry score accurately predicts complications following laparoscopic renal cryoablation. J Urol 2012;188:1796-800.
19. da Silva RD, Jaworski P, Gustafson D, Nogueira L, Kang F, et al. How I do it: laparoscopic renal cryoablation (LRC). Can J Urol 2014;21:7574-7.
20. Schmit GD, Atwell TD, Leibovich BC, Callstrom MR, Kurup AN, et al. Percutaneous cryoablation of anterior renal masses: technique, efficacy, and safety. Am J Roentgenol 2010;195:1418-22.
21. Zondervan PJ, Buijs M, de la Rosette JJ, van Delden O, van Lienden K, et al. Cryoablation of small kidney tumors. Int J Surg 2016;36:533-40.
22. Caputo PA, Zargar H, Ramirez D, Andrade HS, Akca O, et al. Cryoablation versus partial nephrectomy for clinical T1b renal tumors: a matched group comparative analysis. Eur Urol 2017;71:111-7.
23. Weld KJ, Figenshau RS, Venkatesh R, Bhayani SB, Ames CD, et al. Laparoscopic cryoablation for small renal masses: three-year follow-up. Urology 2007;69:448-51.

24. Gill IS, Novick AC, Soble JJ, Sung GT, Remer EM, et al. Laparoscopic renal cryoablation: initial clinical series. Urology 1998;52:543-51.
25. Allen BC, Remer EM. Percutaneous cryoablation of renal tumors: patient selection, technique, and postprocedural imaging. Radiographics 2010;30:887-900.
26. Pan XW, Cui XM, Huang H, Huang Y, Li L, et al. Radiofrequency ablation versus partial nephrectomy for treatment of renal masses: a systematic review and meta-analysis. Kaohsiung J Med Sci 2015;31:649-58.
27. Olweny EO, Park SK, Tan YK, Best SL, Trimmer C, et al. Radiofrequency ablation versus partial nephrectomy in patients with solitary clinical T1a renal cell carcinoma: comparable oncologic outcomes at a minimum of 5 years of follow up. Eur Urol 2012;61:1156-61.
28. Johnson BA, Sorokin I, Cadeddu JA. Ten-year outcomes of renal tumor radio frequency ablation. J Urol 2019;201:251-8.
29. Pessoa RR, Autorino R, Laguna MP, Molina WR, Gustafson D, et al. Laparoscopic versus percutaneous cryoablation of small renal mass: systematic review and cumulative analysis of comparative studies. Clin Genitourin Cancer 2017;15:513-9.e5.
30. Zargar H, Atwell TD, Cadeddu JA, de la Rosette JJ, Janetschek G, et al. Cryoablation for small renal masses: selection criteria, complications, and functional and oncologic results. Eur Urol 2016;69:116-28.
31. Kim EH, Tanagho YS, Saad NE, Bhayani SB, Figenshau RS. Comparison of laparoscopic and percutaneous cryoablation for treatment of renal masses. Urology 2014;83:1081-7.
32. Atwell TD, Vlaminck JJ, Boorjian SA, Kurup AN, Callstrom MR, et al. Percutaneous cryoablation of stage T1b renal cell carcinoma: technique considerations, safety, and local tumor control. J Vasc Interv Radiol 2015;26:792-9.
33. Goel RK, Kaouk JH. Probe ablative treatment for small renal masses: cryoablation vs. radio frequency ablation. Curr Opin Urol 2008;18:467-73.
34. Atwell TD, Schmit GD, Boorjian SA, Mandrekar J, Kurup AN, et al. Percutaneous ablation of renal masses measuring 3.0 cm and smaller: comparative local control and complications after radiofrequency ablation and cryoablation. AJR Am J Roentgenol 2013;200:461-6.
35. Adamy A, Chong KT, Chade D, Costaras J, Russo G, et al. Clinical characteristics and outcomes of patients with recurrence 5 years after nephrectomy for localized renal cell carcinoma. J Urol 2011;185:433-8.
36. Du Y, Grüllich C, Hadaschik B, Hatiboglu G, Hohenfellner M, et al. Local recurrence after curative surgical treatment of renal cell cancer: a study of 91 patients. Clin Genitourin 2016;14:e379-85.
37. Guillotreau J, Haber GP, Autorino R. Robotic partial nephrectomy versus laparoscopic cryoablation for the small renal mass. Eur Urol 2012;61:899-904.
38. Capogrosso P, Capitanio U, La Croce G, Nini A, Salonia A, et al. Follow-up after treatment for renal cell carcinoma: the evidence beyond the guidelines. Eur Urol Focus 2016;1:272-81.
39. Chang SL, Cipriano LE, Harshman LC, Garber AM, Chung BI. Cost-effectiveness analysis of nephron sparing options for the management of small renal masses. J Urol 2011;185:1591-7.
40. Bhan SN, Pautler SE, Shayegan B, Voss MD, Goeree RA, et al. Active surveillance, radiofrequency ablation, or cryoablation for the nonsurgical management of a small renal mass: a cost-utility analysis. Ann Surg Oncol 2013;20:3675-84.
41. Badwan K, Maxwell K, Venkatesh R, Figenshau RS, Brown D, et al. Comparison of laparoscopic and percutaneous cryoablation of renal tumors: a cost analysis. J Endourol 2008;22:1275-7.
42. Link RE, Permpongkosol S, Gupta A, Jarrett TW, Solomon SB, et al. Cost analysis of open, laparoscopic, and percutaneous treatment options for nephron-sparing surgery. J Endourol 2006;20:782-9.
43. Arnoux V, Descotes JL, Sengel C, Terrier N, Rambeaud JJ, et al. Perioperative outcomes and mid-term results of radiofrequency ablation and partial nephrectomy in indications of renal tumor treatment and imperative nephron-sparing procedure. Prog Urol 2013;23:99-104.
44. Bensalah K, Zeltser I, Tuncel A, Cadeddu J, Lotan Y. Evaluation of costs and morbidity associated with laparoscopic radiofrequency ablation and laparoscopic partial nephrectomy for treating small renal tumours. BJU Int 2008;101:467-71.
45. Bird VG, Carey RI, Ayyathurai R, Bird VY. Management of renal masses with laparoscopic-guided radiofrequency ablation versus laparoscopic partial nephrectomy. J Endourol 2009;23:81-8.
46. Chang X, Liu T, Zhang F, Ji C, Zhao X, et al. Radiofrequency ablation versus partial nephrectomy for clinical T1a renal-cell carcinoma: long-term clinical and oncologic outcomes based on a propensity score analysis. J Endourol 2015;29:518-25.
47. Chang X, Zhang F, Liu T, Ji C, Zhao X, et al. Radio frequency ablation versus partial nephrectomy for clinical T1b renal cell carcinoma: long-term clinical and oncologic outcomes. J Urol 2015;193:430-5.
48. Ji C, Zhao X, Zhang S, Liu G, Li X, et al. Laparoscopic radiofrequency ablation versus partial nephrectomy for cT1a renal tumors: long-term outcome of 179 patients. Urol Int 2016;96:345-53.
49. Kim SH, Lee ES, Kim HH, Kwak C, Ku JH, et al. A propensity-matched comparison of perioperative complications and of chronic kidney disease between robot-assisted laparoscopic partial nephrectomy and radiofrequency ablative therapy. Asian J Surg 2015;38:126-33.
50. Liu N, Huang D, Cheng X, Chong Y, Wang W, et al. Percutaneous radiofrequency ablation for renal cell carcinoma vs. partial nephrectomy: comparison of long-term oncologic outcomes in both clear cell and non-clear cell of the most common subtype. Urol Oncol 2017;35:530.e1-16.
51. Lucas SM, Stern JM, Adibi M, Zeltser IS, Cadeddu JA, et al. Renal function outcomes in patients treated for renal masses smaller than 4 cm by ablative and extirpative techniques. J Urol 2008;179:75-80.
52. Olweny EO, Park SK, Tan YK, Best SL, Trimmer C, et al. Radiofrequency ablation versus partial nephrectomy in patients with solitary clinical T1a renal cell carcinoma: comparable oncologic outcomes at a minimum of 5 years of follow-up. Eur Urol 2012;61:1156-61.
53. Pantelidou M, Challacombe B, McGrath A, Brown M, Ilyas S, et al. Percutaneous radiofrequency ablation versus robotic-assisted partial nephrectomy for the treatment of small renal cell carcinoma. Cardiovasc Interv Radiol 2016;39:1595-603.
54. Raman JD, Raj GV, Lucas SM, Williams SK, Lauer EM, et al. Renal functional outcomes for tumours in a solitary kidney managed by ablative or extirpative techniques. BJU Int 2010;105:496-500.

55. Stern JM, Svatek R, Park S, Hermann M, Lotan Y, et al. Intermediate comparison of partial nephrectomy and radiofrequency ablation for clinical T1a renal tumours. BJU Int 2007;100:287-90.
56. Sung HH, Park BK, Kim CK, Choi HY, Lee HM. Comparison of percutaneous radiofrequency ablation and open partial nephrectomy for the treatment of size- and location-matched renal masses. Int J Hyperthermia 2012;28:227-34.
57. Takaki H, Yamakado K, Soga N, Arima K, Nakatsuka A, et al. Midterm results of radiofrequency ablation versus nephrectomy for T1a renal cell carcinoma. Jpn J Radiol 2010;28:460-8.
58. Kim EH, Tanagho YS, Saad NE, Bhayani SB, Figenshau RS. Comparison of laparoscopic and percutaneous cryoablation for treatment of renal masses. Urology 2014;83:1081-7.
59. El Dib R, Touma NJ, Kapoor A. Cryoablation vs radiofrequency ablation for the treatment of renal cell carcinoma: a meta-analysis of case series studies. BJU Int 2012;110:510-6.
60. Atwell TD, Schmit GD, Boorjian SA, Mandrekar J, Kurup AN, et al. Percutaneous ablation of renal masses measuring 3.0 cm and smaller: comparative local control and complications after radiofrequency ablation and cryoablation. AJR Am J Roentgenol 2013;200:461-6.
61. Tanagho YS, Bhayani SB, Kim EH, Figenshau RS. Renal cryoablation versus robot-assisted partial nephrectomy: Washington University long-term experience. J Endourol 2013;27:1477-86.
62. Guillotreau J, Haber GP, Autorino R, Miocinovic R, Hillyer S, et al. Robotic partial nephrectomy versus laparoscopic cryoablation for the small renal mass. Eur Urol 2012;61:899-904.
63. Klatte T, Shariat SF, Remzi M. Systematic review and meta-analysis of perioperative and oncologic outcomes of laparoscopic cryoablation versus laparoscopic partial nephrectomy for the treatment of small renal tumors. J Urol 2014;191:1209-17.
64. Thompson RH, Atwell T, Schmit G, Lohse CM, Kurup AN, et al. Comparison of partial nephrectomy and percutaneous ablation for cT1 renal masses. Eur Urol 2015;67:252-9.

Mini-invasive Surgery

Original Article

Open Access

Check for updates

Laparoscopic *vs.* open distal gastrectomy for advanced gastric cancer in elderly patients: a retrospective study

Ken Yuu, Kurumi Tsuchihashi, Sho Toyoda, Masayasu Kawasaki, Masao Kameyama

Department of Surgery, Bell Land General Hospital, 500-3, Higashiyama, Naka-ku, Sakai, Osaka 599-8247, Japan.

Correspondence to: Dr. Ken Yuu, Department of Surgery, Bell Land General Hospital, 500-3, Higashiyama, Naka-ku, Sakai, Osaka 599-8247, Japan. E-mail: k_yuu@seichokai.or.jp

How to cite this article: Yuu K, Tsuchihashi K, Toyoda S, Kawasaki M, Kameyama M. Laparoscopic *vs.* open distal gastrectomy for advanced gastric cancer in elderly patients: a retrospective study. *Mini-invasive Surg* 2019;3:6. http://dx.doi.org/10.20517/2574-1225.2018.73

Received: 1 Dec 2018 **First Decision:** 22 Jan 2019 **Revised:** 31 Jan 2019 **Accepted:** 11 Feb 2019 **Published:** 18 Mar 2019

Science Editor: Tetsu Fukunaga **Copy Editor:** Cai-Hong Wang **Production Editor:** Huan-Liang Wu

Abstract

Aim: It is unclear whether elderly patients with advanced gastric cancer can benefit from laparoscopic gastrectomy. This study aimed to compare the surgical and early postoperative outcomes of laparoscopic distal gastrectomy with those of open distal gastrectomy for advanced gastric cancer in elderly patients aged 75 years or older.

Methods: We retrospectively examined all elderly patients who underwent laparoscopic distal gastrectomy or open distal gastrectomy from October 2010 to October 2017 using prospectively collected data. Operative results, hospital courses, and survival rates were compared between the two groups.

Results: Distal gastrectomy was performed in 60 patients, laparoscopically in 20 and through open surgery in 40. The laparoscopic group had significantly lesser intraoperative blood loss (100 mL *vs.* 300 mL; $P < 0.001$) and shorter mean postoperative hospital stays (12 days *vs.* 23 days; $P < 0.001$). The overall 3-year survival rate was 50.1% in the laparoscopic group and 41.7% in the open group ($P = 0.531$).

Conclusion: Laparoscopic distal gastrectomy led to a faster return to a full diet and a shorter postoperative hospital stay in our study, and it was well tolerated by elderly patients with advanced gastric cancer.

Keywords: Aging, gastrectomy, gastric cancer, laparoscopy

INTRODUCTION

In Japan, the 2017 Annual Health, Labour and Welfare Report defined an "elderly" or older person as an individual aged 75 years or older. The average age of the population and the number of elderly patients have been increasing worldwide, particularly in developing countries[1]. Elderly patients usually have various comorbidities such as cardiovascular diseases[2,3] and decreased respiratory function, making them unsuitable for surgery. Age exceeding 70 years is an independent predictor of increased postoperative complications, in-hospital mortality, and longer hospital stays[4-6].

The advantages of laparoscopic surgery demonstrated by several reports include a decreased morbidity rate, decreased pain, and faster recovery[7-9]. It is important to determine whether elderly patients with advanced gastric cancer can benefit from laparoscopic surgery. However, few studies on laparoscopic distal gastrectomy (LDG) in elderly patients, especially those with advanced gastric cancer, have been reported. Therefore, it is necessary to study the safety, efficacy, and outcomes of LDG in elderly patients with advanced gastric cancer. Although several studies have reported the safety and benefits of laparoscopic surgery for gastric cancer in the elderly, most authors preferred to compare the findings in the elderly with those in younger patients[10,11]. These researchers could not illustrate that the laparoscopic surgery for gastric cancer in elderly patients were more effective and safe than traditional open surgery. Therefore, the present study aimed to compare the surgical and early postoperative outcomes of LDG with those of open distal gastrectomy (ODG) for advanced gastric cancer in patients age 75 years or older.

METHODS

We identified 60 patients aged 75 years or older[12] who underwent LDG or ODG for advanced primary gastric cancer at the Department of Surgery of Bell Land General Hospital from October 2010 to October 2017. The patients were retrospectively selected from a prospectively collected database and divided into two groups based on the operative approach: the LDG group and the ODG control group.

Exclusion criteria included urgent or emergent procedures and operations other than distal gastrectomy, such as total or proximal gastrectomy. Preoperative diagnosis was made by upper endoscopy with tumor biopsy, and clinical staging was performed with abdominopelvic computed tomography. Tumors were staged according to the Japanese Classification of Gastric Carcinoma[12].

In this study, laparoscopic surgery was performed by three surgeons who were proven experts in their field as defined by the Japan Society for Endoscopic Surgery. Two of the three surgeons are experts in laparoscopic gastrectomy. The indications for LDG and ODG were the same: clinically diagnosed gastric cancer without distant metastasis and lymph node involvement in the extraperigastric area. The patients were fully informed of their diagnoses and briefed on whether they would undergo LDG or ODG. The choice of LDG or ODG was decided upon by the patient and the attending surgeon after discussing both approaches. Written informed consent was obtained from all patients before the operation.

Data on several factors, including preoperative patient baseline parameters, perioperative variables, postoperative outcomes, and pathologic results, were collected for analysis. The preoperative parameters analyzed were age, sex, body mass index (BMI), American Society of Anesthesiology (ASA) classification, previous abdominal surgery, and comorbidities, which were assessed using the Charlson Comorbidity Index (CCI)[13]. Perioperative variables analyzed included the mode of anastomosis, length of the operation, estimated blood loss, time to first oral diet, and duration of postoperative hospital stay. Postoperative outcomes included postoperative complications, 30-day mortality, and recurrences. Postoperative complications, such as anastomotic leakage and pancreatic fistula, were classified based on the Clavien-Dindo classification[14]. In addition, postoperative complications such as pneumonia and delirium, which

Table 1. Patient demographics of the LDG group and ODG group

Variable	LDG group (n = 20)	ODG group (n = 40)	P value
Age (years)	81.0 ± 5.0	81.4 ± 3.9	0.289
Sex, F/M	5/15	13/27	1
BMI	22.3 ± 3.4	21.4 ± 3.0	0.289
ASA			0.551
1	2	3	
2	15	25	
3	3	12	
Hugh-Jones classification			0.117
1	12	13	
2	7	16	
3	1	9	
4	0	2	
Previous surgeries	9	9	0.134
CCI			0.566
0	5	6	
1	7	10	
2	7	16	
3	1	6	
4	0	2	

ASA: American Society of Anesthesiology; BMI: body mass index; CCI: Charlson comorbidity index; LDG: laparoscopic distal gastrectomy; ODG: open distal gastrectomy

are especially critical in elderly patients, were included in the analysis.

This study was approved by the institutional review board of the Bell Land General Hospital. The study protocol conformed to the principles set in the Declaration of Helsinki and its later amendments.

All statistical analysis were performed with EZR (Saitama Medical Center, Jichi Medical University; http://www.jichi.ac.jp/saitama-sct/SaitamaHP.files/statmedEN.html; Kand, 2012), which is a graphical user interface for R (version 2.13.0; The R Foundation for Statistical Computing, Vienna, Austria)[15].

The characteristics of both groups were compared using the chi-squared and Mann-Whitney U tests. The postoperative survival was analyzed using Kaplan-Meier survival curves and compared with the log-rank test. Significance was established at $P < 0.05$. As the number of patients older than 75 years are low, the sample size of the present study was small. Therefore, we used non-parametric statistical methods.

RESULTS

Patient characteristics

Patient characteristics are shown in Table 1. There were 20 patients in the LDG group and 40 in the ODG group with mean ages of 81.0 ± 5.0 and 81.4 ± 3.9 years, respectively. No significant differences were observed in terms of sex, BMI, ASA classification, previous surgery, or CCI. Since decreased respiratory function is a major risk factor for postoperative pulmonary complications in the elderly, previous studies commonly assessed the predicted functional expiratory volume in 1 s, predicted vital capacity, or arterial oxygen saturation[16,17]. In this study, we used the Hugh-Jones classification to assess respiratory function[18], and no differences were observed between the two groups. The prevalence of comorbidity was high in both groups; only 25.0% of the patients in the LDG group (n = 5) and 15.0% of those in the ODG group (n = 6) had no preoperative comorbidity (CCI = 0).

The surgical procedure and early surgical outcomes are summarized in Table 2. A Billroth I anastomosis was performed in 12 patients in the LDG group and in 18 in the ODG group, while a Roux-en-Y anastomosis was performed in 8 and 20 patients, respectively. The remaining patients in the ODG group underwent a Billroth II anastomosis. There were no conversions to open surgery in the LDG group. D2 lymph node dissection was performed in 15 patients in the LDG group and in 26 patients in the ODG

Table 2. Surgical and oncological outcomes of the LDG group and ODG group

	LDG group (*n* = 20)	ODG group (*n* = 40)	*P* value
Mode of anastomosis			0.473
Billroth I	12	18	
Billroth II	0	2	
Roux-en-Y	8	20	
LN dissection			0.77
D1	2	9	
D1+	3	5	
D2	15	26	
Operative time (min)	328 ± 57	243 ± 57	< 0.001
EBL (mL, range)	100 (0-475)	300 (60-2,464)	< 0.001
Time to first oral diet (days)	4.9 ± 2.4	8.3 ± 8.1	0.0185
Postoperative stay (days, range)	12 (8-39)	23 (10-514)	< 0.001
Postoperative metastasis	3 (15%)	13 (32.5%)	0.0766

EBL: estimated blood loss; LDG: laparoscopic distal gastrectomy; ODG: open distal gastrectomy

group. There was a significant reduction in the estimated blood loss in the LDG group compared with that in the ODG group ($P < 0.001$). The time to first oral diet was significantly shorter in the LDG group than in the ODG group ($P = 0.00185$).

Postoperative hospital stay was significantly shorter in the LDG group than in the ODG group ($P < 0.001$). The clinical pathway was used after gastrectomy in the hospital.

Postoperative complications

Postoperative complications occurred in 8 patients (40.0%) in the LDG group and in 24 patients (60.0%) in the ODG group ($P = 0.176$). In terms of abdominal complications, only the rate of paralytic ileus, defined as bowel obstruction treated by a long nasogastric tube, was significantly lower in the LDG group ($P = 0.040$). No significant differences were found in the rates of other complications [Table 3]. Pneumonia occurred in 3 patients in the ODG group, but it did not occur in the LDG group ($P = 0.544$). Postoperative complications included all grades of Clavien-Dindo classification. A total of 4 patients (10.0%) in the ODG group died within 30 days due to postoperative complications: pneumonia in 2, anastomotic leakage in 1, and remnant stomach necrosis in 1. In the LDG group, only 1 patient died of enteritis due to methicillin-resistant *Staphylococcus aureus* on postoperative day 7.

Pathological results

Table 4 describes the pathological findings in the 2 groups. No significant differences were noted in terms of depth of invasion, nodal catalog, and pathological stage. Stage 4 disease was observed in 1 patient in the LDG group and in 6 patients in the ODG group. Curative surgery was not performed in 7 patients: 1 patient who had liver metastasis (LDG group), 4 patients who had dissemination (ODG group), and 2 patients who had liver metastases (ODG group). No significant differences were found in terms of tumor diameter, the mean number of harvested lymph nodes, and the mean number of positive lymph node metastases between the two groups.

Prognosis

The LDG and ODG groups did not differ significantly in terms of the pathological stage according to the Japanese Classification of Gastric Carcinoma[12]. The median follow-up period in the LDG and ODG groups was 11.7 months (range, 0.3-54.8 months), and the 3-year overall survival was 50.1% and 41.7%, respectively ($P = 0.531$) [Figure 1].

DISCUSSION

As life expectancy continues to increase, the number of elderly patients with malignancies and concomitant comorbidities has increased as well. The proportion of elderly patients among the total gastric

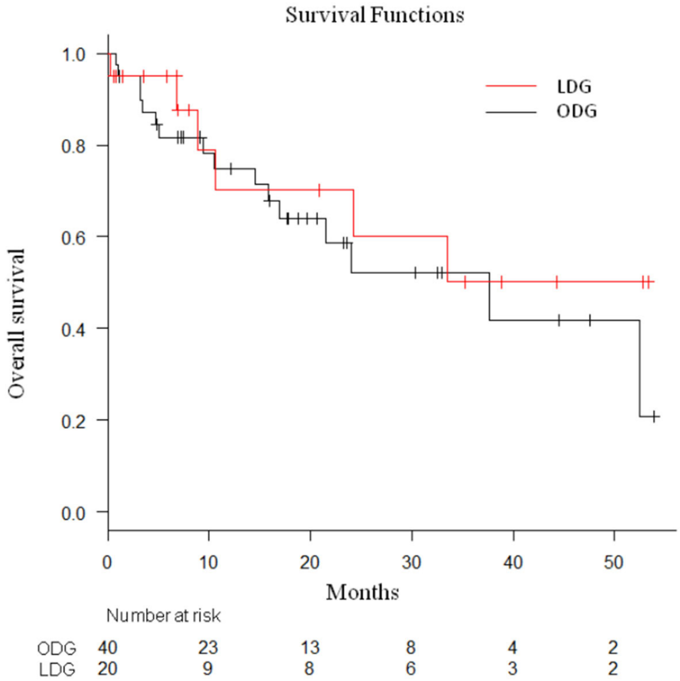


Figure 1. Kaplan-Meier overall survival curves of the LDG group and the ODG group. LDG: laparoscopic distal gastrectomy; ODG: open distal gastrectomy

Table 3. Postoperative complications in the LDG group and ODG group

	LDG group (*n* = 20)	ODG group (*n* = 40)	*P* value
Abdominal morbidity[1]			
Anastomotic leakage	0	3 (7.5%)	0.544
Pancreatic fistula	3 (15.0%)	4 (10.0%)	0.676
Abdominal abcess	1 (5.0%)	3 (7.5%)	1
Anastomotic ulcer	2 (10.0%)	1 (2.5%)	0.272
Wound dehiscence	0	1 (2.5%)	1
Paralytic ileus	0	5 (12.5%)	0.040
Other morbidity[1]			
Wound infection	0	6 (15.0%)	0.083
Pneumonia	0	3 (7.5%)	0.544
Acute cardiac failure	1 (5.0%)	2 (5.0%)	1
Delirium	1 (5.0%)	3 (7.5%)	1
Overall	8 (40.0%)	24 (60.0%)	0.176
Mortality	1 (5.0%)	4 (10.0%)	0.656

[1]Including overlapping cases. LDG: laparoscopic distal gastrectomy; ODG: open distal gastrectomy

cancer population is expected to increase gradually over the next few decades. As aging is associated with a gradual loss of reserve capacity[19], age exceeding 70 years is an independent risk factor for postoperative mortality, complications, and longer hospital stays after gastric cancer surgery[4,5].

According to the Japanese gastric cancer treatment guidelines, laparoscopic surgery is one of the most reliable treatments for early gastric cancer[20]. With the increase in the number of laparoscopic gastrectomies being performed, elderly patients might benefit from their less invasive nature. However, it is important to determine whether these advantages are applicable to elderly patients because the carbon dioxide pneumoperitoneum required for laparoscopy may be harmful and the patients' frequent comorbidities and reduced physiological reserves indicate increased risk of postoperative morbidity and mortality[21,22]. Limited data exist on the efficacy of laparoscopic gastrectomy in elderly patients, especially those with advanced gastric cancer. We performed the current study to compare LDG in elderly patients with advanced gastric cancer to ODG and determine its feasibility and efficacy.

Table 4. Pathological data of the LDG group and ODG group

	LDG group (*n* = 20)	ODG group (*n* = 40)	*P* value
Depth of invasion			0.156
pT1	0	0	
pT2	8	6	
pT3	2	3	
pT4a	9	27	
pT4b	1	4	
Nodal catalog			0.215
pN0	8	11	
pN1	3	9	
pN2	5	3	
pN3a	3	10	
pN3b	1	7	
Stage			0.62
IA	0	0	
IB	4	3	
IIA	1	4	
IIB	6	8	
IIIA	3	4	
IIIB	1	4	
IIIC	4	11	
IV	1	6	
Diameter of tumor (cm)	5.9 ± 2.2	6.1 ± 2.2	0.762
Number of lymph node removed	35.5 (14-65)	33.5 (5-96)	0.994
Number of positive lymph node metastasis	2 (0-12)	2.5 (0-47)	0.213

LDG: laparoscopic distal gastrectomy; ODG: open distal gastrectomy

LDG for advanced gastric cancer was shown to be more effective than open surgery in elderly patients, resulting in reduced blood loss, faster first oral diet initiation, and shorter hospital stays. Conversely, the longer operative time may lead to a higher rate of morbidity, including delirium, pneumonia, and cardiac failure. Acute cardiac failure and pneumonia are the most common minor complications of distal gastrectomy for gastric cancer. Some reports have suggested that the adverse cardiopulmonary effects of pneumoperitoneum occur only when the intra-abdominal pressure is more than 15 mmHg, while low pressures do not affect cardiopulmonary output[23-25]. Therefore, laparoscopic surgery may be safe even in high-risk patients. However, the operative time was longer in the LDG group than in the ODG group, and longer operative times are associated with postoperative delirium and pneumonia[26]. Our results revealed no significant differences in postoperative morbidities, suggesting that high-risk patients, including the elderly may be able to tolerate the prolonged laparoscopic operative times. In accordance with previous reports, laparoscopic surgery led to a faster return to a full diet and a shorter postoperative hospital stay in our study[27].

In fact, a shorter abdominal incision leads to less pain and, subsequently, earlier ambulation. Early ambulation may prevent postoperative delirium as evidenced by the findings of Schweickert *et al.*[28], who found a shorter duration of intensive care unit-associated delirium in patients who received physical and occupational therapy. Since postoperative pain is one cause of delirium, less pain after surgery may help prevent postoperative delirium[29]. Therefore, it is more important to reduce pain after surgery than to shorten operative time, especially in elderly patients. In addition, early ambulation prevents pneumonia resulting from atelectasis. Based on these advantages, LDG may provide superior short-term outcomes in elderly patients with advanced gastric cancer.

A 2011 report stated that the average life expectancy at 80 years in Japan had increased by 8.39 years in men and 11.36 years in women. However, Endo *et al.*[2] reported that the overall survival of gastric cancer patients was longer in the operation group than in the best supportive care group. The oncologic results of LDG in elderly patients have not been determined. In a study of the overall gastric cancer patient population, Hu *et al.*[30] reported that the cumulative 3-year overall survival rate after laparoscopy-assisted gastrectomy for advanced gastric cancer was 75.3%; in our study, it was 50.1% and 41.7% in the LDG and

ODG groups, respectively, which is lower than the overall rate. This may be because elderly patients have concurrent ailments that affect prognosis and survival. Indeed, in the present study, 49 patients (81.7%) had preoperative comorbid diseases. Concurrent disease was the cause of death in 2 patients in the LDG group and in 4 patients in the ODG group. Since elderly patients are expected to have a shorter residual life span, quality of life should also be considered when choosing a surgical procedure[31,32].

The elderly patients in the ODG group were more likely to require inpatient rehabilitation due to their diminished mobility and more persistent postoperative wound pain, which seriously hamper the recovery of activities of daily living[33]. Prolonged hospitalization after surgery can lead to worse quality of life in elderly patients. Several reports have demonstrated that laparoscopic surgery leads to a faster return to a full diet and a shorter postoperative hospital stay, as shown in our own study. These data indicate that LDG may be superior to conventional open surgery in terms of the length of the hospital stay, even for advanced gastric cancer.

Our overall rate of postoperative complications was higher than that in previous studies on the overall gastric cancer patient population. Hu *et al*.[30] reported a postoperative complication rate of 10.2% in 1,184 patients with advanced gastric cancer. The most common major complication in the LDG group was pancreatic fistula, which tends to reflect surgical inexperience and a learning curve[34]. Pancreatic fistulas occurred in 3 patients undergoing LDG in 2010, the year we started performing D2 lymphadenectomy. As experience accumulates, the incidence rate of major pancreatic fistulas may decrease. Although the mortality rate was not significantly different between the 2 groups, 4 deaths occurred in the ODG group, suggesting that radical gastrectomy may sometimes be excessively stressful for elderly patients, especially those with advanced gastric cancer. Surgery should be performed more meticulously and quickly than usual in elderly patients. The choice of surgical procedure in elderly patients with short life expectancies must guarantee disease control as well as acceptable short- and long-term survival and quality of life[35].

Our study had some limitations inherent to retrospective and non-randomized studies, where selection and observer biases with regard to the operative approach adopted are possible. Furthermore, our study was limited by the small number of cases. Surgeons may have encouraged earlier discharge of the patients in the LDG group. A high-volume, prospective, and randomized study is needed to confirm our findings.

According to the Japanese gastric cancer treatment guidelines, laparoscopic surgery is one of the most reliable treatments for early gastric cancer. It is important to determine whether elderly patients with advanced gastric cancer can benefit from laparoscopic surgery. Our results demonstrated that LDG for advanced gastric cancer in patients older than 75 years was associated with lesser intraoperative blood loss and shorter hospital stays than ODG, with no differences in survival. Patient age alone should not rule out the feasibility of either LDG or ODG.

DECLARATIONS

Acknowledgments

We are grateful to the study participants and their caregivers. The authors thank participating surgeons from the Bell Land General Hospital. We would like to thank Editage (www.editage.jp) for English language editing.

Authors' contributions

Designed the study and acquisition, analysis, and interpretation of the data: Yuu K
Collected the data: Yuu K, Tsuchihashi K, Toyoda S, Kawasaki M
Supervised this study: Kameyama M

Availability of data and materials
Not applicable.

Financial support and sponsorship
None.

Conflicts of interest
All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

REFERENCES
1. Frasson M, Braga M, Vignali A, Zuliani W, Di Carlo V. Benefits of laparoscopic colorectal resection are more pronounced in elderly patients. Dis Colon Rectum 2008;51:296-300.
2. Endo S, Dousei T, Yoshikawa Y, Hatanaka N, Kamiike W, et al. Prognosis of gastric carcinoma patients aged 85 years or older who underwent surgery or who received best supportive care only. Int J Clin Oncol 2013;18:1014-9.
3. Kim EJ, Seo KW, Yoon KY. Laparoscopy-assisted distal gastrectomy for early gastric cancer in the elderly. J Gastric Cancer 2012;12:232-6.
4. Polanczyk CA, Marcantonio E, Goldman L, Rohde LE, Orav J, et al. Impact of age on perioperative complications and length of stay in patients undergoing noncardiac surgery. Ann Intern Med 2001;134:637-43.
5. Monson K, Litvak DA, Bold RJ. Surgery in the aged population: surgical oncology. Arch Surg 2003;138:1061-7.
6. Story DA. Postoperative complications in elderly patients and their significance for long-term prognosis. Curr Opin Anaesthesiol 2008;21:375-9.
7. Kim MC, Jung GJ, Kim HH. Morbidity and mortality of laparoscopy-assisted gastrectomy with extraperigastric lymph node dissection for gastric cancer. Dig Dis Sci 2007;52:543-8.
8. Kitano S, Shiraishi N, Fujii K, Yasuda K, Inomata M, et al. A randomized controlled trial comparing open vs laparoscopy-assisted distal gastrectomy for the treatment of early gastric cancer: an interim report. Surgery 2002;131:S306-11.
9. Mochiki E, Nakabayashi T, Kamimura H, Haga N, Asao T, et al. Gastrointestinal recovery and outcome after laparoscopy-assisted versus conventional open distal gastrectomy for early gastric cancer. World J Surg 2002;26:1145-9.
10. Kim MG, Kim HS, Kim BS, Kwon SJ. The impact of old age on surgical outcomes of totally laparoscopic gastrectomy for gastric cancer. Surg Endosc 2013;27:3990-7.
11. Park HA, Park SH, Cho SI, Jang YJ, Kim JH, et al. Impact of age and comorbidity on the short-term surgical outcome after laparoscopy-assisted distal gastrectomy for adenocarcinoma. Am Surg 2013;79:40-8.
12. Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma: 3rd English edition. Gastric Cancer 2011;14:101-12.
13. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chron Dis1987;40:373-83.
14. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-13.
15. Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant 2013;48:452-8.
16. Kawamura H, Yokota R, Homma S, Kondo Y. Comparison of respiratory function recovery in the early phase after laparoscopy-assisted gastrectomy and open gastrectomy. Surg Endosc 2010;24:2739-42.
17. Inokuchi M, Kojima K, Kato K, Motoyama K, Sugita H, et al. Feasibility of laparoscopy-assisted gastrectomy for patients with chronic obstructive pulmonary disease. Surg Endosc 2013;27:2102-9.
18. Fletcher CM. The clinical diagnosis of pulmonary emphysema; an experimental study. Proc R Soc Med 1952;45:577-84.
19. Evers BM, Townsend CM Jr, Thompson JC. Organ physiology of aging. Surg Clin North Am 1994;74:23-39.
20. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines (ver.3). Tokyo: Kanehara; 2010.
21. Mayol J, Martinez-Sarmiento J, Tamayo FJ, Fernández-Represa JA. Complications of laparoscopic cholecystectomy in the ageing patient. Age Ageing 1997;26:77-81.
22. Turrentine FE, Wang H, Simpson VB, Jones RS. Surgical risk factors, morbidity, and mortality in elderly patients. J Am Coll Surg 2006;203:865-77.
23. Odeberg S, Ljungqvist O, Svenberg T, Gannedahl P, Bäckdahl M, et al. Haemodynamic effects of pneumoperitoneum and the influence

of posture during anaesthesia for laparoscopic surgery. Acta Anaesthesiol Scand 1994;38:276-83.
24. Rauh R, Hemmerling TM, Rist M, Jacobi KE. Influence of pneumoperitoneum and patient positioning on respiratory system compliance. J Clin Anesth 2001;13:361-5.
25. Gutt CN, Oniu T, Mehrabi A, Schemmer P, Kashfi A, et al. Circulatory and respiratory complications of carbon dioxide insufflation. Dig Surg 2004;21:95-105.
26. Lu J, Huang CM, Zheng CH, Li P, Xie JW, et al. Short- and long-term outcomes after laparoscopic versus open total gastrectomy for elderly gastric cancer patients: a propensity score-matched analysis. J Gastrointest Surg 2015;19:1949-57.
27. Usui S, Yoshida T, Ito K, Hiranuma S, Kudo SE, et al. Laparoscopy-assisted total gastrectomy for early gastric cancer: comparison with conventional open total gastrectomy. Surg Laparosc Endosc Percutan Tech 2005;15:309-14.
28. Schweickert WD, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet 2009;373:1874-82.
29. Avidan MS, Fritz BA, Maybrier HR, Muench MR, Escallier KE, et al. The prevention of delirium and complications associated with surgical treatments (PODCAST) study: protocol for an international multicentre randomised controlled trial. BMJ Open 2014;4:e005651.
30. Hu Y, Ying M, Huang C, Wei H, Jiang Z, et al. Oncologic outcomes of laparoscopy-assisted gastrectomy for advanced gastric cancer: a large-scale multicenter retrospective cohort study from China. Surg Endosc 2014;28:2048-56.
31. Wu CW, Lo SS, Shen KH, Hsieh MC, Lui WY, et al. Surgical mortality, survival, and quality of life after resection for gastric cancer in the elderly. World J Surg 2000;24:465-72.
32. Kitamura K, Sugimachi K, Saku M. Evaluation of surgical treatment for patients with gastric cancer who are over 80 years of age. Hepatogastroenterology 1999;46:2074-80.
33. Zheng L, Lu L, Jiang X, Jian W, Liu Z, et al. Laparoscopy-assisted versus open distal gastrectomy for gastric cancer in elderly patients: a retrospective comparative study. Surg Endosc 2016;30:4069-77.
34. Park SH, Mok YJ, Kim JH, Park SS, Kim SJ, et al. Clinical significance of gastric outlet obstruction on the oncologic and surgical outcomes of radical surgery for carcinoma of the distal stomach. J Surg Oncol 2009;100:215-21.
35. Bandoh T, Isoyama T, Toyoshima H. Total gastrectomy for gastric cancer in the elderly. Surgery 1991;109:136-42.

Mini-invasive Surgery

Review

Open Access

Check for updates

Laparoscopic lymph nodes dissection for advanced gastric cancer: the current status and the perspective

Masanari Shimada, Susumu Amaya, Yoshinori Munemoto, Takeshi Mitsui

Department of Surgery, Fukui-ken Saiseikai Hospital, Fukui 918-8503, Japan.

Correspondence to: Dr. Masanari Shimada, Department of Surgery, Fukui-ken Saiseikai Hospital, Wadanaka Funabashi 7-1, Fukui 918-8503, Japan. E-mail: masanari.shimada@gmail.com

How to cite this article: Shimada M, Amaya S, Munemoto Y, Mitsui T. Laparoscopic lymph nodes dissection for advanced gastric cancer: the current status and the perspective. *Mini-invasive Surg* 2019;3:7. http://dx.doi.org/10.20517/2574-1225.2018.78

Received: 19 Dec 2018 **First Decision:** 18 Feb 2019 **Revised:** 25 Feb 2019 **Accepted:** 26 Feb 2019 **Published:** 27 Mar 2019

Science Editor: Tetsu Fukunaga **Copy Editor:** Cai-Hong Wang **Production Editor:** Huan-Liang Wu

Abstract
The laparoscopic gastrectomy (LG) with D2 lymph node dissection (LND) for advanced gastric cancer (AGC) have been widely done. However, the applicability to more advanced disease is still under debate. Actually, there are a lot of technical demands against D2 LND for AGC, e.g., total omentectomy, splenic hilar node dissection, and the management for bulky lymph nodes, etc. Recently, extensive research has been gradually performed in the field of LG for AGC and demonstrated that LG for AGC is a safe and feasible procedure with better short-term outcomes compared with open gastrectomy. Also, large-scaled phase III trials are ongoing, and their long-term outcomes are awaited the publication in the near future. LG with D2 LND by expert surgeons under the cautious indications could be acceptable treatment for locally AGC. On the other hand, we should keep searching for solutions to the technical or oncological issues, and long-term outcome of phase III study should be warranted for standard treatment. Robotic surgery, LG following neoadjuvant chemotherapy, or conversion therapy using LG for several stage IV patients may help us clear the technical hurdles, and may show survival advantages in the future.

Keywords: Laparoscopic gastrectomy, advanced gastric cancer, lymph node dissection, distal gastrectomy, total gastrectomy

INTRODUCTION

Laparoscopic gastrectomy (LG) for gastric cancer has been popular rapidly with the improvement of technique and the progress of surgical devices. In the latest Gastric Cancer Treatment Guidelines 2018 (ver.5) published by Japanese Gastric Cancer Association[1], laparoscopic distal gastrectomy (LDG) for clinical stage I disease is accepted for one of the options in daily clinical practice. Recently, extensive research has been gradually performed in the field of LG for advanced gastric cancer (AGC) and demonstrated that LG for AGC is a safe and feasible procedure with better short-term outcomes compared with open gastrectomy (OG). However, there are few randomized clinical trials (RCT) reporting the long-term outcome of LG for AGC previously. Moreover, it also remains controversial whether LG can be performed for AGC from the aspect of technical and oncological issues. Clinically, we often encounter the situations that the disease is unexpectedly diagnosed with advanced disease in laparoscopic inspection. Moreover, if it comes to that the histological examination may reveals serosa invasions or multiple lymph node metastases even if only D1 or D1+ lymph node dissection (LND) has been done because of the clinical stage I, we are sorry D2 LND had not been performed in such cases. So, surgeons must prepare to perform D2 LND in laparoscopic gastrectomy and recognize the acceptable indications and limitations for AGC. Now, we summarized the main points of surgical procedure of D2 LND and the future perspectives.

PREVIOUS STUDIES ABOUT RADICAL LG FOR AGC

Recently, many retrospective comparative studies and several prospective RCTs have reported that LG for AGC was safe and feasible when compared to the short-term and long-term outcomes observed with OG[2-13]. Table 1 summarizes these studies about LG for AGC in recent years. Propensity score matching analysis (PSM) was often used for comparison the LG and OG groups in some retrospective studies[8,10,12]. Especially, some authors demonstrated the technical safety of LDG with D2 LND for locally AGC in the multi-institutional, prospective, phase II study[2-5,11]. Moreover, the 3- year or 5-year overall or disease-free survival rates have been gradually reported from China, Korea, and Japan[7-13]. Majority of them reported that LG is feasible and safe for the treatment of AGC with D2 LND compared with OG, and no significant differences were observed in long-term over all survival (OS) and disease free survival (DFS) between the LG group and OG group. However, Li *et al.*[6] suggested higher-level tumor stage may increase the operative risk and should be performed with caution by surgeons with considerable experience of LG. Also, Lin *et al.*[8] reported although the OS curve at each stage did not differ significantly, the survival rate increased overall for patients with T4aN3bM0 in the OG group. Additionally, because the patient selections in their studies are different slightly in each and there is the difference that laparoscopic total gastrectomy (LTG) is embedded in the studies or not, we should give the result careful consideration. Collectively, it seems that LG with D2 LND could be acceptable treatment for AGC under definite conditions by expert surgeons.

CLINICAL INDICATIONS AND LIMITATIONS DEALING WITH LND FOR AGC

Tumor infiltration

Recently, the result of JCOG1001 (UMIN000003688) has been published, which demonstrated no survival difference between omentectomy *vs.* bursectomy for T3/T4 tumors diagnoses with surgical findings in OG[14]. Therefore, bursectomy is not recommended as a standard procedure for AGC in Japan. However, the significance for omentectomy only does not become clear yet, because it is determined that omentum should be resected in both omentectomy group and bursectomy group in JCOG1001 study. Some reports indicated that in some metastatic nodes extra-nodal expansion is recognize, which means cancer cell spread out of lymph node capsule to adjacent adipose tissue[15,16]. Extra-nodal expansion is pointed out to be a poor prognostic factor[15]. Based on these reports, if the prognosis will be improved with omentectomy, it is expected to be significant clinically for T4 tumor. Then, omentectomy is performed for patients having tumors deeper than T3 in a lot of institutes at the moment. Presently, RCT is scheduled to launch, which validate the non-inferiority of omentum-preserving surgery for T3/T4 tumors.

Bulky positive nodes and large primary tumor

Generally, bulky lymph node is, by definition, “one node ≥ 3 cm in diameter” or “nearby more than one nodes ≥ 1.5 cm in diameter”, and neoadjuvant chemotherapy (NAC) is often performed in such patients.

Table 1. The latest studies evaluating safety or survival rate about laparoscopic gastrectomy for advanced gastric cancer

Authors	Inaki *et al.*[2] (2015)	Hu *et al.*[3] (2016)	Lee *et al.*[4] (2016)	Okabe *et al.*[5] (2016)	Li *et al.*[6] (2016)	Hao *et al.*[7] (2016)	Lin *et al.*[8] (2016)	Lee *et al.*[9] (2018)	Li *et al.*[10] (2018)	Park *et al.*[11] (2018)	Kinoshita *et al.*[12] (2018)	Xu *et al.*[13] (2018)
Country	Japan	China	Korea	Japan	China	China	China	Korea	China	Korea	Japan	China
Analysis	Phase II	Phase II	Phase III	Phase II	PSM	Retrospective	PSM	Retrospective	PSM	Phase II	Multicenter Cohort PSM	Retrospective Cohort
Sample size of LG cases	86	528	526	73	101	579	539	160	410	100	305	430
Eligibility	cT2-4 N0-2	cT2-4a N0-3	cT2-4a N0-2	cT2-4b N0-3	-	cT2-3	pT2-4a N0-3b	cT2-4	pT2-4a N0-3b	cT2-4a N0-3	c-Stage II/III	cT2-4a N0-3b
Surgery	LDG 100%	LDG 97.9% LTG 2.1%	LDG 100%	LDG 56% LTG 43% UR 1%	LDG 37.6% LTG 62.4%	LPG 9.7% LDG 63.8% LTG 25.8%	LTG 63.1% LDG 36.9%	LTG 10% LSTG 90%	LDG 38.6% LTG 61.4%	LDG 94% LTG 4%	LDG 51.5% LTG 42.0% LPG 0.7% UR 2.0% Bypass 3.9%	LDG 39.8% LTG 60.2%
Operative time (min)	296	217.3	-	366	297.4	257.8	-	174	-	257.4	365	283.8
Blood loss (mL)	30	105.5	231.2	60	131.9	154.5	-	99.5	-	-	140	273.7
Conversion	1 (1.2%)	6.4%	-	0	-	35 (5.57%)	-	Excluded	-	2 (2%)	4 (1.3%)	Excluded
p-Stage	IA 26.7% IB 20.9% II 20.9% III 31.5%	IA 16.8% IB 12.3% IIA 12.7% IIB 13.7% IIIA 13.3% IIIB 14.1% IIIC 14.8% IV 2.1%	Awaiting the results	CR 1% IA 3% IIA 1% IIB 7% IIIA 11% IIIB 7% IIIC 8% IV 4%	II 57.4% IIIA 23.8% IIIB 18.8%	IB 14.8% IIA 22.6% IIB 26.3% IIIA 36.3%	IB 9.5% IIA 8.2% IIB 13.9% IIIA 12.4% IIIB 20.4% IIIC 35.6%	IA 13.8% IB 11.9% IIA 27.5% IIB 20.6% IIIA 11.9% IIIB 15.0% IIIC 8.8%	IB 12.2% IIA 21.5% IIB 19.3% IIIA 22.0% IIIB 20% IIIC 5.1%	IA 27% IB 15.0% IIA 18.0% IIB 11.0% IIIA 8.0% IIIB 15.0% IIIC 5.0% IV 1.0%	IA 4.3% IB 5.9% IIA 15.7% IIB 15.4% IIIA 15.4% IIIB 19.7% IIIC 15.4% IV 8.2%	IB 10.7% IIA 16.0% IIB 20.9% IIIA 18.1% IIIB 22.8% IIIC 11.4%
Morbidity	15%	15.2%	16.4%	≥ Grade II 20.5%	21.8%	6.4%	-	14.3%	-	17%	≥ Grade 2 20.1%	Grade II 2.8% ≥ Grade III 2.6%
Mortality	0%	0.4%	0.38%	1.4%	1%	-	-	0%	-	0%	0.3%	0.2%
Lomg-term outcome	Ongoing in phaseIII study	Ongoing in phaseIII study	Ongoing in phaseIII study	-	-	5-year OS 57.65% RR 31.2%	5-year OS 58.8%	3-year OS 80.5& DFS 73.7%	5-year OS 52.0% DFS 46.8%	3-year DFS 80.1%	5-year OS 53.0% RFS 72%	5-year OS 51.2% DFS 52.8%

PSM: propensity score method; c: clinical; p: pathological; LDG: laparoscopic distal gastrectomy; LPG: laparoscopic proximal gastrectomy; LTG: laparoscopic total gastrectomy; LSTG: laparoscopic subtotal gastrectomy; UR: unresected; p-Stage: pathological stage; CR: complete response of the primary tumor; OS: overall survival; DFS: disease-free survival; RFS: relapse-free survival; LG: laparoscopic gastrectomy

NAC with S-1 plus cisplatin followed by D2 gastrectomy with para-aortic lymph node dissection is slightly recommended only in the event of highly metastases-positive nodes[17]. On the other hand, recently randomized phase III trial of gastrectomy with or without neoadjuvant S-1 plus cisplatin for type 4 or large type 3 gastric cancer: (JCOG0501) has been published in ASCO 2018 meeting[18], which demonstrated no survival difference between with NAC group *vs*. without NAC group. Laparoscopic procedure for such bulky lymph nodes, type 3 tumor > 8 cm, and type 4 tumor has a limitation to handle with endoscopic forceps with concerns of spillage of cancer cells. Thus, primary open surgery with D2 LND and adjuvant chemotherapy remains the standard treatment for type 4 or large type 3 tumors.

Probably, majority of surgeons will be convinced of the indication of LG about positive nodes and large tumor as below: (1) lymph nodes are not bulky; (2) no invasion to other organ or major vessels; (3) tumor size is less than 8cm in diameter; and (4) non-type4 tumor. In that context, Okabe *et al*.[5] disclosed a phase II study (KUGC04), which demonstrated safety and efficacy of LG for gastric cancer of clinical stage II or higher, including patients with prior chemotherapy, tumors requiring TG, tumors that invaded adjacent organs, and patients with bulky nodes metastasis. Solid evidence of the surgical and oncological safety of LG for AGC requires performance of a multicenter, prospective study with experienced surgeons.

Splenic hilar dissection for proximal gastric cancer

In Japan, splenic hilar nodes (No.10) have been included within the extent of D2 LND in the treatment of proximal AGC for a long time. However, the final result of JCOG 0110 (UMINC000000004) has been disclosed, which compared splenectomy *vs*. non-splenectomy for proximal AGC not invading greater curvature line. There was no difference in long-term survival rate. Furthermore, splenectomy was associated with increased incidence of morbidity[19]. Therefore, splenectomy is not recommended as a standard treatment, except for tumors invading the greater curvature line. Conversely, there is a possibility that such tumors invading the greater curvature line or tumors with metastases of splenic hilar lymph node may be indicated for splenic hilar dissection. Laparoscopic approach has a great advantage for procedures in deep surgical fields around spleen. However, for complicated cases, such as invading the splenogastric ligament or the pancreatic tail, there are strong doubts about whether laparoscopic maneuver is applicable or not.

THE TECHNICAL TIPS OF LND FOR AGC

Preoperative evaluation

Preoperative esophagogastroduodenoscopy, contrast enhanced computed tomography, and positron emission tomography are important for accurate diagnosis on tumor depth, invasion adjacent organs, lymph node metastases, or distant metastases. Three-dimensional computed tomography is also helpful to recognize the branching of celiac artery or anatomical diversity of the splenic hilar vessels[20].

Positions of trocars

Reverse Trendelenberg position with head elevated about 15-20°. The surgeon stands on the patient's right side, the assistant is on the left side, and the assistant for camera stand between the patient's legs. A scope port is inserted via umbilical mini-laparotomy. For manipulation, 5 mm trocars are inserted on bilateral subcostal midclavicular line, and 12 mm trocars are inserted on bilateral lateroabdominal region, which arranged in an inverted trapezoidally. Especially, because the raised pancreatic head or vertebral body get in the way of dissection in case of dissection around esophagus or deep suprapancreatic lymph node dissection, right lateroabdominal trocar should be arranged slightly medially and cranially.

Laparoscopic inspection

At first, it is identified that there is no metastasis on the surface of the liver and peritoneal dissemination in the omentum, mesocolon, and mesenterium. Subsequently, intraoperative cytology of ascites in the pelvic cavity or peritoneal lavage specimen is examined. If the intraoperative cytology detects free cancer cells, it is considered to be "non-curative factor (CY1)". However, if there is no "non-curative factor" other than CY1, it is often recommend now that we should convert LG into OG with D2 LND for standard radical surgery and extensive intraoperative peritoneal lavage using a large amount of saline solution.

Dividing the greater omentum and dissection of the gastrosplenic ligament

Omentectomy is performed for almost patients having tumors deeper than T3. Discussion of the greater omentum is started near transverse colon. Surgeon's left forceps and the assistant's right forceps elevate

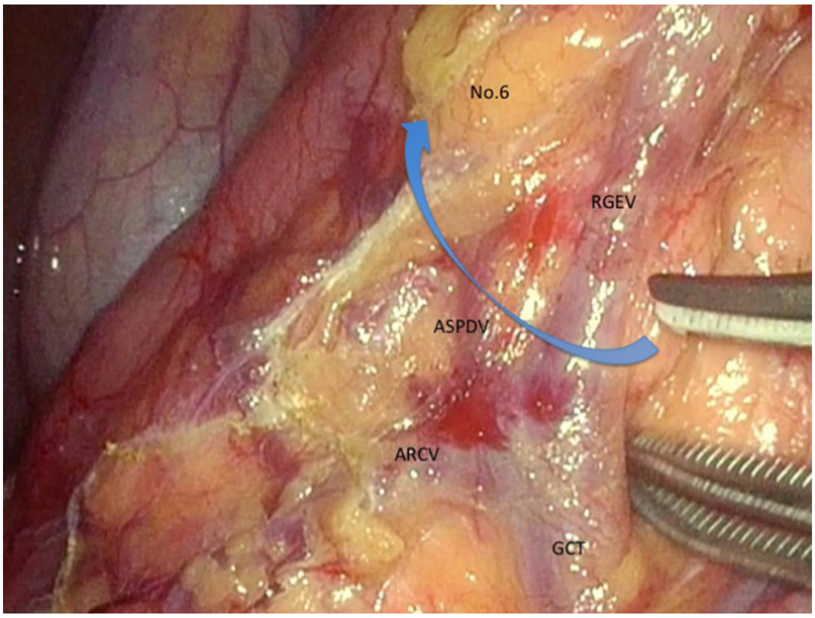


Figure 1. We present the boundary of No.6 lymph node station. The operator should identify anterior superior pancreaticoduodenal vein (ASPDV) and elevates No.6 lymphoid tissues ventrally and softly. ARCV: accessory right colic vein; GCT: gastrocolic trunk; RGEV: right gastroepiploic vein

the greater omentum; moreover, the wide triangulation is formed by the traction of fatty appendices of transverse colon with the assistant's left forceps. The triangulated counter traction makes it possible for surgeons to resect the greater omentum. Then, the splenocolic ligament is divided and the root of left gastroepiploic artery and vein (LGEAV) are identified in the pancreatic tail. After LGEAV are ligated and cut, the gastrosplenic ligament including short gastric artery (SGA) and vein are dissected toward cranial side. Surgeon is careful not to injure the branch around the spleen. In the area of superior border of spleen, because the operative field often becomes limited by excess fatty tissue, in such occasions the precursor cutting of esophagus may be able to show good operative field toward caudal side later. Alternatively the approach that goes into the left gastrophrenic ligament can confirm the superior border of spleen and the most cranial branch of SGA. Therefore, the mobility of the gastrosplenic ligament is improved by cutting the most cranial branch of SGA, and the gastrosplenic ligament is spread like a "screen". This approach is flexible enough to respond to variety of pancreatic tail or splenic hilum[21].

Dissection of infra-pyloric nodes (No.6)

The surgeon moves to the patient's left side during the dissection of No.6 lymph node station. After the omentectomy has been finished close to the hepatic flexure, the layer of "embryologic failure of fusion" which consists of the anterior lobe of transverse mesocolon and the anterior pancreatic fascia is dissected for the mobilization of transverse colon. Thereby, we are able to finally determine the range to dissect and ready to dissect No.6 lymph node station. The inferior limit of infra-pyloric nodes is anterior superior pancreaticoduodenal vein (ASPDV) [Figure 1]. The right gastroepiploic vein is clipped and cut at the point in which ASPDV flows. Then, the lymph nodes and fat tissue in front of ASPDV is elevated and dissected toward descending duodenum. Subsequently, the neural layer around the right gastroepiploic artery (RGEA), which is called "outermost layer", is identified and dissected keeping the layer. Then, the lymphoid tissue on the left side of RGEA is softly elevated ventrally. Nerve bundle around RGEA is cut and RGEA is clipped and cut. Because the lymphoid tissue around infra-pyloric artery (IPA) remain formed into a screen, IPA is cut and lymphoid tissue attaching to duodenum is peeled up.

Cutting the duodenum

The assistant lift up the posterior wall of the stomach, and the branches of superior duodenal artery is cut from dorsal side. Then, the duodenal bulb is stapled and cut. In patients suspected of duodenal invasion of

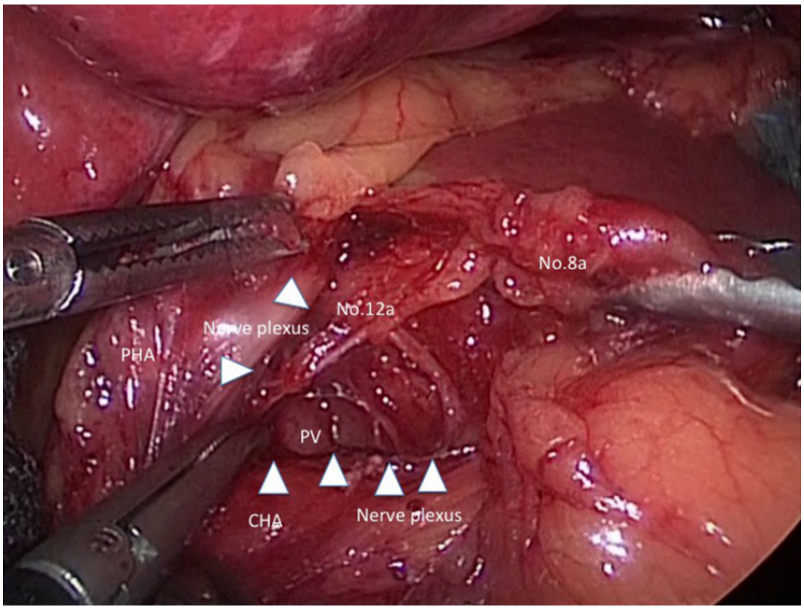


Figure 2. We present a scene in suprapancreatic lymph node dissection. The outermost layer existing between nerve plexus around common hepatic artery (CHA) and No.8a lymph nodes is traced by white arrowheads. PV: portal vein; PHA: proper hepatic artery

gastric cancer, we have to cut the duodenum at the level of superior duodenal angulus. Additionally, the staple line of duodenal stump should be reinforced by intracorporeal suture to prevent the duodenal stump fistula. Recently, it is reported that the method using barbed suture can be performed in a short operation time without any technical difficulties[22].

Dissection of suprapancreatic nodes (No.5, 8a, 9, 12a)

At first, the pancreatic capsule is cut along the lines with superior edge of pancreas from the root of gastroduodenal artery to near the root of posterior gastric artery (PGA). The assistant's right forceps grasps the gastropancreatic fold ventrally and the left forceps rotates the pancreas dorsocaudally. There are some pancreatic rotating techniques with forceps, gauze, sponge, cotton *etc*.[23-26], however surgeons should avoid the pancreatic injury by delicate compression and coordination with surgeon's devices.

Subsequently, the outermost layer existing between nerve plexus around common hepatic artery (CHA) and No.8a lymph nodes is probed with dissecting forceps [Figure 2]. The ventral side of CHA, proper hepatic artery, and the dorsal side of right gastric artery (RGA) is exposed continuously if the outermost layer is kept dissecting. Then, RGA is clipped and cut at the root and No.5 lymph node dissection is finished.

Next, if the assistant's right forceps grasps and tract No.8a ventrally, the assistant's left forceps and the surgeon's left forceps tracts the nerve plexus around CHA caudally, No.12a lymph node at the hepatoduodenal ligament is pulled out and the left wall of portal vein (PV) is exposed dorsalward. Because the visual reference of PV determine the dorsal limit of No.12a lymph node dissection, the cranial edge of No.12a lymph node is sealed and cut by ultrasonically activated device *etc*. near hepatic portal region.

Then, the assistant's right forceps grasps and lifts up the gastropancreatic fold ventrally and straight again, and the surgeon's left forceps grasps and lift up the capsule of dissected lymph nodes. The surgeon keeps dissecting from No.8a lymph node to proximal region of splenic artery while he sustains the outermost layer. The left gastric vein is clipped and cut along the way and the left outermost layer of left gastric artery (LGA) is identified preferentially. Herein, the approach that goes into the left gastrophrenic ligament is also

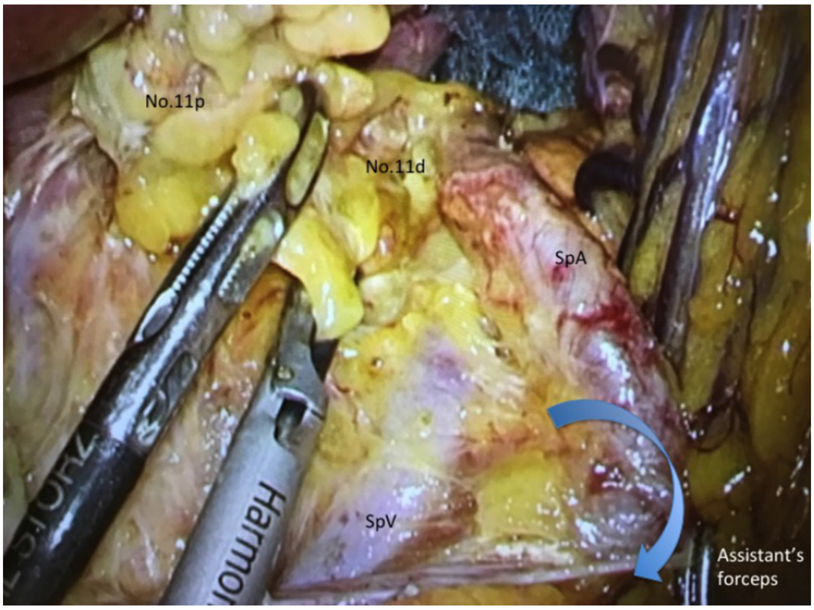


Figure 3. We present a scene in dissection of lymph nodes along splenic artery (SpA) The assistant's left forceps grasps connective tissue around SpA and make SpA straight. Then, we can have visual contact with the dorsal side of the splenic vessels. SpV: splenic vein

effective. In other words, the dissection from the left outermost layer of LGA to crura of the diaphragm is performed at once. The right outermost layer of LGA is similarly identified, and LGA remain celiac nerves-covered. Then, LGA and surrounding celiac nerves is double clipped and cut. No.9 lymph node around celiac axis is lead to improvement in mobility by dissecting the outermost layer around the celiac and hepatic nerves, and No.9 lymph node leading to No.16 (para-aortic nodes) should be clipped at the root to prevent lymphorrhea.

Dissection of lymph nodes along splenic artery and splenic hilar nodes (No.11p, 11d, 10)

The most common technical difficulty encountered during LTG with D2 LND is dissection of the lymph nodes among splenic artery (SpA) and splenic hilar lymph nodes (No.10, 11p, and 11d).

At the first setout, the dorsal layer of Toldt's fusion fascia is dissected widely. The assistant's left forceps grasps connective tissue around SpA and make SpA straight; moreover, the assistant's right forceps rotates the lower edge of pancreatic tail dorsally. Then, we can have visual contact with the dorsal side of the splenic vessels [Figure 3], and No.11p and No.11d lymph nodes are dissected toward the root if of LGEAV, which have been initially ligated. Hur *et al.*[27] reported that taping the splenic artery was helpful in dissecting lymph nodes No.10 and 11d during spleen- and pancreas-preserving LG. The PGA is clipped and cut along the way wherever possible. We should try to preserve the caudal pancreatic artery and vein in the region of pancreatic tail. In splenic hilar region, surgeons are careful not to suffer injuries to pancreatic parenchyma hidden behind the SpA. Finally, the SGA, which arising from the SpA, is clipped and cut at the root.

Throughout the surgery

The intraoperative characteristics about AGC with metastatic lymph nodes are as below: (1) the Surgical field of view is restricted because of the decline of organ mobility; (2) the identification of the dissectable layer and vessels is difficult; (3) the oozing derives from the fatty tissue around lymph nodes; (4) the mists and fluids, which produced when the energy devices are activated, increase significantly.

In D2 LND for AGC, making an operating field against the metastatic lymph node and the tumor is the first important procedure. We should start dissecting on the normal tissues and keep the dissecting layer toward each landmark of surgical scenes, while we try to prevent the organ injury by delicate manipulation. For non-touch isolation of the tumor, gauze is frequently used to retract or lift up stomach, and to absorb bleeding or lymphatic fluid, which can make dry field.

FUTURE PERSPECTIVE

Ongoing prospective studies

To provide answers to the extent of laparoscopic LND in AGC, phase III trials to confirm the non-inferiority of this procedure to open are ongoing. In Japan, the short-term outcome of the randomized controlled trial to evaluate laparoscopic *vs.* open surgery for AGC (JLSSG0901) has been published in the 30th annual meeting of the Japan Society for Endoscopic Surgery in December 2017, which demonstrated no significant differences in grade 3 and higher postoperative complications between two groups (3.1% *vs*. 4.7%)[28]. In China, CLASS-01 (NCT01609309) has been conducted and the short-term outcomes were already published, demonstrating no difference between LG and OG (15.2% *vs*. 12.9%) in morbidity rate[3]. The final outcomes, namely 3-year DFS, are awaited the publication before long. In Korea, the short-term outcomes of KLASS-02 (NCT01456598) were disclosed in ASCO 2016 meeting[4], which demonstrated less complication rate (16.4% *vs*. 24.3%), less use of analgesics, and faster recovery in LG group. Its primary endpoint, or 3-year relapse free survival, will be analyzed also anytime soon. We should wait for the final results of these three phase-III trials. Especially, not only long-term survival rate but also difference of recurrence pattern should be carefully checked the specific feature in recurrences after LG. Concerning LTG, a Korean group has launched multicenter randomized controlled trial for application of LTG with LND for gastric cancer (KLASS-06; NCT03385018) in 2018. However, some researchers suggested that LTG for AGC should be carried out on a trial basis until the definitive results are available, and surgeons should be particularly attentive to No.10 or 11d LND without lessening the quality of LND compared with open total gastrectomy[29]. The data from these studies are expected to decide future directions for the indication of LG for AGC.

Neo adjuvant chemotherapy

A few phase III trials and retrospective studies have provided supportive evidence that NAC results in high compliance, as well as other favorable factors such as high rate of R0 resection and tumor regression, which lead to a better prognosis[17,30,31]. There have been many RCT comparing LG with OG as mentioned above. However, very few on the comparison between LG + NAC and OG + NAC. Recently, a phase II trial to which evaluate the safety and efficacy of LG after NAC for distal advanced gastric cancer and which provide theoretical basis for conducting a multicenter phase III verification clinical trial conducted in China[32]. Long term follow up and piling up the cases will be necessary in the future.

Conversion surgery

The term “conversion therapy” describes a therapeutic concept in which the treatment strategy is converted by chemotherapy to curative surgery through an oncosurgical approach. The terms “conversion surgery” or “adjuvant surgery” can be applied to the operations performed for conversion therapy. Yoshida *et al.*[33] proposed that the indications for conversion therapy include patients with marginally resectable metastasis, some patients who are incurable and unresectable except certain circumstances of local palliation needs, and patients with noncurable metastasis in whom an R0 resection can be expected after a satisfactory response to chemotherapy. There were long-term survivors who underwent conversion surgery for such patients. The median survival time of the patients who underwent surgical resection was 30.5 months, as opposed to those who received chemotherapy alone at 11.3 months[34]. If the feasibility of this concept will be estimated in the near future by large-scale retrospective and prospective cohort studies, laparoscopic approach may be applied to treatment for minimal invasive surgery.

Robotic surgery

Robotic surgical instruments seem to have potential to cover disadvantages of LG, such as insufficiency of forceps’ degree of freedom or surgeons’ physiological tremor at the tip of device[35]. It is suggested by experts that the use of a surgical robot may be beneficial for more complicated procedures, including more advanced cancer disease[36]. Although a number of robot-assisted gastrectomy (RAG) are rapidly increasing since RAG has been covered by insurance in April 2018 in some limited institutes, several issues remain to be solved regarding clinical indication, short- and long-term outcomes, cost- effectiveness, and stress of surgeons[37-39]. Recently, Li *et al.*[40] reported a retrospective PSM analysis that the overall postoperative complication rate was 13.4% and 11.6% in the RAG and LG groups, with no significant difference, and the 3-year OS and recurrence rates of the RAG and LG groups were also comparable (78.6% *vs.* 74.1%; 18.8% *vs.* 21.4%; respectively). Moreover, multicenter prospective study of RAG *vs.* LG for gastric cancer including AGC has been published in 2016, which demonstrated no significant differences between groups were noted in overall complication and mortality rates, estimated blood loss, rates of open conversion, diet build-up, or length of hospital stay, except for operative time and total costs[41].

Thus, although RAG has evident benefits, it is difficult to assess and compare some advantages at the moment with respect to traditional surgery. Larger randomized prospective trials, well-designed cost-effectiveness analysis, and high-quality comparative-effectiveness research are needed before robotic resection can be considered an acceptable alternative for patients with AGC. Probably, the main indication for RAG is when it serves as an adjunct to laparoscopic resection in selected patients with local advanced tumors requiring a D2 LND.

CONCLUSION

LG with D2 lymph node dissection by expert surgeons under the cautious indications could be acceptable treatment for locally AGC. On the other hand, we should keep searching for solutions to the technical or oncological issues, and long-term outcome of phase III study should be warranted for standard treatment.

DECLARATIONS

Authors' contributions

Retrieved the data and cited literatures: Shimada M
Provided technical and clinical advices for Shimada M: Amaya S, Munemoto Y, Mitsui T
Read and approved the final manuscript: All authors

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Japanese Gastric Cancer Association. Gastric Cancer Treatment Guidelines 2018 (ver.5). Tokyo: Kanehara-shuppan; 2018. pp. 17-8. (in Japanese)
2. Inaki N, Etoh T, Ohyama T, Uchiyama K, Katada N, et al. A multi-instistional, prospective, phase II feasibility study of laparoscopy-assisted distal gastrectomy with D2 lymph node dissection for locally advanced gastric cancer (JLSSG0901). World J Surg 2015;39:2734-41.
3. Hu Y, Huang C, Sun Y, Su X, Cao H, et al. Morbidity and mortality of laparoscopic versus open D2 distal gastrectomy for advanced gastric cancer: a randomized controlled trial. J Clin Oncol 2016;34:1350-7.
4. Lee HJ, Hyung WJ, Yang HK, Han SU, Park YK, et al. Morbidity of laparoscopic distal gastrectomy with D2 lymphadenectomy compared with open distal gastrectomy for locally advanced gastric cancer: Short term outcomes from multicenter randomized controlled trial (KLASS-02). J Clin Oncol 2016;34:asbtr 4062.
5. Okabe H, Tsunoda S, Obama K, Tanaka E, Hisamori S, et al. Feasibility of laparoscopic radical gastrectomy for gastric cancer of clinical stage II or higher: early outcomes in a phase II study (KUGC04). Ann Surg Oncol 2016;23:S516-23.
6. Li Q, Wang J, Zhang G, Wang J, Yang B, et al. Feasibility and safety comparison of laparoscopy-assisted versus open gastrectomy for advanced gastric carcinoma with D2 lymphadenectomy. Jpn J Clin Oncol 2016;46:323-8.
7. Hao Y, Yu P, Qian F, Zhao Y, Shi Y, et al. Comparison of laparoscopy-assisted and open radical gastrectomy for advanced gastric cancer: a retrospective study in a single minimally invasive surgery center. Medicine 2016;95:25.
8. Lin JX, Huang CM, Zheng CH, Li P, Xie JW, et al. Is all advanced gastric cancer suitable for laparoscopy-assisted gastrectomy with extended lymphadenectomy? A case-control study using a propensity score method. Ann Surg Oncol 2016;23:1252-60.
9. Lee S, Lee H, Lee J. Feasibility and safety of totally laparoscopic radical gastrectomy for advanced gastric cancer: comparison with early gastric cancer. J Gastric Cancer 2018;18:152-60.
10. Li Z, Li B, Bai B, Yu P, Lian B, et al. Long-term outcomes of laparoscopic versus open D2 gastrectomy for advanced gastric cancer. Surgical Oncology 2018;27:441-8.
11. Park YK, Yoon HM, Kim YW, Park JY, Ryu KW, et al. Laparoscopy-assisted versus open D2 distal gastrectomy for advanced gastric cancer: results from a randomized phase II multicenter clinical trial (COACT 1001). Ann Surg 2018;267:638-45.
12. Kinoshita T, Uyama I, Terashima M, Noshiro H, Nagai E, et al. Long-term outcomes of laparoscopic versus open surgery for clinical stage II/III gastric cancer: a multicenter cohort study in Japan (LOC-A study). Ann Surg 2018; doi: 10.1097/SLA.0000000000002768.
13. Xu Y, Hua J, Li J, Shi L, Xue H, et al. Long-term outcomes of laparoscopic versus open gastrectomy for advanced gastric cancer: a large cohort study. Am J Surg 2019;217:750-6.
14. Kurokawa Y, Doki Y, Mizusawa J, Terashima M, Katai H, et al. Bursectomy versus omentectomy alone for resectable gastric cancer (JCOG1001): a phase 3, open-label, randomised controlled trial. Lancet Gastroenterol Hepatol 2018;3:460-8.
15. Etoh T, Sasako M, Ishikawa K, Katai H, Sano T, et al. Extranodal metastasis is an indicator of poor prognosis in patients with gastric carcinoma. Br J Surg 2006;93:369-73.
16. Lee IS, Park YS, Ryu MH, Song MJ, Yook JH, et al. Impact of extranodal extension on prognosis in lymph node-positive gastric cancer. Br J Surg 2014;101:1576-84.
17. Tsuburaya A, Mizusawa J, Tanaka Y, Fukushima N, Nashimoto A, et al. Neoadjuvant chemotherapy with S-1 and cisplatin followed by D2 gastrectomy with para-aortic lymph node dissection for gastric cancer with extensive lymph node metastasis. Br J Surg 2014;101:653-60.
18. Iwasaki Y, Terashima M, Mizusawa J, Katayama H, Nakamura K, et al. Randomized phase III trial of gastrectomy with or without neoadjuvant S-1 plus cisplatin for type 4 or large type 3 gastric cancer: Japan Clinical Oncology Group study (JCOG0501). J Clin Oncol 2018;36:abstr 4046.
19. Sano T, Sasako M, Mizusawa J, Yamamoto S, Katai H, et al. Randomized controlled trial to evaluate splenectomy in total gastrectomy for proximal gastric carcinoma. Ann Surg 2017;265:277-83.
20. Kinoshita T, Shibasaki H, Enomoto N, Sahara Y, Sunagawa H, et al. Laparoscopic splenic hilar lymph node dissection for proximal gastric cancer using integrated three-dimensional anatomic simulation software. Surg Endosc 2016;30:2613-9.
21. Uyama I, Suda K, Sato S. Textbook for Endoscopic Surgery of Fujita Health University. Nankodo Co., Ltd.; 2015. p. 64. (in Japanese)
22. Kim SY, Nam SH, Min JS, Kim MC. Laparoscopic reinforcement suture on staple-line of duodenal stump using barbed suture during laparoscopic gastrectomy for gastric cancer. Ann Surg Treat Res 2017;93:305-9.
23. Yamaguchi T, Fukunaga T, Hiki N. Laparoscopic gastric surgical procedures: distinctive (innovative) operative style of cancer institute hospital, medical view. Japan; 2011. pp. 56-69. (in Japanese)
24. Eto T, Kitano S. Laparoscope assisted distal gastrectomy. Gastroenterological Surgery 2011;34:752-60. (in Japanese)
25. Nobuoka T, Ito T, Kyuno T, Nishidate T, Imamura M, et al. Laparoscopic distal gastrectomy. Gastroenterological Surgery 2014;37:1775-83. (in Japanese)
26. Shimada M, Amaya S, Tatemichi K, Tawara H, Furutani Y, et al. Delicate pancreatic rotating technique using “Thoraco Cotton” in laparoscopic gastrectomy. Int J Gastroenterol Disord Ther 2017;4:133.
27. Hur H, Jeon HM, Kim W. Laparoscopic pancreas- and spleen-preserving D2 lymph node dissection in advanced (cT2) upper-third gastric cancer. Surg Oncol 2008;97:169-72.
28. Etoh T, Ohtsubo D, Misawa K, Kinoshita T, Cho H, et al. Is laparoscopic distal gastrectomy for advanced gastric cancer feasible? Short-term outcomes from a multi-institutional, phase III study (JLSSG0901). Proceeding of the 30th annual meeting of the Japan Society for Endoscopic Surgery, 2017 Dec 7-9. Kyoto, Japan; 2017.
29. Kawaguchi Y, Shiraishi K, Akaike H, Ichikawa D. Current status of laparoscopic total gastrectomy. Ann Gastroenterol Surg 2019;3:14-23.

30. Cunningham D, Allum WH, Stennning SP, Thompson JN, Van de Velde CJ, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med 2006;355:11-20.
31. Ychou M, Boige V, Pignon JP, Conroy T, Bouché O, et al. Perioperative chemotherapy compared with surgery alone for resectable gastroesophageal adenocarcinoma: an FNCLCC and FFCD multicenter phase III trial. J Clinic Oncol 2011;29:1715-21.
32. Li Z, Shan F, Ying X, Zhang L, Ren H, et al. Laparoscopic or open distal gastrectomy after neoadjuvant chemotherapy for advanced gastric cancer: study protocol for a randomised phase III trial. BMJ Open 2018;8:e021633.
33. Yoshida K, Yamaguchi K, Okumura N, Tanahashi T, Kodera Y. Is conversion therapy possible in stage IV gastric cancer: the proposal of new biological categories of classification. Gastric Cancer 2016;19:329-38.
34. Yamaguchi K, Yoshida K, Tanahashi T, Takahashi T, Matsuhashi N, et al. The long-term survival of stage IV gastric cancer patients with conversion therapy. Gastric Cancer 2018;21:315-23.
35. Terashima M, Tokunaga M, Tanizawa Y, Bando E, Kawamura T, et al. Robotic surgery for gastric cancer. Gastric Cancer 2015;18:449-57.
36. Kinoshita T, Kaito A. Current status and future perspectives of laparoscopic radical surgery for advanced gastric cancer. Transl Gastroenterol Hepatol 2017;2:43.
37. Kim MC, Heo GU, Jung GJ. Robotic gastrectomy for gastric cancer: surgical techniques and clinical merits. Surg Endosc 2010;24:610-5.
38. Hashizume M, Sugimachi K. Robot-assisted gastric surgery. Surg Clin North Am 2003;83:1429-44.
39. Song J, Oh SJ, Kang WH, Hyung WJ, Choi SH, et al. Robot-assisted gastrectomy with lymph node dissection for gastric cancer: lessons learned from an initial 100 consecutive procedures. Ann Surg 2009;249:927-32.
40. Li Z, Li J, Li B, Bai B, Liu Y, et al. Robotic versus laparoscopic gastrictomy with D2 lymph node dissection for advanced gastric cancer: a propensity score-matched analysis. Cancer Manag Res 2018;10:705-14.
41. Kim HI, Han SU, Yang HK, Kim YW, Lee HJ, et al. Multicenter prospective comparative study of robotic versus laparoscopic gastrectomyfor gastric adenocarcinoma. Ann Surg 2016;263:103-9.

Mini-invasive Surgery

Editorial

Open Access

Check for updates

Preface of the special issue on "A bespoke approach to rectal cancer resection and management"

Gordon N. Buchanan

Consultant Colorectal Surgeon, Lister Hospital, London SW1W 8RH, UK.

Correspondence to: Mr. Gordon Buchanan, Consultant Colorectal Surgeon, Lister Hospital, Chelsea Bridge Road, London SW1W 8RH, UK. E-mail: gordon.buchanan@hcaconsultant.co.uk

How to cite this article: Buchanan GN. Preface of the special issue on "A bespoke approach to rectal cancer resection and management". *Mini-invasive Surg* 2019;3:8. http://dx.doi.org/10.20517/2574-1225.2019.24

Received: 5 Mar 2019 **Accepted:** 11 Mar 2019 **Published:** 28 Mar 2019

Science Editor: Charles F. Bellows **Copy Editor:** Cai-Hong Wang **Production Editor:** Huan-Liang Wu

Rectal cancer is increasingly managed by super-specialist colorectal and oncological teams - this has only become possible through the belief and drive of many key figures who often, despite lack of support from their peers, persevered in order to define the aspect of care they truly believed beneficial to improve outcomes. It is this collective work across decades that has enabled patients to have choice in scenarios that were often previously both bleak and debilitating. It is a great honour to act as guest editor for this special edition where many of these key international opinion leaders have generously contributed to help coalesce the goal for a bespoke approach to rectal cancer.

Tebala *et al.*[1] discuss the role of enhanced recovery and demonstrate how it can shorten stay and potentially reduce complications in this complex set of patients.

Chouhan *et al.*[2], with input both from the greatly experienced Korean and Australasian teams, have discussed in great depth the potential benefits of the robotic platform and even in early trials noted the trend to reduced conversion *vs.* laparoscopic resection in the obese male - as numbers grow this almost certainly will become more evident. They liken the robot to an open approach with its wrist movement but providing a more magnified view and the benefits of a minimally invasive surgery (MIS) approach. They provide some evidence that the robotic approach may improve survival potentially combined with better pathological outcomes; these benefits are further reviewed by Chen *et al.*[3] from Taiwan who found this technique safe in low lying rectal cancer.

Yellinek and Wexner[4], writing from the Cleveland clinic, discuss an alternative to the robot, namely transanal total mesorectal excision (TaTME), the importance of a registry and training programme though conclude that the single port robot may provide a method for better adopting this technique, potentially as a combined approach and ongoing trial data is awaited. De Nardi[5] suggests that TaTME has comparable functional outcomes compared with the abdominal approach though the COLOR III trial results are eagerly awaited to assess this.

Ishida *et al.*[6] recognise the difficulty associated with learning reduce port surgery, though again note that this technique once mastered may yield benefits in terms reduced operating time over single incision laparoscopic surgery, particularly with advancements in needlescopic surgery.

Ambe and Möslein[7] discuss the role of extended resections in certain mutational and hereditary analyses, making the point that each case must be considered on its own merits after fully informed discussion with patients about the risks and benefits of each approach - this detailed piece provides an up to date review of most of the important hereditary and mutational conditions, how they are classified and defined as well as many operative illustrations pointing out the various surgical approaches possible.

Kumar[8] looks beyond TME and the role of MIS surgery in exenterative surgery, pelvic lymphadenectomy and even abdomino-sacral resection.

Funahashi[9] and colleagues outline their experience in Japanese patients of intersphincteric resection in low lying rectal cancer and how it can lead to organ preservation in many without compromising pathological outcomes - they notes the improved quality of life after preserving as much of the internal anal sphincter as possible.

O'Donohue *et al.*[10] explore whether laparoscopic rectal surgery is non inferior, particularly assessing the COREAN, ALaCaRT and ACOSOG Z6051 trials. The concept of non-inferiority in the short term, *vs.* equivalent long term outcomes should not cloud the picture of the many advantages of an MIS approach, that are likely to be borne out with larger population based studies.

Westwood and West[11] emphasise how pathologists enhance feedback and thus quality of rectal cancer specimens and thus, patient outcomes. This quality control was largely the work of Quirke, coupled with imaging expertise from Brown G working with resection material generated via Heald in TME surgery - initially surgeons felt affronted by resections being graded though with importance on outcome, now entirely value the essential role of feeding this back via their multidisciplinary teams.

Erkan, Kelly and Monson[12] in Florida review the role of the transanal minimally invasive surgery (TAMIS) platform in locally resecting rectal cancer, particularly in T1 lesions or after chemo-radiotherapy and more controversially T2/4 lesions even in palliative scenarios - again Adegbola *et al.*[13] from St Mark's, UK, additionally discuss the role of TAMIS with a robotic platform in exenterative surgery and other scenarios - i.e., trying to avoid major resectional surgery altogether.

Myint[14] discusses the alternative of brachytherapy to radical resection and that patients with knowledge of this may reject MDT recommendations in favour of a more conservative approach - the OPERA database (organ preservation) will help provide useful outcome information in this regard.

All of these articles are well written and many beautifully illustrated, giving a concise appraisal of state of the art techniques. Some highlighted above do not take away all the other well-constructed opinion pieces that expand on the themes generated through principles of TME surgery and multidisciplinary input into this group of patients.

DECLARATIONS

Authors' contributions

Buchanan GN contributed solely to this preface.

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

The author declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Tebala GD, Gordon-Dixon A, Imtiaz M, Shrestha A, Toeima M. Enhanced recovery after rectal surgery: what we have learned so far. Mini-invasive Surg 2018;2:32.
2. Chouhan H, Shin J, Kim SH. Is robotic rectal resection the preferred option for resectable cancer? Mini-invasive Surg 2018;2:18.
3. Chen PJ, Huang CW, Tsai HL, Yeh YS, Su WC, et al. Robotic-assisted total mesorectal excision in low-lying rectal cancer. Mini-invasive Surg 2018;2:43.
4. Yellinek S, Wexner SD. The role of transanal total mesorectal excision in rectal surgery. Mini-invasive Surg 2018;2:22.
5. De Nardi P. Functional results and quality of life after transanal total mesorectal excision. Mini-invasive Surg 2018;2:20.
6. Ishida T, Shigeta K, Okabayashi K, Tsuruta M, Hasegawa H, et al. Reduced-port surgery for rectal cancer. Mini-invasive Surg 2018;2:31.
7. Ambe PC, Möslein G. Surgical management of hereditary colorectal cancer. Mini-invasive Surg 2018;2:37.
8. Kumar NAN, Kammar P, Saklani A. Minimal invasive approach for beyond total mesorectal excision/extended resections in rectal cancer. Mini-invasive Surg 2018;2:19.
9. Funahashi K, Koike J, Shiokawa H, Ushigome M, Kaneko T, et al. Clinical feasibility of sphincter-preserving resection with transanal rectal dissection for low-lying rectal cancer in Japanese patients: a single-center cohort study. Mini-invasive Surg 2018;2:27.
10. O'Donohue PF, Warren CD, Chow CFK. Is laparoscopic rectal surgery really not non-inferior? Mini-invasive Surg 2018;2:24.
11. Westwood AC, West NP. The importance of pathological quality control for rectal surgery. Mini-invasive Surg 2018;2:38.
12. Erkan A, Kelly JJ, Monson JRT. Current state of transanal minimally invasive surgery in the management of rectal cancer. Mini-invasive Surg 2018;2:30.
13. Adegbola SO, Sahnan K, Pellino G, Warusavitarne J. Transanal minimal invasive surgery - pushing the boundaries of transanal surgery. Mini-invasive Surg 2018;2:40.
14. Myint AS, Gerard JP. Minimally invasive contact X-ray brachytherapy as an alternative option in patients with rectal cancer not suitable for bespoke surgical resection. Mini-invasive Surg 2018;2:34.

Mini-invasive Surgery

Review

Open Access

Laparoscopic resection of liver tumors

Ankush Golhar, Vinayak Nikam, Prashantha Rao, Ravi Mohanka

Department of Hepato-Biliary Surgery and Liver Transplant, Global Hospital, Mumbai 400012, India.

Correspondence to: Dr. Ravi Mohanka, Chief Surgeon and Head of Department, Department of Hepato-Biliary Surgery and Liver Transplantation, Global Hospital, Mumbai 400012, India. E-mail: ravimohanka@gmail.com

How to cite this article: Golhar A, Nikam V, Rao P, Mohanka R. Laparoscopic resection of liver tumors. *Mini-invasive Surg* 2019;3:9. http://dx.doi.org/10.20517/2574-1225.2018.58

Received: 21 Aug 2018 **First Decision:** 23 Oct 2019 **Revised:** 23 Feb 2019 **Accepted:** 4 Mar 2019 **Published:** 17 Apr 2019

Science Editor: Fernando Andrés Alvarez **Copy Editor:** Cai-Hong Wang **Production Editor:** Huan-Liang Wu

Abstract

Laparoscopic liver resection is technically challenging compared to open liver surgery and has a steep learning curve. Tumors located in the posterior sector, centrally, in proximity of major vascular pedicles or in a background of liver cirrhosis are surgically more complex with a higher risk of blood loss. There is emerging consensus about indications for laparoscopic liver resection. While laparoscopic approach is considered standard for left lateral sectionectomy and minor laparoscopic liver resections in antero-lateral segments, with increasing experience, major resections, parenchyma sparing resections and even donor hepatectomies are being performed laparoscopically with good outcomes. Laparoscopic liver surgery is feasible and safe for well selected patients by well-trained surgeons with short-term advantages and non-inferior long-term oncologic outcomes.

Keywords: Laparoscopic liver surgery, liver tumors, hepatocellular cancer

INTRODUCTION

Laparoscopic liver resection (LLR) is performed for benign as well as malignant liver tumors. Its adoption has been relatively slow, although the benefits of LLR compared to open liver resection (OLR) are similar to other laparoscopic surgeries, such as lesser peri-operative blood loss, shorter hospital stay and fewer post-operative complications[1]. The first international consensus conference to define its role was held at Louisville (USA) in 2008 where it was suggested that LLR was best suited for solitary lesions smaller than 5 cm in diameter, located in the anterior segments of liver, away from the hepatic hilum or the vena cava so that an adequate resection margins could be obtained[1]. The conference also recommended creation of an international registry for ongoing assessment of outcomes with its increasing adoption by surgeons[1]. More

Table 1. Salient features of recommendations by the First European Guidelines Meeting on Laparoscopic Liver Surgery

Indications for LLR	Comments
1. CRLM	LLR is a valid alternative to OLR in experienced hands for CRLM. As compared to OLR, LLR has better short term outcomes and equivalent oncological and long term survival outcomes for CRLM
	When feasible parenchyma sparing approach should be adopted during LLR, but it should not lead to alteration in the present indications for liver resection in CRLM
	Combined liver and colon resection should be adopted in highly selected cases only for CRLM. Timing of colon and liver resection in synchronous disease is similar to OLR
2. Benign tumors and non-colorectal liver metastases	Benign tumors and tumors with malignant potential are suitable for LLR with satisfactory short term post-operative outcomes. LLR should not alter the indications for liver resection in such tumors
	LLR is an acceptable approach for metastases from neuroendocrine and non-colorectal liver metastases
3. HCC	In selected patients LLR offers better short term post-operative outcomes such as decreased morbidity and hospital stay without compromising oncological outcomes
	Indications LLR are similar to those for OLR in case of HCC. Laparoscopic resection for tumors located in postero-superior (Segment 1, 4a, 7, 8) segments should be done only at experienced centers
	In experienced hands major LLR is appropriate option to OLR in highly selected patients
	Outcomes of left and right laparoscopic hepatectomy should be reported separately as they vary significantly. Laparoscopic right hepatectomy should be further developed in major liver centers
	In patients with HCC, as for other indications, selective use of intermittent Pringle's maneuver may help decrease the blood loss without detrimental effect on liver function
	In patients with cirrhosis, LLR may be associated with less risk of post-operative ascites and liver decompensation. Minor LLR for single and peripheral HCC in selected Child B patients warrants cautious approach and further evaluation is needed
4. LDH	LDH requires expertise in both liver transplantation and laparoscopic liver surgery
	Laparoscopic left lateral sectionectomy for pediatric liver transplantation offers reduction in blood loss, morbidity and hospital stay and should be considered equivalent to OLR
	Adult liver transplantation: LDH is not yet standardized in terms of donor selection and surgical technique. Its safety and postoperative outcomes needs to be evaluated in experienced center further

CRLM: colorectal liver metastases; LLR: laparoscopic liver resection; OLR: open liver resection; LDH: laparoscopic donor hepatectomy; HCC: hepatocellular carcinoma

recently, the second international consensus conference held at Morioka (Japan) in 2014, recommended that minor LLR to be considered as a standard practice and major LLR as an innovative procedure, under exploration[2]. The first European Guidelines Meeting on Laparoscopic Liver Surgery at Southampton in February 2017 summarized available evidence for LLR for different liver tumors, types of resections and clinical situations. Few salient points relevant to this article have been summarized in Table 1[3].

TECHNICAL CHALLENGES IN LAPAROSCOPIC LIVER SURGERY

Detailed understandings of the hilar and segmental anatomy of the liver and adequate experience with OLR are pre-requisites for performing LLR[3]. The laparoscopic view is caudo-cranial for hilar dissection as well as the parenchymal transection compared to the antero-posterior view in OLR[4]. Liver being a heavy and deep seated organ, especially its right lobe, may be difficult to maneuver. Liver tumors most often develop in a background of liver cirrhosis with stiff parenchymal tissue and collaterals due to portal hypertension, which makes the operation more difficult and increases the risk of bleeding[4]. Tumors located in postero-superior or central segments, large tumors and intra-abdominal adhesions secondary to previous hepato-pancreato-biliary (HPB) surgeries can further make LLR more difficult[4]. The learning curve for LLR is steep requiring about 45 to 60 cases before improvements in operative time, blood loss and post-operative complications are apparent[5,6].

TECHNIQUE OF LAPAROSCOPIC LIVER SURGERY

LLR may be performed purely laparoscopic, hand-assisted, using the hybrid technique or by robotic assisted approaches[4,5,7,8]. Port placement varies by tumor location, type of resection planned, patient positioning and surgeon's preference[7]. Generally an umbilical port is used for the camera and directed towards the tumor and about 4 to 5 working ports for graspers, suction, ultrasonic or sealing energy devices, cavitron ultrasonic surgical aspirator (CUSA) and others are placed on either side of the camera port at a reasonable distance[7]. In hand-assisted technique, in addition to the regular ports a hand-port is used to help mobilize the liver and retract both cut surfaces during the transection[7]. The hybrid technique involves mobilization laparoscopically followed by parenchymal transection and specimen extraction through a small open incision and may combine the benefits of both techniques[8]. Robot assisted LLR offers the advantage of a 3 dimensional vision and dexterity of robotic arms whereas parenchymal transection is performed laparoscopically with access to better retractors and CUSA. Robot assisted LLR may be more suited for postero-superior segment tumors[4].

LLR involves the following steps, not necessarily in the same order:

- Hilar dissection followed by inflow control is obtained fairly early during the LLR. Inflow control may be obtained by intra-fascial or Glissonian approach depending on tumor factors and surgeon's preferences, as both are safe[3,6,9]. Biliary anatomy can be deciphered using fluorescence, conventional contrast or combined cholangiography[10]. Either intrabiliary injection of 0.025-0.5 mg/mL indocyanine green (ICG) or intravenous injection of 2.5 mg ICG fifteen minutes before fluoroscopy can be used to identify biliary anatomy and plan division of the bile ducts[10].
- Approach for laparoscopic right hepatectomy may be by anterior approach or conventional approach after mobilisation of liver[3,11,12].
- The transection plane is identified for left or right hepatic resection by unilateral clamping vascular inflow of same side at the hilum or by fluorescence imaging with ICG[10]. After clamping the portal pedicle supplying segment to be removed, boundaries of hepatic segments can be visualized following injection of 0.25-2.5 mg/mL ICG into the portal veins or by intravenous injection of 2.5 mg ICG[10]. For segmental or non-anatomical resection, the transection plane may be identified using the Glissonian approach or intra-operative Doppler Ultrasonography[3,13].
- Cholecystectomy: some surgeons although disconnect the cystic artery and duct, retain the gall bladder for retraction until later in the case.
- Pringle's maneuver, the practice is variable with few centers not using it at all and others using it in all cases[3,11]. Parenchymal transection is the most challenging part of the surgery with large variations in technique, instruments, equipment used between different surgeons also depending on the tumor size, location and nature of background liver[3,14]. Various transection techniques have been described including the use of the modern dissectors/ aspirators [laparoscopic CUSA, WaterJet (Helix Hydro-Jet Erbe Elektromedizin GmbH, Tuebingen, Germany), *etc.*], sealing devices [Harmonic scalpel (Ethicon Endo Surgery INC - Johnson & Johnson Medical SPA, Somerville, NJ), Ligasure (Valleylab Inc., Boulder, Colorado, USA), bipolar sealing devices, *etc.*], and vascular staplers[3,14]. Superficial transection can be performed with any energy device, but deeper transection should be performed with an appropriate device to identify deep vascular structures[3]. While large vessels should be secured with vascular staplers or Hem-o-lok clips (Weck Closure Systems, Research Triangle Park, Durham, NC, USA Manufacturer), smaller vessels can be divided using metal or Hem-o-lok clips or sealed with an energy device[3,14]. Staplers for parenchymal transection should be used with caution because it lacks precision and identification of the underlying structures[3]. Argon Plasma Coagulator (APC) should be used for haemostasis with extreme caution due to the potential risk of gas embolism[3]. More recently, a novel technique has been described, called "superficial pre-coagulation, sealing and transection method", which utilizes a soft coagulation system to create a 5 mm zone of pre-coagulation causing shrinkage and blockage of micro-vessels and bile ducts smaller than 1 mm without causing sparks and tissue desiccation[15]. This is followed by liver parenchymal dissection using CUSA in a bloodless plane created by pre-coagulation[15]. Use of the laparoscopic hanging maneuver is also reported by few surgeons[3,16]. Intra-operative Doppler Ultrasonography (IOUS) is used for confirming adequate tumor margin from the cut surface[11].
- The specimen may be extracted using an appropriate retrieval bag generally through a midline or pfannenstiel incision.

TECHNICALLY COMPLEX SITUATIONS

For centrally located or deep tumors, visual guidance and tactile feedback are limited, and IOUS may be essential for tumor localization, assessment for satellite nodules, planning the resection plane and determining spatial relationship of the tumor with major blood vessels[13]. Sub-capsular tumors can be identified by intra-operative fluorescence imaging following preoperative intravenous injection of ICG (0.5 mg per kg body weight) usually given within two weeks of surgery[10]. “Diamond technique” has been described for centrally located parenchymal sparing liver resection[17].

Anatomic liver resection for tumors located in postero-superior (segment 7, segment 8) segments and segment 4a are technically difficult because of difficulty of access and are associated with more blood loss, risk of conversion to open surgery or change to hemi-hepatectomy[18-21]. Strategies such as use of a spacer, left lateral position, intercostal ports, hand-assisted, robot-assisted or other approaches have demonstrated reduced blood loss and need for conversion in such tumors[18-21].

Only few cases of isolated laparoscopic caudate lobe resection are reported as it is technically challenging[22,23]. Laparoscopy provides good vision of the caudate lobe between the hilar plate and the vena cava from the right side. Division of the gastro-hepatic ligament facilitates visualization and resection from the left side[22,23]. LLR is safe and non-inferior to OLR in the cirrhotic liver too, with lesser blood loss and shorter hospital stay reported in few studies[24].

LLR DIFFICULTY SCORING SYSTEMS AND SELECTION CRITERIA

The degree of difficulty of LLR depends upon multiple factors[25]. A retrospective analysis has found a good agreement between the difficulty level assessed by the surgeon and a difficulty index based on tumor location, extent of liver resection, tumor size, proximity to major vessels, and liver function[25]. Although such scoring systems need further refinement and prospective validation, they can be helpful in assessment of trainee surgeon’s skills, guide their training, better estimate risks of the procedure[25]. Appropriate patient selection, practicing and honing LLR skills is paramount for success[25]. Most laparoscopic liver surgeons would accept tumor size of < 5 cm, fewer than three lesions without macroscopic vascular invasion or the need for biliary reconstruction as criteria for LLR[2,26].

RESULTS OF LAPAROSCOPIC VERSUS OPEN HEPATECTOMY

Short term outcomes

Comparison of LLR and OLR

LLR has been found to be significantly better compared to OLR for minor hepatectomies for short-term outcomes such as the operation time, blood loss, and post-operative hospital stay[27]. Although there are numerous case-reports and retrospective series of LLR, few well-designed randomized controlled trials (RCTs) and meta-analyses are currently available[27-35]. Meta-analyses show that LLR has clinical benefits over OLR with significant reduction in blood loss, blood transfusion, complications and hospital stay with comparable operative time and resection margin positivity. However potential biases due to low statistical power of many studies included in the meta-analyses cannot be undermined[28-35]. The results of these studies are summarized in Table 2.

Long term outcomes

Hepatocellular carcinoma

Current evidence suggests that local tumor recurrence, disease free survival and overall survival are similar between laparoscopic and open resections[39-42]. The results of these studies are summarized in Table 3. Although meta-analyses indicate that LLR for hepatocellular carcinoma (HCC) is comparable to OLR in oncological and survival outcomes, they lacked RCTs[36-39].

Table 2. Previous studies comparing laparoscopic and open liver resection

Author	Type	Blood loss	Transfusion	Operative time	Hospital stay	Complications	Resection margin
Simillis *et al*.[28] (2007)	Meta-analysis 8 studies	LLR < OLR	No significant difference	No significant difference	LLR < OLR	No significant difference	No significant difference
Zhou *et al*.[29] (2011)	Meta-analysis 21 studies	LLR < OLR	LLR < OLR	No significant difference	LLR < OLR	LLR < OLR	No significant difference
Rao *et al*.[30] (2012)	Systematic review 10 studies	LLR < OLR	LLR < OLR	No significant difference	LLR < OLR	LLR < OLR	No significant difference
Fancellu *et al*.[31] (2011)	Meta-analysis 9 studies	LLR < OLR	LLR < OLR	No significant difference	LLR < OLR	LLR < OLR	No significant difference
Li *et al*.[32] (2012)	Meta-analysis 10 studies	LLR < OLR	LLR < OLR	No significant difference	LLR < OLR	LLR < OLR	No significant difference
Xiong *et al*.[33] (2012)	Meta-analysis 16 studies	LLR < OLR	LLR < OLR	No significant difference	LLR < OLR	LLR < OLR	No significant difference
Yin *et al*.[34] (2013)	Meta-analysis 15 studies	LLR < OLR	LLR < OLR	No significant difference	LLR < OLR	LLR < OLR	No significant difference
Fretland *et al*.[35] (2018)	RCT	No significant difference	No significant difference	No significant difference	LLR < OLR	LLR < OLR	No significant difference

LLR: laparoscopic liver resection; OLR: open liver resection; RCT: randomized controlled trials

Colorectal liver metastases

Recently published meta-analysis on LLR for colorectal liver metastases (CRLM) concluded that LLR is a beneficial alternative to OLR in selected patients and does not compromise oncological outcomes including surgical margins, tumor recurrence, disease-free survival or 5-year overall survival, with even a possibility of better 3-year overall survival[40]. Even though this meta-analysis used propensity matching for compensating for selection bias, differences in proportions of major and minor resections and studies with low statistical power might be a potential source of bias[40]. In a recently completed randomized control trial (OSLO-COMET trial) of 280 patients with CRLM, randomized either to laparoscopic (n = 133) or open (n = 147) liver resection; blood loss, operative time and resection margins were similar in both groups[38] while the post-operative hospital stay was shorter with laparoscopic surgery (53 h *vs.* 96 h), complications were significantly less (19% *vs.* 31%), costs were similar at four months while patients in the laparoscopic group gained 0.011 quality adjusted life years[35].

ADVANCES IN LLR

The scope for LLR is increasing with improvements in LLR skills, availability of surgical gadgets and use of the robotic platform[41]. Robotic assistance is promising to aid difficult LLRs such as postero-superior resections, non-anatomical resections along angulated or curvilinear resection planes, those requiring complex vascular and biliary reconstructions, but these need further refinement in skills and prospective validation[41]. Even single incision laparoscopic liver resection has been reported in very suitable tumors[42-44]. Few surgeons have reported the feasibility and safety of laparoscopic re-resections for malignant liver tumors, with a satisfactory conversion rate of 15%, although with significantly greater blood loss and operative time compared to primary LLR[45,46]. Laparoscopic re-resection of liver tumors may be feasible even after previous OLR, up to two prior LLRs, after previous major hepatectomy, even in cirrhotic livers and postero-superiorly located tumors[47]. Recent advances in LLR also include laparoscopic living donor hepatectomy and laparoscopic associating liver partition and portal vein ligation amongst others[48].

SUMMARY

LLR is becoming widely accepted for the treatment of both benign and malignant liver tumors especially HCC and CRLM. Laparoscopic left lateral sectionectomy and minor laparoscopic liver resection are now

Table 3. Studies comparing long-term outcomes of laparoscopic and open liver resection for HCC

Study	Type	1-year survival	3-year survival	5-year survival	1-year DFS	3-year DFS	5-year DFS	Overall and DFS
Parks *et al.*[36] (2014)	Meta-analysis	L - 92% O - 91.3%	L - 77.7% O - 76.5%	L - 61.9% O - 56.5%	NA	NA	NA	NA
Kim *et al.*[37] (2014)	Case matched with PSM	L - 100% O - 96.5%	L - 100% O - 92.2%	L - 92.2% O - 87.7%	L - 81.7% O - 78.6%	L - 61.7% O - 60.9%	L - 54% O - 40.1%	NSD
Han *et al.*[38] (2015)	Case matched with PSM	L - 91.6% O - 93.1%	L - 87.5% O - 87.8%	L - 76.4% O - 73.2%	L - 69.7% O - 74.7%	L - 52% O - 49.5%	L - 44.2% O - 41.2%	NSD
Takahara *et al.*[39] (2015)	Case matched with PSM	L - 95.8% O - 95.8%	L - 86.2% O - 84%	L - 76.8% O - 70.9%	L - 83.7% O - 79.6%	L - 58.3% O - 50.4%	L - 40.7% O - 39.3%	NSD

HCC: hepatocellular carcinoma; DFS: disease free survival; PSM: propensity score matching; L: laparoscopic liver resection; O: open liver resection; NSD: no significant difference; NA: not available

considered standard approaches. Major laparoscopic hepatectomy has been shown to be feasible and safe at few select experienced centers. Few meta-analyses have shown that LLR is better than OLR with better short-term and cosmetic outcomes. Long-term oncologic and survival outcomes have been found to be similar to open liver resection in case-matched studies. Although LLR has a steep learning curve, indications for it are expanding fast with advances in laparoscopic techniques and skills.

CONCLUSION

LLR is a safe and effective approach to liver surgery for well selected patients in the hands of well trained surgeons with experience in hepatobilliary and laparoscopic surgery. The current scientific support in its favour is limited to case series, expert consensus recommendations, guidelines, meta-analyses with very few matched controlled studies and a single randomised controlled trial.

The learning curve is still a problem.

Randomized trials and structured training will help benefit more patients with the advancement in this technique.

DECLARATIONS

Authors' contributions

Wrote part of the article: Golhar A, Rao P
Wrote part of the article and reviewed: Nikam V
Conceptualized the article, researched and wrote the outline and part of the article: Mohanka R

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Buell JF, Cherqui D, Geller DA, O'Rourke N, Iannitti D, et al. The international position on laparoscopic liver surgery: The Louisville Statement, 2008. Ann Surg 2009;250:825-30.
2. Wakabayashi G, Cherqui D, Geller DA, Buell JF, Kaneko H, et al. Recommendations for laparoscopic liver resection: a report from the second international consensus conference held in Morioka. Ann Surg 2015;261:619-29.
3. Hilal MA, Aldrighetti L, Dagher I, Edwin B, Torisi RI, et al. The Southampton consensus Guidelines for laparoscopic liver surgery. Ann surg 2018;268:11-8.
4. Boggi U, Caniglia F, Vistoli F, Costa F, Pieroni E, et al. Laparoscopic robot-assisted resection of tumors located in posterosuperior liver segments. Updates Surg 2015;67:177-83.
5. Brown KM, Geller DA. What is the Learning Curve for Laparoscopic Major Hepatectomy? J Gastrointest Surg 2016;20:1065-71.
6. Lin CW, Tsai TJ, Cheng TY, Wei HK, Hung CF, et al. The learning curve of laparoscopic liver resection after the Louisville statement 2008: Will it be more effective and smooth? Surg Endosc 2016;30:2895-903.
7. Fong Y, Jarnagin W, Conlon KC, Demattero R, Dougherty E, et al. Hand assisted laparoscopic liver resection: Lessons from initial experience. Archives of Surgery 2000;135:845-9.
8. Koffron AJ, Kung RD, Auffenberg GB, Abecassis MM. Laparoscopic liver surgery for everyone: the hybrid method. Surgery 2007;142:463-8; discussion 468.e1-2.
9. Machado MA, Surjan RC, Basseres T, Schadde E, Costa FP, et al. The laparoscopic Glissonian approach is safe and efficient when compared with standard laparoscopic liver resection: Results of an observational study over 7 years. Surgery 2016;160:643-51.
10. Kudo H, Ishizawa T, Tani K, Harada N, Ichida A, et al. Visualization of subcapsular hepatic malignancy by indocyanine-green fluorescence imaging during laparoscopic hepatectomy. Surg Endosc 2014;28:2504-8.
11. Chen HW, Deng FW, Wang FJ, Li JY, Lai EC, et al. Laparoscopic Right Hepatectomy Via an Anterior Approach for Hepatocellular Carcinoma. JSLS 2018;22:e2017.00084.
12. Soubrane O, Schwarz L, Cauchy F, Perotto LO, Brustia R, et al. A conceptual technique for laparoscopic right hepatectomy based on facts and oncologic principles: the caudal approach. Ann Surg 2015;261:1226-31.
13. Torzilli G, Makuuchi M. Intraoperative ultrasonography in liver cancer. Surg Oncol Clin N Am 2003;12:91-103.
14. Otsuka Y, Kaneko H, Cleary SP, Buell JF, Cai X, et al. What is the best technique in parenchymal transection in laparoscopic liver resection? Comprehensive review for the clinical question on the 2nd International Consensus Conference on Laparoscopic Liver Resection. Journal of Hepato-Biliary-Pancreatic Sciences. 2015;22:363-70.
15. Itano O, Ikoma N, Takei H, Oshima G, Kitagawa Y. The superficial precoagulation, sealing, and transection method: a "bloodless" and "ecofriendly" laparoscopic liver transection technique. Surg Laparosc Endosc Percutan Tech 2015;25:e33-6.
16. Dokmak S, Ben Safta Y, Ftériche FS, Aussilhou B, Belghiti J. Pure laparoscopic right hepatectomy with the hanging maneuver for multiple hepatocellular adenomas. Ann Surg Oncol 2014;21:3800-1.
17. Cipriani F, Shelat VG, Rawashdeh M, Francone E, Aldrighetti L, et al. Laparoscopic parenchymal-sparing resections for nonperipheral liver lesions, the diamond technique: technical aspects, clinical outcomes, and oncologic efficiency. J Am Coll Surg 2015;221:265-72.
18. Kim YK, Han HS, Yoon YS, Cho JY, Lee W. Total anatomical laparoscopic liver resection of segment 4 (S4), extended S4, and subsegments S4a and S4b for hepatocellular carcinoma. J Laparoendosc Adv Surg Tech A 2015;25:375-9.
19. Ikeda T, Toshima T, Harimoto N, Yamashita Y, Ikegami T, et al. Laparoscopic liver resection in the semiprone position for tumors in the anterosuperior and posterior segments, using a novel dual-handling technique and bipolar irrigation system. Surg Endosc 2014;28:2484-92.
20. Lee W, Han HS, Yoon YS, Cho JY, Choi Y, et al. Role of intercostal trocars on laparoscopic liver resection for tumors in segments 7 and 8. J Hepatobiliary Pancreat Sci 2014;21:65-8.
21. Morise Z. Laparoscopic liver resection for posterosuperior tumors using caudal approach and postural changes: a new technical approach. World J Gastroenterol 2016;22:10267-74.
22. Salloum C, Lahat E, Lim C, Doussot A, Osseis M, et al. Laparoscopic isolated resection of caudate lobe (Segment 1): a safe and versatile technique. J Am Coll Surg 2016;222:e61-6.
23. Dulucq JL, Wintringer P, Stabilini C, Mahajna A. Isolated laparoscopic resection of the hepatic caudate lobe: surgical technique and a report of 2 cases. Surgical Laparoscopy Endoscopy & Percutaneous Techniques 2006;16:32-5.
24. Twaij A, Pucher PH, Sodergren MH, Gall T, Darzi A, et al. Laparoscopic vs open approach to resection of hepatocellular carcinoma in patients with known cirrhosis: systematic review and meta-analysis. World J Gastroenterol 2014;20:8274-81.
25. Ban D, Kudo A, Ito H, Mitsunori Y, Matsumura S, et al. The difficulty of laparoscopic liver resection. Updates Surg 2015;67:123-8.
26. Shelat VG, Cipriani F, Basseres T, Armstrong TH, Takhar AS, et al. Pure laparoscopic liver resection for large malignant tumors: does size matter? Ann Surg Oncol 2015;22:1288-93.
27. Carswell KA, Sagias FG, Murgatroyd B, Rela M, Heaton N, et al. Laparoscopic versus open left lateral segmentectomy. BMC surgery 2009;9:14.
28. Simillis C, Constantinides VA, Tekkis PP, Darzi A, Lovegrove R, et al. Laparoscopic versus open hepatic resections for benign and malignant neoplasms - a meta-analysis. Surgery 2007;141:203-11.
29. Zhou YM, Shao WY, Zhao YF, Xu DH, Li B. Meta-analysis of laparoscopic versus open resection for hepatocellular carcinoma. Dig Dis Sci 2011;56:1937-43.
30. Rao A, Rao G, Ahmed I. Laparoscopic or open liver resection? Let systematic review decide it. Am J Surg. 2012;204:222-31.

31. Fancellu A, Rosman AS, Sanna V, Nigri GR, Zorcolo L, et al. Meta-analysis of trials comparing minimally-invasive and open liver resections for hepatocellular carcinoma. J Surg Res 2011;171:e33-45.
32. Li N, Wu YR, Wu B, Lu MQ. Surgical and oncologic outcomes following laparoscopic versus open liver resection for hepatocellular carcinoma: a meta-analysis. Hepatol Res 2012;42:51-9.
33. Xiong JJ, Altaf K, Javed MA, Huang W, Mukherjee R, et al. Meta-analysis of laparoscopic vs open liver resection for hepatocellular carcinoma. World J Gastroenterol 2012;18:6657-68.
34. Yin Z, Fan X, Ye H, Yin D, Wang J. Short- and long-term outcomes after laparoscopic and open hepatectomy for hepatocellular carcinoma: a global systematic review and meta-analysis. Ann Surg Oncol 2013;20:1203-15.
35. Fretland AA, Dagenborg VJ, Bjørnelv GM, Kazaryan AM, Kristiansen R, et al. Laparoscopic versus open resection for colorectal liver metastases. Annals of surgery. 2018;267:199-207.
36. Parks KR, Kuo YH, Davis JM, O' Brien B, Hagopian EJ. Laparoscopic versus open liver resection: a meta-analysis of long-term outcome. HPB (Oxford) 2014;16:109-18.
37. Kim H, Suh KS, Lee KW, Yi NJ, Hong G, et al. Long-term outcome of laparoscopic versus open liver resection for hepatocellular carcinoma: a case-controlled study with propensity score matching. Surg Endosc 2014;28:950-60.
38. Han HS, Shehta A, Ahn S, Yoon YS, Cho JY, et al. Laparoscopic versus open liver resection for hepatocellular carcinoma: case-matched study with propensity score matching. J Hepatol 2015;63:643-50.
39. Takahara T, Wakabayashi G, Beppu T, Aihara A, Hasegawa K, et al. Long-term and perioperative outcomes of laparoscopic versus open liver resection for hepatocellular carcinoma with propensity score matching: a multi-institutional Japanese study. J Hepatobiliary Pancreat Sci 2015;22:721-7.
40. Zhang XL, Liu RF, Zhang D, Zhang YS, Wang T. Laparoscopic versus open liver resection for colorectal liver metastases: a systematic review and meta-analysis of studies with propensity score-based analysis. Int J Surg 2017;44:191-203.
41. Tranchart H, Ceribelli C, Ferretti S, Dagher I, Patriti A. Traditional versus robot-assisted full laparoscopic liver resection: a matched-pair comparative study. World J Surg 2014;38:2904-9.
42. Ban D, Kudo A, Irie T, Ochiai T, Aihara A, et al. Advances in reduced port laparoscopic liver resection. Asian J Endosc Surg. 2015;8:11-5.
43. Tan EK, Lee VT, Chang SK, Ganpathi IS, Madhavan K, et al. Laparoendoscopic single-site minor hepatectomy for liver tumors. Surg Endosc 2012;26:2086-91.
44. Shetty GS, You YK, Choi HJ, Na GH, Hong TH, et al. Extending the limitations of liver surgery: outcomes of initial human experience in a high-volume center performing single-port laparoscopic liver resection for hepatocellular carcinoma. Surg Endosc 2012;26:1602-8.
45. Goh BK, Teo JY, Chan CY, Lee SY, Cheow PC, et al. Review of 103 Cases of Laparoscopic Repeat Liver Resection for Recurrent Hepatocellular Carcinoma. J Laparoendosc Adv Surg Tech A 2016;26:876-81.
46. Shelat VG, Serin K, Samim M, Besselink MG, Al Saati H, et al. Outcomes of repeat laparoscopic liver resection compared to the primary resection. World J Surg 2014;38:3175-80.
47. Hu M, Zhao G, Xu D, Liu R. Laparoscopic repeat resection of recurrent hepatocellular carcinoma. World J Surg 2011;35:648-55.
48. Schön MR, Justinger C. Laparoscopic liver resection. Chirurg. 2017;88:469-75.

Muttin *et al. Mini-invasive Surg* 2019;3:10
DOI: 10.20517/2574-1225.2018.005

Mini-invasive Surgery

Review

Open Access

Check for updates

The role of the renal biopsy and surveillance in the management of small renal masses

Fabio Muttin[1], **Eric Barret**[2]

[1]Unit of Urology, Division of Experimental Oncology, Urological Research Institute (URI), IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, 20132 Milano, Italy.
[2]Department of Urology, Institut Mutualiste Montsouris, Paris 75014, France.

Correspondence to: Dr. Eric Barret, Department of Urology, Institut Mutualiste Montsouris, Paris 75014, France. E-mail: eric.barret@imm.fr

How to cite this article: Muttin F, Barret E. The role of the renal biopsy and surveillance in the management of small renal masses. *Mini-invasive Surg* 2019;3:10. http://dx.doi.org/10.20517/2574-1225.2018.005

Received: 30 Nov 2018 **First Decision:** 14 Jan 2019 **Revised:** 7 Mar 2019 **Accepted:** 11 Mar 2019 **Published:** 17 Apr 2019

Science Editor: Richard Lawrence John Naspro **Copy Editor:** Cai-Hong Wang **Production Editor:** Huan-Liang Wu

Abstract

Cross-sectional imaging shows a limited diagnostic accuracy for the histological discrimination of small renal masses (SRM). In this scenario, a renal tumor biopsy is a safe, feasible and effective diagnostic tool that can guide treatment strategy by providing the histological characterization of a SRM. Although nephron-sparing surgery is still considered the gold standard treatment for patients with SRM, more and more evidence suggests that active surveillance (AS) is a reasonable alternative option, especially in old and comorbid patients. Indeed, owing to the relatively slow growth and favorable biology of SRM, AS followed up by, if necessary, a delayed intervention provides an optimal oncological outcome with low rates of systemic progression or death.

Keywords: Small renal masses, cross-sectional imaging, renal biopsy, surveillance

INTRODUCTION

Traditionally, kidney cancer is one of the few tumors that is only treated if there is a radiological probability of malignancy. This concern is related to the limited diagnostic accuracy of computed tomography and magnetic resonance imaging in the histologic characterization of small renal masses (SRM)[1]. In recent years, a percutaneous renal tumor biopsy (RTB) has emerged as a promising diagnostic tool that may help in the clinical decision-making process by distinguishing benign from malignant radiological inconclusive renal lesions, and thus may be considered suitable for patients who are candidates for either active surveillance or nephron-sparing treatments[1-3].

Renal tumor biopsy

In the context of SRM, RTB has been used to identify low- and high-risk malignant renal tumors, to reveal a suspected metastasis in a non-renal neoplasm, to exclude lymphoma or abscess or, when an ablative therapy (e.g., radiofrequency ablation) is planned, to obtain the histology or to confirm the success of the treatment[4]. Contraindications include comorbid and frail patients only suitable for conservative management irrespective of biopsy results; patients with coagulation impairment; patients with a contrast-enhanced renal mass for whom surgery is already planned[1,4].

According to a patient's habits, anatomical tumor location and personal experience, ultrasounds and computed tomography are conventionally used for guidance when RTBs are performed. Tissue sampling can be realized with fine needle aspiration (FNA) and/or core biopsy (CB)[1,4]. In FNA, a twenty-one-gauge needle is inserted through a coaxial sheath to obtain multiple cytologic samples while limiting discomfort and the risk of tumor seeding. For CB, an eighteen-gauge needle with the same coaxial technique provides better diagnostic samples when at least 10 mm long cores are taken from the central and peripheral zones while avoiding necrotic areas.

In a recent systematic review and meta-analysis, CBs have been found to have a better diagnostic accuracy for the detection of malignancy compared to FNA, with a sensitivity of 99.1% *vs*. 93.2% and a specificity of 99.7% *vs*. 89.8%, respectively[3]. Higher diagnostic accuracy is reached when large solid exophytic lesions are biopsied or when a combination of the two techniques is performed[1,2]. A non-diagnostic result can occur in up to 8%-14.7% of all RTB (range 0%-22.6% for CB and 0%-36% for FNA). However, a repeated biopsy is diagnostic in > 90% of cases. After surgical resection, the positive and negative predictive values of RTB are > 99% and 70%, respectively[2,3,5,6]. When focusing on SRM only, RTB shows a sensitivity of 99.7% and a specificity of 98.2%. Furthermore, after surgical resection of SRM only, the concordance rate for tumor histotype is 96% while the concordance rate for tumor grade is 66.7% and increases to 86.5% when a simplified low-high grading system is used[3].

Overall, RTB is feasible and safe when the coaxial technique is used. Morbidity after percutaneous sampling is low (8.1%) and complications include spontaneous resolving subcapsular/perinephric hematoma (4.3%-4.9%), clinically significant pain (1.2%-3%), self-limiting hematuria (1%-3.15%), pneumothorax (0.6%), hemorrhage requiring blood transfusions (0.4%-0.7%) and infections. Fewer than 1% of the patients experience major complications such as a gross hematuria or a pseudoaneurysm that requires embolization. Anecdotal cases are reported for tumor seeding along the needle tract[3,5].

Active surveillance

Active surveillance (AS) is defined as the initial monitoring of tumor size by serial abdominal ultrasounds or cross-sectional imaging with delayed treatment (DT) reserved for those patients whose SRMs show clinical progression during the follow-up examination[1]. Indications for AS are still controversial, thought an elderly patient with a high surgical risk or competing risks of death and a very small low-growing renal mass represents the optimal candidate for AS [Table 1]. A recent systematic review of the oncological outcomes of currently published AS data indicates this treatment modality is a safe initial management strategy for SRM, especially for patients with very small tumors (< 2 cm) and elderly and/or sicker patients (> 75 years), followed by DT only if required because of progression. Specifically, metastatic progression and cancer-specific mortality (CSM) rates for cT1a tumors have been found to be low, accounting for 0-6% and 1%, respectively. Conversely, the other-cause mortality (OCM) rate is 1%-45%, reflecting the advanced age and prevalence of comorbidities in these AS patients AS[7].

The data supporting these findings are manifold. Up to 52% of all resected SRM are suitable for AS, with 23% of benign histology and 29% of favorable risk or intermediate risk < 2 cm tumors[8]. Moreover, a significant proportion of SRM which satisfy the criteria of AS are benign tumors or low-grade renal cell

Table 1. Factors favoring active surveillance

Patient-related	Tumor-related
Elderly	Tumor size < 3 cm
Life expectancy < 5 years	Tumor growth < 5 mm/year
High comorbidities	Non-infiltrative on imaging
Excessive perioperative risk	Low complexity
Frailty (poor functional status)	Favorable histology (if RTB is performed)
Patient preference for AS	
Marginal renal function	

RTB: renal tumor biopsy; AS: active surveillance

carcinoma, with relatively indolent biologic and clinical behavior[9,10]. Indeed, most of SRM grow slowly, with a median linear growth rate (LGR) of 0.22 cm/year for cT1a tumors[7]. Conversely, although benign tumors may grow significantly, high median LGR (0.37 cm/year) has been associated with a progression to metastasis and may be mirror more aggressive cancers[7,9,11,12].

Elderly and comorbid patients with SRM have a relative low risk of CSM but a significant risk of OCM, thus questioning their eligibility for surgery, which may also expose the patient to a greater risk of post-operative morbidity[13-17]. In comparative retrospective and prospective analyses, although patients in the AS arm were older with greater comorbidity and smaller tumors with respect to the surgical counterpart, no statistically significant difference in OS and CSS were observed once adjusted for patients and tumor characteristics[10,13,18,19].

Triggers for AS cessation and commencement of treatment are poorly understood and include tumor volume doubling time < 12 months, LGR > 0.5 cm/year, tumor maximal diameter at risk of systemic dissemination (3-4 cm), malignant RTB results, new onset of tumor-related symptoms and/or patient's preference[11,20]. Up to one-third of patients in AS cross over to treatment and most of them within the first 2-3 years[1,2]. For the 1%-26% of cT1a tumors undergoing surgical DT, the median LGR has been found 0.62 cm/year[7]. Furthermore, increasing growth kinetics at the first follow-up imaging appear to be associated with higher treatment crossing over but not with OS, which suggests that rapidly growing masses early in AS may not necessarily require immediate treatment[12].

The optimal follow-up schedule for patients in AS is still unknown and therefore hasn't been standardized. Current recommendations suggest imaging at relatively frequent intervals initially, which may increase as the stability of the lesion is demonstrated: cross-sectional imaging every 3-4 months for the first year, followed by cross-sectional imaging or ultrasound every 4-6 months for the second year and every 6-12 months thereafter[20].

Nephron-sparing surgery

Although AS and ablative therapies have been regarded as attractive treatment modalities, partial nephrectomy (PN) represents the standard of care for the management of SRMs[1,15,21-23]. Indeed, PN has demonstrated comparable cancer control[24-26] but a lower incidence of chronic kidney disease[27-30], cardiovascular events[31,32], overall and competing-cause mortality[31,33-35] when compared to radical nephrectomy.

According to a surgeon's experience and preference, a PN can be performed with open (OPN), laparoscopic (LPN) or robot-assisted (RAPN) approach[1]. Specifically, RAPN provides non-inferior oncological and functional outcomes and an improved morbidity profile with respect to OPN[36,37]. Moreover, RAPN is now considered the preferable minimally invasive approach to PN because it eliminates the technical issues of LPN and reduces the surgical learning curve[38-40].

CONCLUSION

An accurate diagnosis of SRM can be made by using RTB and will further improve the risk-stratification of patients and guide the treatment strategy. Moreover, AS is a viable alternative to standard PN for SRM and should be discussed with candidates for active intervention, according to the baseline health status and the characteristics of the tumor provided by the RTB.

DECLARATIONS

Authors' contributions

Data analysis and interpretation, manuscript writing and editing: Muttin F
Conception and design of the study, supervision and critical revision for important intellectual content: Barret E

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

Both authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable

Copyright

REFERENCES

1. Ljungberg B, Albiges L, Abu-Ghanem Y, Bensalah K, Dabestani S, et al. European association of urology guidelines on renal cell carcinoma: the 2019 update. Eur Urol 2019; doi:10.1016/j.eururo.2019.02.011.
2. Richard PO, Jewett MAS, Bhatt JR, Kachura JR, Evans AJ, et al. Renal tumor biopsy for small renal masses: a single-center 13-year experience. Eur Urol 2015;68:1007-13.
3. Marconi L, Dabestani S, Lam TB, Hofmann F, Stewart F, et al. Systematic review and meta-analysis of diagnostic accuracy of percutaneous renal tumour biopsy. Eur Urol 2016;69:660-73.
4. Herrera-Caceres JO, Finelli A, Jewett MAS. Renal tumor biopsy: indicators, technique, safety, accuracy results, and impact on treatment decision management. World J Urol 2018;362:624.
5. Patel HD, Johnson MH, Pierorazio PM, Sozio SM, Sharma R, et al. Diagnostic accuracy and risks of biopsy in the diagnosis of a renal mass suspicious for localized renal cell carcinoma: systematic review of the literature. J Urol 2016;195:1340-7.
6. Richard PO, Jewett MAS, Tanguay S, Saarela O, Liu ZA, et al. Safety, reliability and accuracy of small renal tumour biopsies: results from a multi-institution registry. BJU Int 2017;119:543-9.
7. Mir MC, Capitanio U, Bertolo R, Ouzaid IP, Salagierski M, et al. Role of active surveillance for localized small renal masses. Eur Urol Oncol 2018;1:177-87.
8. Rahbar H, Bhayani S, Stifelman M, Kaouk J, Allaf M, et al. Evaluation of renal mass biopsy risk stratification algorithm for robotic partial nephrectomy--could a biopsy have guided management? J Urol 2014;192:1337-42.
9. Jewett MAS, Mattar K, Basiuk J, Morash CG, Pautler SE, et al. Active surveillance of small renal masses: progression patterns of early stage kidney cancer. Eur Urol 2011;60:39-44.
10. Pierorazio PM, Johnson MH, Ball MW, Gorin MA, Trock BJ, et al. Five-year analysis of a multi-institutional prospective clinical trial of delayed intervention and surveillance for small renal masses: the DISSRM registry. Eur Urol 2015;68:408-15.
11. Smaldone MC, Kutikov A, Egleston BL, Canter DJ, Viterbo R, et al. Small renal masses progressing to metastases under active surveillance: a systematic review and pooled analysis. Cancer 2012;118:997-1006.

12. McIntosh AG, Ristau BT, Ruth K, Jennings R, Ross E, et al. Active surveillance for localized renal masses: tumor growth, delayed intervention rates, and > 5-yr clinical outcomes. Eur Urol 2018;74:157-64.
13. Lane BR, Abouassaly R, Gao T, Weight CJ, Hernandez AV, et al. Active treatment of localized renal tumors may not impact overall survival in patients aged 75 years or older. Cancer 2010;116:3119-26.
14. Kutikov A, Egleston BL, Canter D, Smaldone MC, Wong YN, et al. Competing risks of death in patients with localized renal cell carcinoma: a comorbidity based model. J Urol 2012;188:2077-83.
15. Pierorazio PM, Johnson MH, Patel HD, Sozio SM, Sharma R, et al. Management of renal masses and localized renal cancer: systematic review and meta-analysis. J Urol 2016;196:989-99.
16. Larcher A, Fossati N, Tian Z, Boehm K, Meskawi M, et al. Prediction of complications following partial nephrectomy: implications for ablative techniques candidates. Eur Urol 2016;69:676-82.
17. Larcher A, Trudeau V, Dell'Oglio P, Tian Z, Boehm K, et al. Prediction of competing mortality for decision-making between surgery or observation in elderly patients with T1 kidney cancer. Urology 2017;102:130-7.
18. Patel N, Cranston D, Akhtar MZ, George C, Jones A, et al. Active surveillance of small renal masses offers short-term oncological efficacy equivalent to radical and partial nephrectomy. BJU Int 2012;110:1270-5.
19. Alam R, Patel HD, Osumah T, Srivastava A, Gorin MA, et al. Comparative effectiveness of management options for patients with small renal masses: a prospective cohort study. BJU Int 2018;351:1296.
20. Ristau BT, Kutikov A, Uzzo RG, Smaldone MC. Active surveillance for small renal masses: when less is more. Eur Urol Focus 2016;2:660-8.
21. Motzer RJ. Kidney Cancer, Version 4.2018, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 2018:1-59.
22. Campbell S, Uzzo RG, Allaf ME, Bass EB, Cadeddu JA, et al. Renal mass and localized renal cancer: AUA guideline. J Urol 2017;198:520-9.
23. Finelli A, Ismaila N, Bro B, Durack J, Eggener S, et al. Management of small renal masses: american society of clinical oncology clinical practice guideline. J Clin Oncol 2017;35:668-80.
24. Zini L, Patard JJ, Capitanio U, Crépel M, la Taille De A, et al. Cancer-specific and non-cancer-related mortality rates in European patients with T1a and T1b renal cell carcinoma. BJU Int 2009;103:894-8.
25. Zini L, Patard JJ, Capitanio U, Mejean A, Villers A, et al. The use of partial nephrectomy in European tertiary care centers. Eur J Surg Oncol 2009;35:636-42.
26. Van Poppel H, Da Pozzo L, Albrecht W, Matveev V, Bono A, et al. A prospective, randomised EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. Eur Urol 2011;59:543-52.
27. Sun M, Bianchi M, Hansen J, Trinh QD, Abdollah F, et al. Chronic kidney disease after nephrectomy in patients with small renal masses: a retrospective observational analysis. Eur Urol 2012;62:696-703.
28. Eckardt KU, Coresh J, Devuyst O, Johnson RJ, Köttgen A, et al. Evolving importance of kidney disease: from subspecialty to global health burden. Lancet 2013;382:158-69.
29. Scosyrev E, Messing EM, Sylvester R, Campbell S, Van Poppel H. Renal function after nephron-sparing surgery versus radical nephrectomy: results from EORTC randomized trial 30904. Eur Urol 2014;65:372-7.
30. Capitanio U, Larcher A, Terrone C, Antonelli A, Volpe A, et al. End-stage renal disease after renal surgery in patients with normal preoperative kidney function: balancing surgical strategy and individual disorders at baseline. Eur Urol 2016;70:558-61.
31. Huang WC, Elkin EB, Levey AS, Jang TL, Russo P. Partial nephrectomy versus radical nephrectomy in patients with small renal tumors--is there a difference in mortality and cardiovascular outcomes? J Urol 2009;181:55-61; discussion 61-2.
32. Capitanio U, Terrone C, Antonelli A, Minervini A, Volpe A, et al. Nephron-sparing techniques independently decrease the risk of cardiovascular events relative to radical nephrectomy in patients with a T1a-T1b renal mass and normal preoperative renal function. European Urology 2015;67:683-9.
33. Sun M, Trinh QD, Bianchi M, Hansen J, Hanna N, et al. A non-cancer-related survival benefit is associated with partial nephrectomy. Eur Urol 2012;61:725-31.
34. Kim SP, Thompson RH, Boorjian SA, Weight CJ, Han LC, et al. Comparative effectiveness for survival and renal function of partial and radical nephrectomy for localized renal tumors: a systematic review and meta-analysis. J Urol 2012;188:51-7.
35. Larcher A, Capitanio U, Terrone C, Volpe A, De Angelis P, et al. Elective nephron sparing surgery decreases other cause mortality relative to radical nephrectomy only in specific subgroups of patients with renal cell carcinoma. J Urol 2016;196:1008-13.
36. Peyronnet B, Seisen T, Oger E, Vaessen C, Grassano Y, et al. Comparison of 1800 robotic and open partial nephrectomies for renal tumors. Ann Surg Oncol 2016;23:4277-83.
37. Larcher A, Capitanio U, De Naeyer G, Fossati N, D'Hondt F, et al. Is robot-assisted surgery contraindicated in the case of partial nephrectomy for complex tumours or relevant comorbidities? A comparative analysis of morbidity, renal function, and oncologic outcomes. Eur Urol Oncol 2018;1:61-8.
38. Pierorazio PM, Patel HD, Feng T, Yohannan J, Hyams ES, et al. Robotic-assisted versus traditional laparoscopic partial nephrectomy: comparison of outcomes and evaluation of learning curve. Urology 2011;78:813-9.
39. Leow JJ, Heah NH, Chang SL, Chong YL, Png KS. Outcomes of robotic versus laparoscopic partial nephrectomy: an updated meta-analysis of 4,919 patients. J Urol 2016;196:1371-7.
40. Larcher A, Muttin F, Peyronnet B, De Naeyer G, Khene ZE, et al. The learning curve for robot-assisted partial nephrectomy: impact of surgical experience on perioperative outcomes. Eur Urol 2019;75:253-6.

Makuuchi *et al. Mini-invasive Surg* 2019;3:11
DOI: 10.20517/2574-1225.2019.03

Mini-invasive Surgery

Review

Open Access

Robotic surgery for gastric cancer

Rie Makuuchi, Satoshi Kamiya, Yutaka Tanizawa, Etsuro Bando, Masanori Terashima

Division of Gastric Surgery, Shizuoka Cancer Center, Nagaizumi-cho, Sunto-gun, Shizuoka 411-5222, Japan.

Correspondence to: Prof. Masanori Terashima, Division of Gastric Surgery, Shizuoka Cancer Center, 1007 Shimonagakubo, Nagaizumi-cho, Sunto-gun, Shizuoka 411-5222, Japan. E-mail: m.terashima@scchr.jp

How to cite this article: Makuuchi R, Kamiya S, Tanizawa Y, Bando E, Terashima M. Robotic surgery for gastric cancer. *Mini-invasive Surg* 2019;3:11. http://dx.doi.org/10.20517/2574-1225.2019.03

Received: 17 Jan 2018 **First Decision:** 26 Feb 2019 **Revised:** 18 Mar 2019 **Accepted:** 18 Mar 2019 **Published:** 19 Apr 2019

Science Editor: Tetsu Fukunaga **Copy Editor:** Cai-Hong Wang **Production Editor:** Huan-Liang Wu

Abstract

The number of robotic gastrectomy (RG) cases is increasing, especially in East Asia. The da Vinci Surgical System for RG allows surgeons to perform meticulous procedures using articulated devices and provides potential advantages over laparoscopic gastrectomy (LG). Meta-analyses including a large number of retrospective studies comparing RG and LG revealed only a limited advantage for RG over LG, such as lower blood loss, and the obvious disadvantage of longer operation times and higher medical cost. Specifically, a multicenter, prospective, single-arm study performed in Japan showed favorable short-term outcomes of RG over LG, while a non-randomized controlled trial in Korea showed similar postoperative complication rates for RG and LG, although the medical costs were significantly higher in RG. A well-designed randomized controlled trial is thus necessary to establish robust evidence comparing the two surgeries. In addition, further development of surgical robotics is expected for RG to be accepted more widely.

Keywords: Gastric cancer, robotic gastrectomy, surgery, minimum invasive surgery

INTRODUCTION

Gastric cancer is the third leading cause of cancer-related deaths and the fifth most common cancer worldwide[1]. Gastrectomy with radical lymphadenectomy is a mainstay of treatment on resectable gastric cancer; however, recent randomized controlled trials have demonstrated inferiorities of such expanded and invasive procedures[2-5]. In contrast, minimally invasive surgery including laparoscopic gastrectomy (LG) and robotic gastrectomy (RG) is attracting attention. LG was first introduced in 1991 in Japan[6], and since then, this procedure is used all over the world. The reported advantages of LG over radical open gastrectomy are faster recovery from the surgical stress, less bleeding, good cosmetic results, and shorter

Table 1. History of surgical robotics

Year	Event
1985	Puma 200 was used for neurosurgical biopsy
1986	ROBODOC was used for artificial joint replacement
1994	AESOP (Computer Motion Inc.) released and approved by the FDA
1998	ZEUS (Computer Motion Inc.) released
1999	da Vinci Surgical System (Intuitive Surgical Inc.) released
2000	da Vinci Surgical System approved by the FDA
2001	First case of intercontinental telesurgery (US-France)
2002	Hashizume performed robot-assisted distal gastrectomy
2003	Merger of Intuitive Surgical Inc. and Computer Motion Inc.

FDA: food and drug administration

hospital stays[7-9]. Nevertheless, this procedure has several drawbacks such as two-dimensional surgical view and the motion restriction using linear forceps. Surgical robotics has introduced in 1990s having the potential to overcome those limitations and is spreading rapidly in the world.

In this review, we provide an historical outline of the development of surgical robotics, and describe the advantages and disadvantages of robot gastrectomy for gastric cancer compared to LG.

HISTORY OF SURGICAL ROBOTICS

The history and development of surgical robotics [Table 1] goes back to the 1950s, with the development of so-called "telepresence robotic arms", although these were not intended for surgical applications, but rather for remotely controlled systems to handle hazardous substances or to perform tasks underwater or in space. In the 1980s, robotic arm development progressed rapidly with advances in computer technology, and in 1985, surgical robotics was first used in a clinical setting to perform a neurological biopsy[10]. A year later, researchers at the IBM Thomas J. Watson Research Center and University of California completed the development of ROBODOC, which became the first surgical robot approved by the USA Food and Drug Administration (FDA) for clinical use in humans[11]. In 1994, Computer Motion Inc. developed Automated Endoscopic System for Optimal Positioning (AESOP; Computer Motion Inc., USA) with the aim of solo-surgery using voice recognition to control the endoscope[12].

The US army also developed medical robotics for the use of telesurgery in the late 1980s with a master-slave manipulator system that was originally designed for battlefield surgery. This system was subsequently introduced into the clinical market as the da Vinci Surgical System (DVSS) by Intuitive Surgical Inc, and in 2000, DVSS became the first robot-assisted surgical system approved by the FDA for use in general laparoscopic surgery[13,14]. Computer Motion Inc. also developed ZEUS in 1998, adding a remote-control function to AESOP[15]. In the beginning, both systems were used only for cardiovascular surgery; however, they were gradually expanded to digestive surgery, urology, and gynecology. In 2001, ZEUS was used for the first case of telesurgery between New York and France to perform cholecystectomy[16]. This operation was called "Lindbergh operation" after the American aviator Charles Lindbergh who was the first person to fly solo across the Atlantic Ocean. The first RG [robotic distal gastrectomy (RDG)] for gastric cancer was reported in 2002 by Hashizume *et al.*[17] using DVSS.

In 2003, Computer Motion Inc merged with Intuitive Surgical Inc., and since then DVSS has been the only FDA-approved surgery-assisting robot, building a near-monopoly. In September 2018, there were 4,814 installed DVSS units worldwide, including 3,110 in the United States, 821 in Europe, and 629 in Asia[18] [Figure 1].

CURRENT STATUS OF RG FOR GASTRIC CANCER

The most apparent advantage of RG over LG is that articulated devices are available in RG. In addition, the motion scaling and tremor suppression functions in RG enable more precise movement, which is believed

Table 2. Summary of the meta-analyses comparing RG and LG with respect to short term outcomes

Author	Year	Country	Number of studies	Number of patients	Morbidity	Blood loss	Operation time	Retrieved LN	Hospital stay	Time to oral intake	Time to first flatus	Medical cost
Hyun *et al.*[26]*	2013	Korea	9	7,200	RG = LG	RG = LG	RG > LG	RG = LG	RG = LG	-	-	-
Shen *et al.*[19]	2014	China	8	1,875	RG = LG	RG < LG	RG > LG	RG = LG	RG = LG	-	-	-
Chuan *et al.*[20]	2015	China	5	1,796	RG = LG	RG < LG	RG > LG	RG = LG	RG = LG	-	-	-
Hu *et al.*[21]	2016	China	12	3,580	RG = LG	RG < LG	RG > LG	RG > LG	RG < LG	-	RG > LG	-
Wang *et al.*[23]	2017	China	3	562	RG = LG	RG = LG	RG > LG	RG = LG	RG = LG	-	-	-
Chen *et al.*[22]	2017	China	19	5,953	RG = LG	RG < LG	RG > LG	RG = LG	RG = LG	RG > LG	RG = LG	RG > LG
Guerra *et al.*[25]	2018	Italy	8	2,026	RG = LG**	-	RG > LG	RG > LG	RG = LG	-	-	-

*This study included open gastrectomy and compared among robotic, laparoscopic, and open gastrectomy; **only pancreatic complications were compared, including acute pancreatitis and pancreatic fistula. LN: lymph nodes; RG: robotic gastrectomy; LG: laparoscopic gastrectomy

to reduce tissue damage and blood loss. Another advantage of RG is a three-dimensional (3D) field of view that facilitates surgeons to recognize depth perception. Recently, 3D images also became available in LG; however, special glasses are necessary and the quality of imaging remains inferior to that in RG. Furthermore, the ergonomics-based surgery console used in RG can reduce the fatigue of operators. While the surgical devices for RG were limited at first, ultrasonically activated device (harmonic), vessel sealers, Endo Wrist staplers, and other instruments are now available.

Short-term outcomes

Retrospective studies

Numerous retrospective, case-control studies comparing RG and LG have been conducted, and several meta-analyses were performed using those studies [Table 2][19-26]. Shen *et al.*[19] conducted 8 studies with a total of 1,875 patients that showed approximately 40 mL lower blood loss in RG than LG; however, the operation time for RG was approximately 50 min longer. The duration of hospital stay, morbidity, and numbers of retrieved lymph nodes were comparable between RG and LG. Other meta-analysis indicated similar results, with the exception of a difference between RG over LG with morbidity. Guerra *et al.*[25] analyzed 8 studies, including 2026 patients, focusing on pancreatic complications. Pancreatic fistula occurred in 2.7% of patients receiving RG and 3.8% of patients receiving LG, for an odds ratio of 0.72. Although the difference was not statistically significant, the authors concluded that RG trended toward lower rates of postoperative pancreas-related events, despite more unfavorable baseline characteristics compared with LG.

Prospective studies

Very limited prospective studies of RG have been conducted thus far. We conducted single-center early and late phase II studies in patients with cStage I gastric cancer to evaluate the safety of RG[27,28], involving 18 and 120 patients, respectively, in each study that found an incidence of intra-abdominal infectious complications of Clavien-Dindo classification grade ≥ II of 0% and 3.3%, respectively. Thus, the null hypotheses were rejected, and the studies concluded that RG can be safely used in cStage I gastric cancer.

In a prospective, multicenter, non-randomized, control study was conducted in Korea from May 2011 to December 2012 to compare the short-term surgical outcomes of RG (n = 223) and LG (n = 211)[29]. No significant difference was observed in the incidence of overall postoperative complications (RG 11.9%, LG 10.3%) and the mortality rate was 0% in both groups; however, the operation time was 40 min longer and the financial cost was 5,000 USD higher for RG than for LG. The authors concluded that RG was not superior to LG, and subsequent sub-group analysis showed a significantly lower amount of blood loss in RG when D2 lymph node dissection than that in LG[30].

A multicenter, prospective, single-arm study conducted in Japan evaluated the safety of RG in 330 patients with cStage I/II gastric cancer enrolled from October 2014 to January 2017, with the primary endpoint of

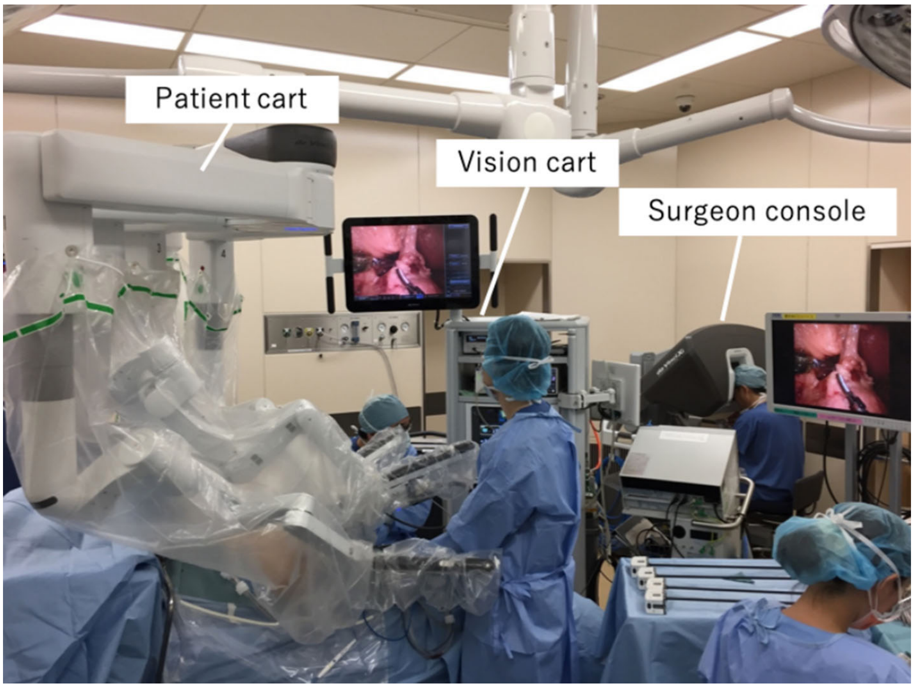


Figure 1. The da Vinci Surgical System comprises the patient cart, vision cart and surgeon console

postoperative complication[31]. The incidence of postoperative complications of Clavien-Dindo grade ≥ III was 2.45%, which was significantly lower than that in the historical control group (6.4%). Based on this result, RG for gastric cancer has been covered by national health insurance since April 2018 in Japan.

Long-term outcomes

A few retrospective case-control studies have been conducted to compare long-term outcomes between RG and LG in Japan and Korea[32-34]. In a study conducted in Japan, data from 84 patients who underwent RG and 437 patients who underwent LG around the same time were retrospectively analyzed; the 3-year overall survival rates were 86.9% and 88.8%, respectively, and did not differ to a statistically significant extent (P = 0.636)[33]. A study conducted in Korea using propensity score matching found 5-year overall survival rates of 93.2% in RG and 94.2% in LG; again the difference was not statistically significant (P = 0.4112)[34]. Although not prospective findings, these results indicate that the long-term outcomes of RG are not inferior to those of LG.

Learning curve

The learning curve for RG is reportedly shorter for experienced surgeons who had performed LG, estimated to total between 10 and 25 cases[35-39], although 40-60 cases is the estimated number needed to reach stabilization in LG[40,41]. Thus, although the 3D imaging and instrument flexibility of RG may help to make the learning curve less steep, the fact that an expert in LG performed the RG in many cases could have affected the results. In contrast, a recent study showed that stabilization of the operation time occurred after 25 cases, even for surgeons without prior LG experience, suggesting that prior LG experience is not necessarily required[42].

Nevertheless, robotic surgery requires surgeons to attain some extent of specialized training. Intuitive Surgical Inc. provides a training program and surgeons have to pass this program and be certificated as a Console Surgeon of DVSS to perform RG using DVSS. Interestingly, this training program targets surgeons from various fields and it is not sufficient to perform RG independently. Therefore, we have developed three-step educational program targeted at qualified surgeons [Table 3], who should perform more than 10

Table 3. Educational Program in Shizuoka Cancer Center

Step	Target item	Purpose
1	Has taken the training courses led by Intuitive Surgical Inc. and acquired surgeon certification	Learn the basic operation of the da Vinci Surgical System and perform repetitive training of surgical techniques and surgical procedures
	Perform at least 10 h of offsite training using the da Vinci Surgical System	Learn the smooth operation of the da Vinci Surgical System
2	Under the guidance of the proctor, perform over 10 robotic gastrectomies (including total gastrectomies, cardia side gastrectomies)*[1-4] Do not cause other organ damage requiring repair, arterial injuries requiring reconstruction, or other intraoperative complications requiring an open conversion	Gain experience in robotic gastrectomy
	Perform one or more robotic total gastrectomies	Gain experience as a surgeon for robotic total gastrectomies to acquire esophagus jejunal anastomosis
3	Achieve a rating of B or higher from the proctor in all items of the surgical evaluation on robotic distal gastrectomy	The proctor evaluates whether or not the target surgeon is appropriate as a robotic surgeon, according to unified standards

*1: The proctor performs surgery mainly for the first case and the operator learns beside or performs part of the surgery; *2: at least the second case should be a case of distal gastrectomy, D1 + dissection, with BMI < 25, PS = 0, and ASA - PS 2 or less; *3: teaching by dual console is desirable until the third case; *4: in the case of a longer than 6 months absence during participation, 2 cases of experience will be added after receiving a retraining program provided by Intuitive Surgical Inc., regardless of the number of experienced cases

cases of RG including one or more cases of total or proximal gastrectomy[43]. A proctor scores the surgeon in accordance to the evaluation list, and when a high score is achieved, the surgeon will be allowed to perform RG independently.

Ergonomics

Robotic surgery provides surgeons with an ergonomically sound work environment because although LG is usually performed in the standing position, RG can be performed in a sitting position at an ergonomically designed surgeon console, which is expected to reduce operator fatigue. A survey study comprising 26 questions was performed to document the discomfort of robotic surgery compared with open and laparoscopic surgery, and to investigate the factors that affect the risk of physical symptoms, involving surgeons with various specialties and 1,215 who practiced all three approaches. This survey demonstrated that robot-assisted surgery was associated with the least physical discomfort and symptoms compared with open and laparoscopic surgery[44]. The breakdown of symptoms indicated that robotic surgery was less likely to lead to neck, back, hip, knee, ankle, foot, shoulder, elbow, and wrist pain than open or laparoscopic surgery, although the frequency of eye and finger pain was higher in robotic surgery. In another survey of 432 surgeons using robotic surgery in various fields, 56.1% complained of physical symptoms or discomfort, with the most frequent complaints being neck stiffness, finger pain, and eye fatigue[45]. Thus, although robotic surgery reduces the physical symptoms and discomfort of surgeons in comparison to open and laparoscopic surgery, more than 50% of surgeons have complained of a certain degree of physical stress, typically finger pain and eye strain.

Disadvantages of robotic compared to laparoscopic gastrectomy

The most critical disadvantage of RG is a lack of tactile perception, which can lead to incomplete ligature and tissue damage due to excessive stress. Visual information can compensate the lack of tactile perception; however, serious injury could still happen outside the field of view. Surgical robotics can potentially apply an unexpectedly strong force that never occurs in conventional surgery. Thus, even slight mishandling of the DVSS may lead to a fatal accident, even with a built-in system to prevent excessive compression to organs.

Requiring a long operation time is another disadvantage in RG. A retrospective study investigating factors contributing to prolongation of the operation time identified “junk time” as a cause of the prolongation[46]. In this study, the authors classified the overall operation time into two groups: the effective time (time required for actual surgical techniques such as port replacement, lymphadenectomy, and reconstruction) and the junk time (setup docking, and adjustment of surgical instruments). They found that junk time was significantly longer in RG, at 41.5 min, than in LG, though effective time was not statistically different between the groups. Although there was no difference in the number of instrument exchanges, the time required to exchange instruments was also significantly longer in RG than in LG. Additionally, the operation time was reduced by about 1 h when ultrasonically activated devices were used[47]. These studies suggest that a smarter and simpler system is needed for the setup and for instrument change, and development of new devices are warranted to reduce the operation time.

FUTURE PERSPECTIVES

A lack of robust evidence regarding RG use appears to be the most important future issue. Although RG has many theoretical advantages over LG, a definite and significant benefit of RG over LG has not been shown in a clinical setting due to the lack of randomized controlled trials (RCT). It cannot be denied that the high cost of RG affects the difficulty in conducting RCT, with some meta-analyses and a prospective study conducted in Korea indicating that RG is 4000-5000 USD more expensive than LG[22,29]. In Japan, RG has been covered by health insurance since April 2018; thus, patients can undergo RG without any extra cost. Thus, while the economic burden on medical institutions remains, the groundwork for RCT has been completed, and a well-designed RCT is needed to investigate the superiority of RG over LG.

Currently, several companies are developing surgical robots, with such market competition expected to decrease the price and further their use. Moreover, we anticipate the near future to bring development of new devices or miniaturization of existing surgical robots, together with innovative development, including concomitant use with 3D imaging[48], artificial intelligence, and virtual reality[49].

CONCLUSION

RG with DVSS facilitates meticulous surgical procedures with 3D imaging, instrument flexibility, tremor suppression, and improved ergonomics. Problems with RG remain including an unacceptable lack in tactile perception, longer operation times, and high medical costs. Moreover, although RG has theoretical advantages over LG, robust evidence is lacking. Well-designed, randomized controlled trials are therefore needed to establish stronger evidence and further develop the field of surgical robotics.

DECLARATIONS

Authors' contributions

Designed the study, reviewed literature, and wrote the manuscript: Makuuchi R
Critical revision of the manuscript and approval of the final version: Kamiya S, Tanizawa Y, Bando E
Writing the manuscript, drafting and critical revision and editing, and approval of the final version: Terashima M

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, et al. Global cancer statistics, 2012. CA Cancer J Clin 2015;65:87-108.
2. Sano T, Sasako M, Mizusawa J, Yamamoto S, Katai H, et al. Randomized Controlled Trial to Evaluate Splenectomy in Total Gastrectomy for Proximal Gastric Carcinoma. Ann Surg 2017;265:277-83.
3. Sasako M, Sano T, Yamamoto S, Kurokawa Y, Nashimoto A, et al. D2 lymphadenectomy alone or with para-aortic nodal dissection for gastric cancer. N Engl J Med 2008;359:453-62.
4. Sasako M, Sano T, Yamamoto S, Sairenji M, Arai K, et al. Left thoracoabdominal approach versus abdominal-transhiatal approach for gastric cancer of the cardia or subcardia: a randomised controlled trial. Lancet Oncol 2006;7:644-51.
5. Terashima M, Doki Y, Kurokawa Y, Mizusawa J, Katai H, et al. Primary results of a phase III trial to evaluate bursectomy for patients with subserosal/serosal gastric cancer (JCOG1001). J Clin Oncol 2017;35:5.
6. Kitano S, Iso Y, Moriyama M, Sugimachi K. Laparoscopy-assisted Billroth I gastrectomy. Surg Laparosc Endosc 1994;4:146-8.
7. Kodera Y, Fujiwara M, Ohashi N, Nakayama G, Koike M, et al. Laparoscopic surgery for gastric cancer: a collective review with meta-analysis of randomized trials. J Am Coll Surg 2010;211:677-86.
8. Katai H, Mizusawa J, Katayama H, Takagi M, Yoshikawa T, et al. Short-term surgical outcomes from a phase III study of laparoscopy-assisted versus open distal gastrectomy with nodal dissection for clinical stage IA/IB gastric cancer: Japan Clinical Oncology Group Study JCOG0912. Gastric Cancer 2017;20:699-708.
9. Katai H, Mizusawa J, Katayama H, Kunisaki C, Sakuramoto S, et al. Single-arm confirmatory trial of laparoscopy assisted total or proximal gastrectomy with nodal dissection for clinical stage I gastric cancer: Japan Clinical Oncology Group study JCOG1401. J Clin Oncol 2018;36:4028.
10. Kwoh YS, Hou J, Jonckheere EA, Hayati S. A robot with improved absolute positioning accuracy for CT guided stereotactic brain surgery. IEEE Trans Biomed Eng 1988;35:153-60.
11. Paul HA, Bargar WL, Mittlestadt B, Musits B, Taylor RH, et al. Development of a surgical robot for cementless total hip arthroplasty. Clin Orthop Relat Res 1992:57-66.
12. Unger SW, Unger HM, Bass RT. AESOP robotic arm. Surg Endosc 1994;8:1131.
13. Falk V, Diegeler A, Walther T, Banusch J, Brucerius J, et al. Total endoscopic computer enhanced coronary artery bypass grafting. Eur J Cardiothorac Surg 2000;17:38-45.
14. Cadiere GB, Himpens J, Germay O, Izizaw R, Degueldre M, et al. Feasibility of robotic laparoscopic surgery: 146 cases. World J Surg 2001;25:1467-77.
15. Reichenspurner H, Damiano RJ, Mack M, Boehm DH, Gulbins H, et al. Use of the voice-controlled and computer-assisted surgical system ZEUS for endoscopic coronary artery bypass grafting. J Thorac Cardiovasc Surg 1999;118:11-6.
16. Marescaux J, Leroy J, Gagner M, Rubino F, Mutter D, et al. Transatlantic robot-assisted telesurgery. Nature 2001;413:379-80.
17. Hashizume M, Shimada M, Tomikawa M, Ikeda Y, Takahashi I, et al. Early experiences of endoscopic procedures in general surgery assisted by a computer-enhanced surgical system. Surg Endosc 2002;16:1187-91.
18. Surgical I. Investors Overview: Featured Documents; Investor Presentation Q4 2018. Available from: https://isrg.gcs-web.com/. [Last accessed on 9 Apr 2019]
19. Shen WS, Xi HQ, Chen L, Wei B. A meta-analysis of robotic versus laparos copic gastrectomy for gastric cancer. Surg Endosc 2014;28:2795-802.
20. Chuan L, Yan S, Pei-Wu Y. Meta-analysis of the short-term outcomes of robotic-assisted compared to laparoscopic gastrectomy. Minim Invasive Ther Allied Technol 2015;24:127-34.
21. Hu LD, Li XF, Wang XY, Guo TK. Robotic versus laparoscopic gastrectomy for gastric carcinoma: a meta-analysis of efficacy and safety. Asian Pac J Cancer Prev 2016;17:4327-33.
22. Chen K, Pan Y, Zhang B, Maher H, Wang XF, et al. Robotic versus laparoscopic gastrectomy for gastric cancer: a systematic review and updated meta-analysis. BMC Surg 2017;17:93.
23. Wang Y, Zhao X, Song Y, Cai A, Xi H, et al. A systematic review and meta-analysis of robot-assisted versus laparoscopically assisted gastrectomy for gastric cancer. Medicine (Baltimore) 2017;96:e8797.
24. Huang KH, Lan YT, Fang WL, Chen JH, Lo SS, et al. Comparison of the operative outcomes and learning curves between laparoscopic and robotic gastrectomy for gastric cancer. PLoS One 2014;9:e111499.
25. Guerra F, Giuliani G, Formisano G, Bianchi PP, Patriti A, et al. Pancreatic complications after conventional laparoscopic radical gastrectomy versus robotic radical gastrectomy: systematic review and meta-analysis. J Laparoendosc Adv Surg Tech A 2018;28:1207-15.
26. Hyun MH, Lee CH, Kwon YJ, Cho SI, Jang YJ, et al. Robot versus laparoscopic gastrectomy for cancer by an experienced surgeon: comparisons of surgery, complications, and surgical stress. Ann Surg Oncol 2013;20:1258-65.
27. Tokunaga M, Sugisawa N, Kondo J, Tanizawa Y, Bando E, et al. Early phase II study of robot-assisted distal gastrectomy with nodal dissection for clinical stage IA gastric cancer. Gastric Cancer 2014;17:542-7.
28. Tokunaga M, Makuuchi R, Miki Y, Tanizawa Y, Bando E, et al. Late phase II study of robot-assisted gastrectomy with nodal dissection for clinical stage I gastric cancer. Surg Endosc 2016;30:3362-7.
29. Kim HI, Han SU, Yang HK, Kim YW, Lee HJ, et al. Multicenter prospective comparative study of robotic versus laparoscopic gastrectomy for gastric adenocarcinoma. Ann Surg 2016;263:103-9.
30. Park JM, Kim HI, Han SU, Yang HK, Kim YW, et al. Who may benefit from robotic gastrectomy? A subgroup analysis of multicenter

prospective comparative study data on robotic versus laparoscopic gastrectomy. Eur J Surg Oncol 2016;42:1944-9.
31. Uyama I, Suda K, Nakauchi M, Kinoshita T, Noshiro H, et al. Clinical advantages of robotic gastrectomy for clinical stage I/II gastric cancer: a multi-institutional prospective single-arm study. Gastric Cancer 2019;22:377-85.
32. Son T, Lee JH, Kim YM, Kim HI, Noh SH, et al. Robotic spleen-preserving total gastrectomy for gastric cancer: comparison with conventional laparoscopic procedure. Surg Endosc 2014;28:2606-15.
33. Nakauchi M, Suda K, Susumu S, Kadoya S, Inaba K, et al. Comparison of the long-term outcomes of robotic radical gastrectomy for gastric cancer and conventional laparoscopic approach: a single institutional retrospective cohort study. Surg Endosc 2016;30:5444-52.
34. Obama K, Kim YM, Kang DR, Son T, Kim HI, et al. Long-term oncologic outcomes of robotic gastrectomy for gastric cancer compared with laparoscopic gastrectomy. Gastric Cancer 2018;21:285-95.
35. D'Annibale A, Pende V, Pernazza G, Monsellato I, Mazzocchi P, et al. Full robotic gastrectomy with extended (D2) lymphadenectomy for gastric cancer: surgical technique and preliminary results. J Surg Res 2011;166:e113-20.
36. Eom BW, Yoon HM, Ryu KW, Lee JH, Cho SJ, et al. Comparison of surgical performance and short-term clinical outcomes between laparoscopic and robotic surgery in distal gastric cancer. Eur J Surg Oncol 2012;38:57-63.
37. Huang KH, Lan YT, Fang WL, Chen JH, Lo SS, et al. Initial experience of robotic gastrectomy and comparison with open and laparoscopic gastrectomy for gastric cancer. J Gastrointest Surg 2012;16:1303-10.
38. Kang BH, Xuan Y, Hur H, Ahn CW, Cho YK, et al. Comparison of surgical outcomes between robotic and laparoscopic gastrectomy for gastric cancer: the learning curve of robotic surgery. J Gastric Cancer 2012;12:156-63.
39. Uyama I, Kanaya S, Ishida Y, Inaba K, Suda K, et al. Novel integrated robotic approach for suprapancreatic D2 nodal dissection for treating gastric cancer: technique and initial experience. World J Surg 2012;36:331-7.
40. Kim MC, Jung GJ, Kim HH. Learning curve of laparoscopy-assisted distal gastrectomy with systemic lymphadenectomy for early gastric cancer. World J Gastroenterol 2005;11:7508-11.
41. Jin SH, Kim DY, Kim H, Jeong IH, Kim MW, et al. Multidimensional learning curve in laparoscopy-assisted gastrectomy for early gastric cancer. Surg Endosc 2007;21:28-33.
42. An JY, Kim SM, Ahn S, Choi MG, Lee JH, et al. Successful robotic gastrectomy does not require extensive laparoscopic experience. J Gastric Cancer 2018;18:90-8.
43. Terashima M. Educational program on robotic gastrectomy in shizuoka cancer center. Available from: https://www.scchr.jp/en/wp-content/uploads/sites/18/2017/02/Educational-Program-on-Robotic-Gastrectomy.pdf. [Last accessed on 9 Apr 2019]
44. Plerhoples TA, Hernandez-Boussard T, Wren SM. The aching surgeon: a survey of physical discomfort and symptoms following open, laparoscopic, and robotic surgery. J Robot Surg 2012;6:65-72.
45. Lee GI, Lee MR, Green I, Allaf M, Marohn MR. Surgeons' physical discomfort and symptoms during robotic surgery: a comprehensive ergonomic survey study. Surg Endosc 2017;31:1697-706.
46. Liu H, Kinoshita T, Tonouchi A, Kaito A, Tokunaga M. What are the reasons for a longer operation time in robotic gastrectomy than in laparoscopic gastrectomy for stomach cancer? Surg Endosc 2019;33:192-8.
47. Hikage M, Tokunaga M, Makuuchi R, Tanizawa Y, Bando E, et al. Impact of an Ultrasonically Activated Device in Robot-Assisted Distal Gastrectomy. Innovations (Phila) 2017;12:453-8.
48. Furukawa J, Miyake H, Tanaka K, Sugimoto M, Fujisawa M. Console-integrated real-time three-dimensional image overlay navigation for robot-assisted partial nephrectomy with selective arterial clamping: early single-centre experience with 17 cases. Int J Med Robot 2014;10:385-90.
49. Iannessi A, Marcy PY, Clatz O, Bertrand AS, Sugimoto M. A review of existing and potential computer user interfaces for modern radiology. Insights Imaging 2018;9:599-609.

Mazzola *et al*. *Mini-invasive Surg* 2019;3:12
DOI: 10.20517/2574-1225.2019.05

Mini-invasive Surgery

Original Article

Open Access

Totally laparoscopic total gastrectomy: challenging but feasible: a single center case series

Michele Mazzola, Monica Gualtierotti, Paolo De Martini, Camillo Leonardo Bertoglio, Lorenzo Morini, Pietro Achilli, Andrea Zironda, Giovanni Ferrari

Division of Oncologic and Mini-invasive General Surgery, ASST Grande Ospedale Metropolitano Niguarda, Milan 20162, Italy.

Correspondence to: Dr. Michele Mazzola, Division of Oncologic and Mini-invasive General Surgery, ASST Grande Ospedale Metropolitano Niguarda, Piazza dell'Ospedale Maggiore 3, Milan 20162, Italy. E-mail: michele.mazzola@ospedaleniguarda.it

How to cite this article: Mazzola M, Gualtierotti M, De Martini P, Bertoglio CL, Morini L, Achilli P, Zironda A, Ferrari G. Totally laparoscopic total gastrectomy: challenging but feasible: a single center case. *Mini-invasive Surg* 2019;3:12. http://dx.doi.org/10.20517/2574-1225.2019.05

Received: 20 Jan 2019 **First Decision:** 12 Feb 2019 **Revised:** 17 Feb 2019 **Accepted:** 4 Mar 2019 **Published:** 21 Apr 2019

Science Editor: Tetsu Fukunaga **Copy Editor:** Cai-Hong Wang **Production Editor:** Huan-Liang Wu

Abstract

Aim: To report the initial monocentric experience of totally laparoscopic total gastrectomy, assessing its feasibility and safety, especially relating to the challenging step of esophago-jejunal (E-J) reconstruction.

Methods: All consecutive patients, underwent laparoscopic total gastrectomy for gastric cancer with curative intent, between January 2017 and June 2018 at our institution, were considered. Data of the selected patients was retrieved from a prospectively collected database. Short and long term outcomes were analyzed.

Results: Ten patients underwent totally laparoscopic total gastrectomy with D2 lymphadenectomy and 4 of these had received preoperative chemotherapy; Two patients also received the lymphadenectomy of the station 10. E-J reconstruction consisted of hemi-double stapling technique with transorally inserted anvil in 1 case, side-to-side overlap anastomosis in 5 cases and end-to-side anastomosis in 4 cases. One patient experienced intraoperative complications needing conversion to laparotomy. Seven patients experienced postoperative complications, three of these were severe according to Dindo-Clavien classification. All the specimens had free proximal resection margins with R0 resection in all the cases. Average postoperative length of hospital stay was 10 days and no patients died during hospitalization. Median overall survival and disease-free survival were 15.5 and 12.5 months respectively.

Conclusion: Totally laparoscopic total gastrectomy is a feasible and safe option in the treatment of gastric cancer. The choice about the type of E-J reconstruction should be based on the single patient's features and on the dexterity of the surgeon who should be able to perform more than one option for a tailored approach.

Keywords: Gastric cancer, totally laparoscopic total gastrectomy, mini-invasive treatment, total gastrectomy

INTRODUCTION

Gastric cancer is the second leading cause of cancer-related mortality worldwide[1]. Although relevant improvements in medical oncology, radical surgery still remains the mainstay of curative treatment[2]. Laparoscopic distal gastrectomy reached a wide diffusion in the last decades, before the treatment of early gastric cancer, and then treating advanced gastric cancer too[3], especially in Eastern countries, demonstrating clear advantages in terms of intraoperative bleeding, length of hospital stay, restoration of bowel function and incidences of minor postoperative complications in comparison with open surgery[4]. Looking at these results, laparoscopic technique has been gradually adopted, including total gastrectomy, confirming the short-term benefits as compared to open technique[5]. On the other hand, laparoscopic total gastrectomy is considered a very demanding procedure, due to the complexity of many steps like omentectomy and lymphadenectomy; however the main reason of complexity is the technical difficulty of esophago-jejunal reconstruction[6].

In order to overcome this complexity, many techniques have been proposed, ranging from hybrid anastomosis by mini-laparotomy, to different kinds of totally laparoscopic ones using a circular or linear stapler, without a clear superiority of one above the others[7]. Furthermore the majority of data on this topic comes from Eastern countries and from case series, making the debate still open[8]. In this scenario, we reported our experience of totally laparoscopic total gastrectomy.

METHODS

All consecutive patients who underwent laparoscopic total gastrectomy for gastric cancer with curative intent, between January 2017 and June 2018 at our institution, were considered. Patients with esophago-gastric junction cancer, with evidence of metastatic disease and/or underwent surgery with palliative intent were excluded.

Exclusion criteria for laparoscopic treatment of gastric cancer were: tumor involvement of adjacent organs, T4a tumor at endoscopic ultrasonography (EUS), tumor located in the greater curvature, preoperative evidence of bulky lymph-nodes, anesthesiologic contraindications to pneumoperitoneum, history of other surgery for gastric cancer, previous laparotomies for major upper abdominal surgery.

All the patients underwent preoperative complete workup consisting of esophago-gastro-duodenoscopy with biopsy, gastric EUS, total body contrast-enhanced computed tomography (ce-CT). Tumor staging was performed according to American Joint Committee on Cancer (AJCC) tumor/node/metastasis classification and staging systems for gastric cancer 8th edition[9].

In all the patients with more than T2 N0 tumors, a perioperative chemotherapy was performed, according to age, comorbidity and performance status and it was followed by a re-staging of the disease. Complications were defined according to the Dindo-Clavien classification; severe complications were considered those of grade > 2[10]. Data of the selected patients was retrieved from a prospectively collected database; all the gathered data was recorded on an electronic spreadsheet and analysed using commercially available software, SPSS 18.0 (IBM, Armonk, NY).

Perioperative management and technical details

All patients received low molecular weight heparin starting the evening before the surgery, 2 g cefazolin 15 min before the skin incision, and 7-10 days preoperatively immunonutrition with 2 brick/day of impact oral.

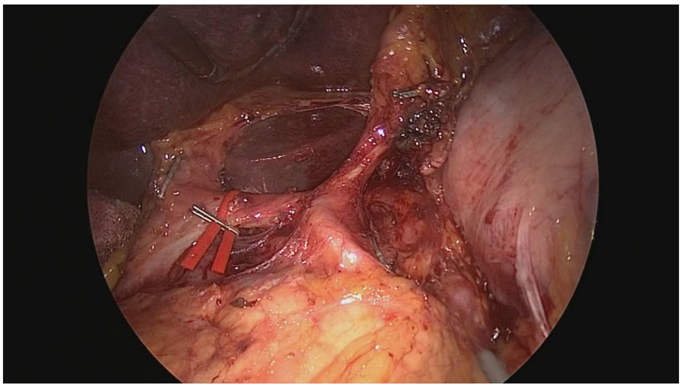


Figure 1. Lymphadenectomy of the stations: 7-8-9-11p-12a

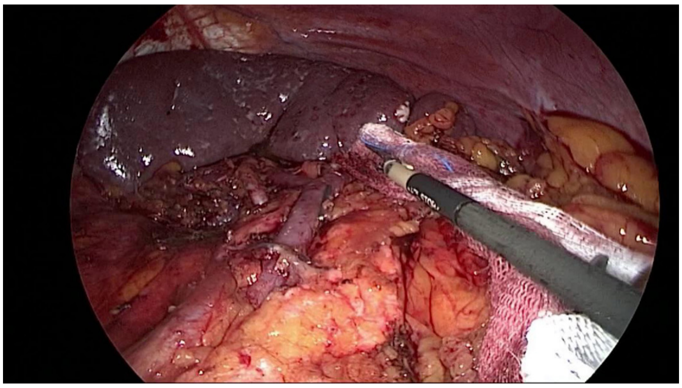


Figure 2. Lymphadenectomy of the stations: 10-11d

Patients were placed in a supine position, with legs apart, with the first surgeon positioned between the legs and one assistant on each side of the patient's abdomen. An open technique according to Hasson was used for the first trocar insertion in suvra-humbilical position; other trocars were placed, 2 on each side of the umbilicus, drawing a "smile" shape line; of these, three were 5 mm and one (on the left hemi-clavear line) 12 mm. A 30 degree scope was always used, with a carbon dioxide 12-14 mmHg pneumoperitoneum.

An exploration of the peritoneal cavity was also performed in order to exclude carcinomatosis and a sample of peritoneal liquid was always obtained for cytological examination.

Coloepiploic detachment and complete omentectomy was the first step of the operation with section of left gastroepiploic vessels at their origin, removing lymph-nodes of stations 4sb and 4sa, section of short gastric vessels, followed by right gastroepiploic vessels section, removing stations 5, 6 and 4d.

Division of the duodenum was performed 2-3 cm distal to pylorus, using 60 mm tristaple Endo Gia reinforced with polyglicolic acid (bioabsorbable staple line reinforcement, GORE SEAMGUARD™). Hepatic pedicle was cleared removing lymph-nodes of the station 12a untill the portal vein became visible and right gastric artery was sectioned. Stomach was pushed upward with better exposition of the suprapancreatic region; lymphadenectomy of stations 7-8a-9-11p-11d was performed and left gastric vessels were divided using clips [Figure 1]. Laimer-Bertelli membrane was divided and cardial branches and of the vagus nerves sectioned, removing lymph-nodes of the stations 1, 2 and 3. Dissection of the station 10 was performed only in the presence of enlarged lymph-nodes at splenic hylum [Figure 2].

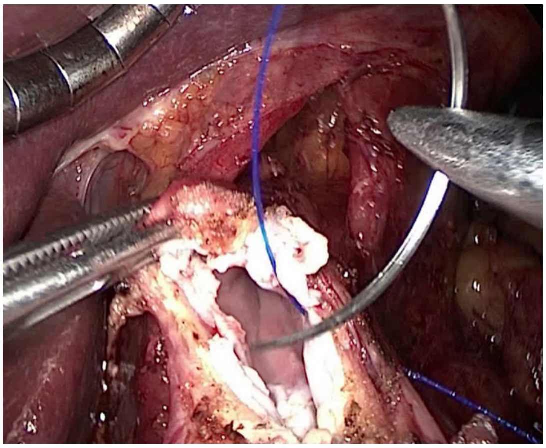


Figure 3. Placement of the hemi hand-sewn purse-string, using polypropylene 2/0 suture, on the anterior esophageal circumference

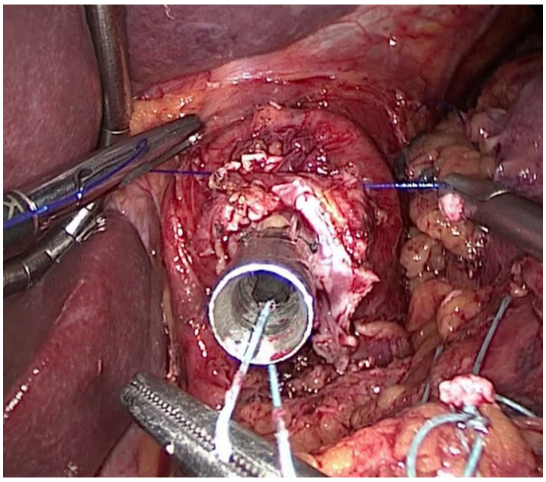


Figure 4. Closure of the hand-sewn purse-string, positioning the anvil in correct position

Roux-en-Y reconstruction was always done using the transmesocolic route and jejuno-jejunal anastomosis was perforemed with the same technique (isoperistaltic side-to-side mechanical anastomosis using 45 mm linear stapler) in all the patients. According to patients' characteristics and surgeon preference, 3 techniques were used for esophago-jejunal (E-J) anastomosis: hemi-double-stapling (HDS) technique using the transorally inserted anvil (OrVil^{TM})[11], modified side-to-side (S-S) overlap anastomosis according to Inaba[12], and modified end-to-side (E-S) anastomosis. For the last one, jejunal loop was always marked with a pen about 20 cm distally to the Treitz ligament and sectioned using a 45 mm linear stapler after it was passed through the mesocolic breach. The anterior hemi-circumference of the distal esophagus was sectioned with monopolar coagulation or an ultrasound device and a hemi hand-sewn purse-string, using polypropylene 2/0 suture, was placed [Figure 3].

After a stitch was placed on its edge, the anvil was introduced in the peritoneal cavity through the suvra-humbilical port, and inserted in the esophagus under laparoscopic vision. The remaining esophageal circumference was sectioned and the hand-sewn purse-string completed, using the stitch on the anvil edge to pull it in the correct position [Figure 4]. The specimen was extracted through mini-laparotomy on the left hemi-clavear trocar; the same mini-laparotomy was used to place the circular stapler in the previously sectioned jejunal loop and to reintroduce it in the peritoneal cavity restoring the pneumoperitoneum

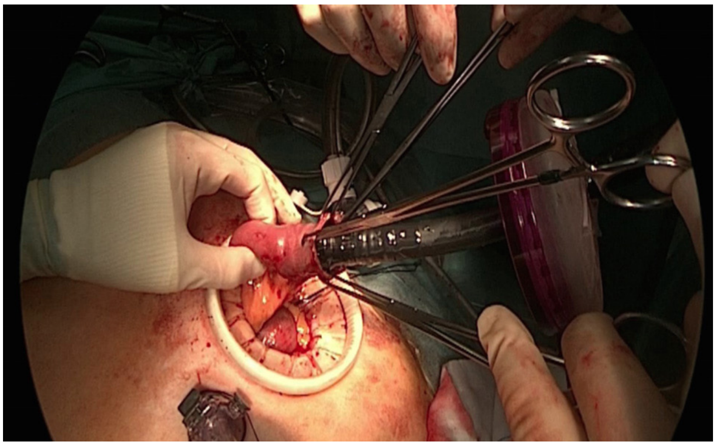


Figure 5. After specimen extraction, the mini-laparotomy on the left hemi-clavear trocar was used to place the circular stapler in the previously sectioned jejunal loop and to reintroduce it in the peritoneal cavity restoring the pneumoperitoneum using a specialized wound-sealing device

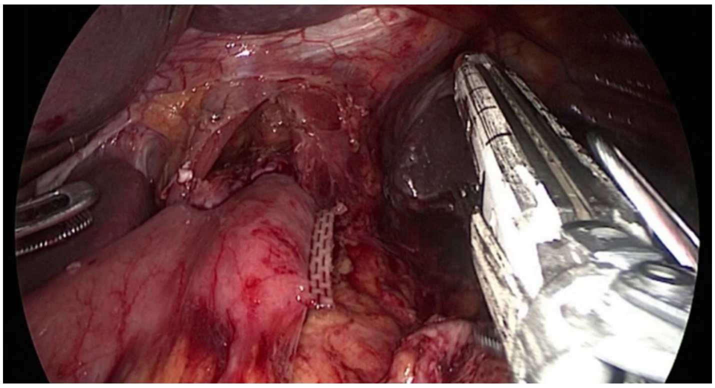


Figure 6. The end-to-side esophago-jejunal anastomosis was performed using 25 mm circular stapler and the jejunal loop extremity was then sectioned using linear 45 mm stapler

using a specialized wound-sealing device (GelPOINT Access Platforms, Applied Medical™) [Figure 5]. The E-S E-J anastomosis was performed using 25 mm circular stapler and the jejunal loop extremity was then sectioned using linear 45 mm stapler [Figure 6]. In all the patients an external close suction drain (type Jackson Pratt) was positioned via the right subcostal 5 mm port and positioned posteriorly to the E-J anastomosis. All the patients resumed oral idric intake on 1st postoperative day and semi liquid diet on 2nd postoperative day, when tolerated. A ce-CT of thorax and abdomen with oral hydrosoluble contrast examination was always performed on 6th postoperative day. After hospital discharge, follow-up was continued in outpatient settings every six months.

RESULTS

Between January 2017 and June 2018 at our institution, 28 patients underwent surgery for middle-upper third gastric cancer with curative intent; among these: 4 had previous gastric surgery for cancer and received degastrogastrectomy, 4 underwent associated transhiatal distal esophagectomy, 1 underwent upper polar gastrectomy. The remaining 19 underwent total gastrectomy; 9 of these received laparotomic treatment because of anesthesiological contraindications to laparoscopy (2 patients), tumor involvement of adjacent organs (4 patients), evidence of bulky nodes (1 patient), evidence of T4a tumor (1 patient), or tumor located on the greater curvature (1 patient). 10 patients underwent totally laparoscopic total

Table 1. Patients' characteristics

Number of patients	10
Sex ratio (M/F)	6/4
Age (year)*	76 (60-93)
BMI (kg/m^2)*	24 (19-32)
ASA score 1/2/3	1/6/3
clinical T1/T2/T3#	1/2/7
clinical EGC/AGC ratio	1/9
clinical N0/N+#	3/7
clinical stage I/IIa/IIb/III#	1/2/2/5
Preoperative CT	4

Data are expressed as number of patients. *Data is expressed as an average with the range in brackets; #clinical staging according AJCC 8th Edition. Pts: patients; M: males; F: females; BMI: body mass index; ASA: American Society of Anaesthesiologists; EGC: early gastric cancer; AGC: advanced gastric cancer; CT: chemotherapy

gastrectomy with D2 lymphadenectomy and 4 of these had received preoperative chemotherapy; in 2 cases the lymphadenectomy of the station 10 was performed. Demographic and preoperative features of these patients are reported in Table 1. After an uneventful resective phase in all patients, 1 of these received E-J anastomosis using HDS technique with transorally inserted anvil, 5 received S-S overlap anastomosis and 4 underwent E-S anastomosis. Only one patient experienced intraoperative complications; the only case reported was related to an esophageal injury during S-S E-J anastomosis needing the only conversion to laparotomy of the series; after conversion an E-S E-J anastomosis with a hand-sewn purse-string was done without further complications; other intraoperative details are reported in Table 2. Although no 30 day fatal events occurred, 7 patients experienced postoperative complications, 3 of these were severe according to Dindo-Clavien classification[10]; they consisted of ileus due to internal hernia, and abdominal abscess in splenic fossa needing reoperation; the last one was the only E-J anastomotic leakage and occurred in a patient who underwent laparoscopic E-S anastomosis and treated with endoscopic transanastomotic stent positioning. At pathological examination all the specimens had free proximal resection margins and all the patients received R0 resection; average numbers of harvested lymph-nodes was 29. Clinical staging was confirmed in 5 patients; on the other hand, 2 patients were under-staged and 3 over-staged; this miss-staging didn't affect the curative intent of surgery and no peritoneal carcinosis was detected at laparoscopy.

Average postoperative length of hospital stay was 10 days and no patients died during hospitalization. With a minimum follow-up of 6 months, median overall survival (OS) and disease-free survival (DFS) were 15.5 and 12.5 months respectively. All the patients included in perioperative chemotherapy program were able to complete the post operative treatment. Postoperative outcomes are described in Table 3.

DISCUSSION

Laparoscopic surgery is a valid option for the treatment of gastric cancer; although only the minor part of the data about it comes from randomized clinical trials (RCTs)[13,14]. A large number of results from non RCTs and case series assessed its safety and feasibility[4,15], however the majority of the reported data refers to distal gastrectomy[16] and only a few parts of the ongoing RCTs include total gastrectomy[17-19].

Nevertheless it gained wide diffusion in Eastern countries, with a slow adoption in Europe and USA too[11,20], showing less blood loss, fewer analgesic uses, earlier passage of flatus, quicker resumption of oral intake, earlier hospital discharge, and reduced postoperative morbidity, with longer operative time, in comparison with open total gastrectomy[5]. Our data, obtained from a non selected series of European older adults, was consistent with these evidences, reporting 3 cases of severe adverse events, 2 of these requiring reoperation; 1 of these was due to an internal hernia and since that occurance we always have sutured the jejunal mesentery without occurance of further cases.

Table 2. Intraoperative outcomes

Duration of surgery (min)*	**369 (275-440)**
Type of anastomosis:	
HDS technique with transorally inserted anvil	1
S-S overlap anastomosis	5
E-S anastomosis	4
Intraoperative complication	1
Associated procedures	6
Conversion to open surgery	1

Data is expressed as number of patients. *Data is expressed as an average with range in brackets. HDS: hemi-double-stapling; S-S: side-to-side; E-S: end-to-side

Table 3. Postoperative outcomes

Length of hospital stay (day)*	10 (8-58)
Overall complications	7
Severe complications	3
Reoperations	2
Anastomotic leakage	1
Anastomotic stenosis	0
Abdominal abscess	1
POPF	0
Duodenal stump leak	0
Wound infection	0
Ileus caused by internal hernia	1
Number of LNs harvested$	29 (15-38)
Number of LNs positive$	5 (0-22)
Tumor dimension (mm)	49 (17-130)
Pathological T1b/T2/T3/T4a#	1/1/6/2
Pathological N0/N1/N2/N3a/N3b	3/1/1/4/1
Pathological staging Ib/IIa/IIIa/IIIb/IIIc#	2/2/1/4/1
Median OS* (months)	15.5 (6-32)
Median DFS* (months)	12.5 (6-28)

Data is expressed as number of patients. *Continuous variables are reported as mean values and range; $data is expressed as an average with range in brackets; #clinical staging according AJCC 8th Edition. POPF: postoperative pancreatic fistula; LNs: lymph-nodes; OS: overall survival; DFS: disease free survival

Some critical aspects of this procedure however still make it open to debate, one of these being the possibility to perform a correct lymphadenectomy, especially to dissect the station 10. A large meta-analysis, comparing open and laparoscopic total gastrectomy, reported no statistical differences between the two techniques in terms of lymph-nodes clearance, 5-year OS and DFS, and free proximal resection margins, confirming their same oncological safety and adequacy[5]. This data was confirmed by another meta-analysis, including totally laparoscopic total gastrectomy only, reporting no difference in the number of the harvested lymph-nodes[21]. Furthermore a recent RCT[22] reported an incidence of positive lymph-nodes in the station 10 of 2.4%, in a cohort of well selected patients, all candidates to total gastrectomy, concluding that, for these kind of patients, the station 10 lymphadenectomy is not mandatory; however in case of macroscopic lymph-nodes at splenic hilum it seems possible to perform a laparoscopic spleen-preserving dissection[23]. Our small series confirmed this data with a mean number of lymph-nodes harvested of 29; D2 lymphadenectomy and complete omentectomy were always performed in all the patients and they didn't cause intraoperative nor postoperative complications; 2 patients needed, in addition, the spleen-preserving lymphadenectomy of the station 10 for slightly enlarged, suspicious, lymph-nodes without further morbidity.

Therefore the major concern of laparoscopic total gastrectomy seems related to the E-J reconstruction. The first attempt to overcome this obstacle was to perform a midline mini-laparotomy for a hybrid approach;

however several authors reported important limits of this approach due to the difficulty to use a purse-string instrument in a very narrow space, and to place a suture without clear visualization[24,25]. Actually various totally laparoscopic techniques are used, based on circular or linear staplers[7]; some authors achieved excellent results independently from the technique, without a clear superiority of a particular model[1], even if leakage and stenosis seemed to occur more frequently using circular stapler compared to linear ones[8]. However the incidence of anastomotic-related complications widely varied among the studies with anastomotic leakage and stricture rate of 3.5% (0.9%-8.5%) and 2.2% (0%-9%) respectively[1]. Differences between laparoscopic total gastrectomies with open ones were not found, neither regarding anastomotic-related complications, with a slightly, but not significantly, disadvantage of laparoscopy in term of stenosis[26]. The feasibility and good outcomes of totally laparoscopic reconstruction were supported by our data; in the majority of patients, anastomosis was performed laparoscopically, under pneumoperitoneum, with a good visualization; just in one case an esophageal disruption occurred during linear stapler insertion needing laparotomic conversion to re-do the anastomosis. With a mean follow up of 16 month, only 1 anastomotic-related complication occurred: anastomotic leakage diagnosed at imaging on 6th postoperative day and treated by means of endoscopically positioned stent with good recovery. As reported in literature, overlap technique is quite easy to perform and not demanding a long time; in addition it seemed to have lower incidence of anastomotic stenosis compared to Orvill technique[27]; on the other hand it doesn't allow ability to check for malignancy with frozen section the esophageal margin[6] and can be very challenging in obese patients with thickened and fixed mesentery, as the patient in our series who experienced esophageal injury. For patients with these anthropometric features, we used a modified E-S double stapling technique using 25 mm circular stapler, introduced in the peritoneal cavity via a wound sealing device in the place of the left hemi-clavear trocar, reproducing the same familial anastomosis usually used in the open total gastrectomy. This technique, although perceived as more time-consuming and technically challenging, allowed to perform a tension-free anastomosis in obese patients too, overcoming the problem of the deep and dorsal position of the anastomotic site and the hindering visualization and manipulation.

Small sample size, retrospective and non comparative analysis constitute the main limits of this study, and firm conclusions cannot be drawn, but it adds to a still lacking amount of literature, especially in Western countries, some results confirming the feasibility and the safety of totally laparoscopic total gastrectomy in the hands of experienced surgeons with a steep learning curve.

In conclusion, totally laparoscopic total gastrectomy is a feasible option in the treatment of gastric cancer. The choice about the method for E-J reconstruction should be based on the individual patient's features and on the dexterity of the surgeon, which should be able to perform more than one option for a tailored approach.

DECLARATIONS

Authors' contributions

Made substantial contributions to conception and design of the study: Mazzola M., Gualtierotti M, De Martini P, Ferrari G
Performed data analysis and interpretation: Mazzola M, Gualtierotti M
Performed data acquisition: Morini L, Achilli P, Zironda A

Availability of data and materials

Not appliable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Copyright

REFERENCES

1. Okabe H, Tsunoda S, Tanaka E, Hisamori S, Kawada H, et al. Is laparoscopic total gastrectomy a safe operation? A review of various anastomotic techniques and their outcomes. Surg Today 2015;45:549-58.
2. Coburn N, Cosby R, Klein L, Knight G, Malthaner R, et al. Staging and surgical approaches in gastric cancer: A clinical practice guideline. Curr Oncol 2017;24:324-31.
3. Inaki N, Etoh T, Ohyama T, Uchiyama K, Katada N, et al. A Multi-institutional, Prospective, Phase II Feasibility Study of Laparoscopy-Assisted Distal Gastrectomy with D2 Lymph Node Dissection for Locally Advanced Gastric Cancer (JLSSG0901). World J Surg 2015;39:2734-41.
4. Best LM, Mughal M, Gurusamy KS. Laparoscopic versus open gastrectomy for gastric cancer. Cochrane Database Syst Rev 2016;3:CD011389.
5. Wang W, Zhang X, Shen C, Zhi X, Wang B, et al. Laparoscopic versus open total gastrectomy for gastric cancer: An updated meta-analysis. PLoS One 2014;9:e88753.
6. Treitl D, Hochwald SN, Bao PQ, Unger JM, Ben-David K. Laparoscopic Total Gastrectomy with D2 Lymphadenectomy and Side-to-Side Stapled Esophagojejunostomy. J Gastrointest Surg 2016;20:1523-9.
7. Wei G, Zheng J, Li Y. Reconstruction after LATG : technical tips and pitfalls.Transl Gastroenterol Hepatol 2017;2:41.
8. Umemura A, Koeda K, Sasaki A, Fujiwara H, Kimura Y, et al. Totally laparoscopic total gastrectomy for gastric cancer: Literature review and comparison of the procedure of esophagojejunostomy. Asian J Surg 2015;38:102-12.
9. Amin MB. AJCC Cancer Staging System, 8th Edition : UPDATE. Am Jt Comm Cancer 2013. Avaliable from: http://cancerstaging.org/About/Pages/8th-Edition.aspx. [Last accessed on 9 Apr 2019]
10. Dindo D, Demartines N, Clavien PA. Classification of Surgical Complications. Ann Surg 2004;240:205-13.
11. Lafemina J, Viñuela EF, Schattner MA, Gerdes H, Strong VE. Esophagojejunal reconstruction after total gastrectomy for gastric cancer using a transorally inserted anvil delivery system. Ann Surg Oncol 2013;20:2975-83.
12. Inaba K, Satoh S, Ishida Y, Taniguchi K, Isogaki J, et al. Overlap method: Novel intracorporeal esophagojejunostomy after laparoscopic total gastrectomy. J Am Coll Surg 2010;211:225-9.
13. Kitano S, Shiraishi N, Fujii K, Yasuda K, Inomata M, et al. A randomized controlled trial comparing open vs laparoscopy-assisted distal gastrectomy for the treatment of early gastric cancer: An interim report. Surgery 2002;131:306-11.
14. Lee JH, Han HS, Lee JH. A prospective randomized study comparing open vs laparoscopy-assisted distal gastrectomy in early gastric cancer: early results. Surg Endosc 2005;19:168-73.
15. Lin JX, Huang CM, Zheng CH, Li P, Xie JW, et al. Surgical outcomes of 2041 consecutive laparoscopic gastrectomy procedures for gastric cancer: A large-scale case control study. PLoS One 2015;10: e0114948.
16. Kim YW, Yoon HM, Yun YH, Nam BH, Eom BW, et al. Long-term outcomes of laparoscopy-assisted distal gastrectomy for early gastric cancer: Result of a randomized controlled trial (COACT 0301). Surg Endosc Other Interv Tech 2013;27:4267-76.
17. Straatman J, van der Wielen N, Cuesta MA, Gisbertz SS, Hartemink KJ, et al. Surgical techniques, open versus minimally invasive gastrectomy after chemotherapy (STOMACH trial): study protocol for a randomized controlled trial. Trials 2015;16:123.
18. Haverkamp L, Brenkman HJ, Seesing MF, Gisbertz SS, van Berge Henegouwen MI, et al. Laparoscopic versus open gastrectomy for gastric cancer, a multicenter prospectively randomized controlled trial (LOGICA-trial). BMC Cancer 2015;15:556.
19. Hyung WJ, Yang HK, Han SU, Lee YJ, Park JM, et al. A feasibility study of laparoscopic total gastrectomy for clinical stage I gastric cancer: a prospective multi-center phase II clinical trial, KLASS 03. Gastric Cancer 2019;22:214-22.
20. Kostakis ID, Alexandrou A, Armeni E, Damaskos C, Kouraklis G, et al. Comparison Between Minimally Invasive and Open Gastrectomy for Gastric Cancer in Europe: A Systematic Review and Meta-analysis. Scand J Surg 2017;106:3-20.
21. Malczak P, Torbicz G, Rubinkiewicz M, Gajewska N, Sajuk N, et al. Comparison of totally laparoscopic and open approach in total gastrectomy with D2 lymphadenectomy - systematic review and meta-analysis. Cancer Manag Res 2018;10:6705-14.
22. Sano T, Sasako M, Mizusawa J, Yamamoto S, Katai H, et al. Randomized Controlled Trial to Evaluate Splenectomy in Total Gastrectomy for Proximal Gastric Carcinoma. Ann Surg 2017;265:277-83.
23. Tu RH, Li P, Xie JW, Wang JB, Lin JX, et al. Development of lymph node dissection in laparoscopic gastrectomy: safety and technical tips. Transl Gastroenterol Hepatol 2017;2:23.
24. Bo T, Peiwu Y, Feng Q, Yongliang Z, Yan S, et al. Laparoscopy-Assisted vs. Open Total Gastrectomy for Advanced Gastric Cancer:

Long-Term Outcomes and Technical Aspects of a Case-Control Study. J Gastrointest Surg 2013;17:1202-8
25. Jeong O, Ryu SY, Zhao XF, Jung MR, Kim KY, et al. Short-term surgical outcomes and operative risks of laparoscopic total gastrectomy (LTG) for gastric carcinoma: Experience at a large-volume center. Surg Endosc 2012;26:3418-25.
26. Inokuchi M, Otsuki S, Fujimori Y, Sato Y, Nakagawa M, et al. Systematic review of anastomotic complications of esophagojejunostomy after laparoscopic total gastrectomy. World J Gastroenterol 2015;21:9656-65.
27. Kawamura H, Ohno Y, Ichikawa N, Yoshida T, Homma S, et al. Anastomotic complications after laparoscopic total gastrectomy with esophagojejunostomy constructed by circular stapler (OrVilTM) versus linear stapler (overlap method). Surg Endosc 2017;31:5175-82.

Mini-invasive Surgery

Commentary

Open Access

Check for updates

Overview of gastroesophageal junction cancers

Aung Myint Oo, Saleem Ahmed

Department of General Surgery, Tan Tock Seng Hospital, Singapore 308433, Singapore.

Correspondence to: Dr. Saleem Ahmed, Department of General Surgery, Tan Tock Seng Hospital, Singapore 308433, Singapore. E-mail: medicsaleem@gmail.com; Dr. Aung Myint Oo, Department of General Surgery, Tan Tock Seng Hospital, Singapore 308433, Singapore. E-mail: myint_oo_aung@ttsh.com.sg

How to cite this article: Oo AM, Ahmed S. Overview of gastroesophageal junction cancers. *Mini-invasive Surg* 2019;3:13. http://dx.doi.org/10.20517/2574-1225.2019.02

Received: 14 Jan 2019 **First Decision:** 25 Mar 2019 **Revised:** 10 Apr 2019 **Accepted:** 17 Apr 2019 **Published:** 6 May 2019

Science Editor: Tetsu Fukunaga **Copy Editor:** Cai-Hong Wang **Production Editor:** Huan-Liang Wu

Abstract

Oesophageal and gastroesophageal junction (GEJ) malignancy is the fastest growing cancer in the Western population. This together with the deadly nature of the disease has attracted increased attention from doctors and researchers alike. The increasing incidence has been primarily attributed to the increase in rates of obesity that in turn causes increased gastroesophageal reflux disease leading to Barrett's oesophagus and eventually adenocarcinoma of the oesophagus especially at the GEJ. We discuss the epidemiology, risk factors and the management of GEJ tumours.

Keywords: Cardioesophageal, gastroesophageal, upper gastrointestinal, cancer, tumour

INTRODUCTION

Oesophageal and gastroesophageal junction (GEJ) malignancy is the fastest growing cancer in the Western population, especially in United States of America (USA), rising by 6-fold annually on the background of declining rates of most other cancers[1,2]. This together with the deadly nature of the disease has attracted increased attention from doctors and researchers alike. The increasing incidence has been primarily attributed to the increase in rates of obesity that in turn causes increased gastroesophageal reflux disease (GERD) leading to Barrett's oesophagus and eventually adenocarcinoma of the oesophagus especially at the GEJ[3].

DEFINITION

The definition of GEJ cancers has been an area of controversy and disagreement and have in the past been considered either a gastric or oesophageal cancer as they lie in between the two. GEJ tumours also go by many other names including distal oesophageal cancers, proximal gastric cancers and cancers of cardia. This has led to discrepancies in the literature regarding the classification, pathophysiology, surgical approach and prognosis. The most widely accepted definition for GEJ cancer is that proposed by Siewert *et al.*[4] and led to the tumours being classified as a distinct entity from gastric or oesophageal cancers. He proposed that GEJ tumours be classified as those having epicentre of the cancer within 5 cm proximal or distant to the Z-line. The Union for International Cancer Control (UICC) has adopted a similar definition and suggests that tumours that extend into the oesophagus classified and staged using an oesophageal scheme while those without oesophageal extension are staged using the gastric cancer scheme even if they occur within 5 cm distant to the GEJ[5]. American Joint Committee on Cancer (AJCC) suggests that cancers involving the GEJ that have their epicentre within the proximal 2 cm of the cardia (Siewert Type I/II) are to be staged as oesophageal tumours while those that are more than 2 cm distal to the cardia should be staged as gastric cancer[6].

The importance of accurate and reproducible definition of GEJ cancer is important as the tumour biology, management is different and importantly the prognosis is considered worse than that of oesophageal and gastric cancer. Even within GEJ tumours there is marked heterogeneity, Siewert Type II and III are known to have better prognosis than Siewert I[3]. GEJ tumours are known to demonstrate aggressive behaviour with early local invasion and systemic dissemination. As the GEJ tumours borders both the thoracic and abdominal cavities there is lymph outflow and therefore lymph node metastasis to both these regions. Moreover, the close relationship of the GEJ cancer to an anatomically complex region bordering multiple organs means complete resection can only be achieved by multi-visceral resection[7].

EPIDEMIOLOGY

GEJ tumour incidence has dramatically increased in Western population and the distal oesophageal cancer type is the dominant oesophageal cancer type in the USA. Similarly, the rates of proximal gastric cancer have increased while that of distal gastric cancer has dropped. The rates of GEJ tumours has increased between 4%-10% every year in USA since 1976[8-10]. The overall proportion of proximal gastric cancer, cancer of the cardia and distal oesophageal cancer accounted for about 30%-40% of all gastric carcinoma in Western countries and interestingly, China, far higher than other Eastern centres such as Japan and Korea[3,8,9]. However, these numbers have to be taken with a pinch of salt. Historically, the confusion in the labelling of GEJ tumours with them being previously labelled as oesophageal or gastric cancers or even "unspecified" under the World Health Organization's International Classification of Diseases for Oncology codes could lead to an erroneous result. A study conducted in Sweden revealed that the true incidence could be up to 45% higher or 15% lower than reported in its national registry[11]. The secular trend of rising incidence of GEJ tumours has to be interpreted with caution.

RISK FACTORS

The etiology of GEJ tumours is still unclear. Much of its alarming rise has been blamed on increasing trends of obesity and GERD. This is likely to explain the rise in Siewert I tumours, which arise from areas of intestinal metaplasia in the distal oesophagus contributed by chronic GERD due to obesity. However, it is still unclear if metaplasia is due to acid reflux or bile reflux into oesophagus. Analysis of oesophageal fluid in patients with GERD found that they contain 10 times more bile than normal controls[12]. Animal studies also have shown that duodenal fluid induces Barrett's oesophagus and oesophageal adenocarcinoma[13,14]. This might explain why use of acid suppression agents has not lowered the rates of GEJ tumours[1].

Increasing rates of GERD due to acid or bile irritation does not explain the rise in Siewert Type II and III tumours. An analysis of GEJ tumours by Siewert *et al.*[15] found that in contrast to Siewert Type I tumours intestinal metaplasia was only found in 10% of patients with Type II and rare in patients with Type III tumours which suggests chronic GERD cannot fully explain the surge in Type II and III tumours and that other factors maybe at play.

Obesity has been consistently implicated as a risk factor for development of GEJ. Apart from the mechanical pathway resulting in increased reflux, there maybe independent inflammatory and hormonal mediators. An Australian study, showed that obesity in combination with frequent reflux were risk factors for development of GEJ tumours than either acting alone suggesting that synergistic as opposed to additive effects was most likely[16].

Infection with *H. pylori* is associated with increased rates of gastric cancer via mechanisms of chronic inflammation however there is an inverse association with *H. pylori* infection and incidence of GEJ tumours. A study by Whiteman *et al.*[17] found that *H. pylori* was inversely associated with GEJ adenocarcinoma tumours with odds ratio (OR) 0.41. It is not well understood how the infection confers a protective benefit but the potential mechanism include decreased acid production and microbiome alteration[18]. It is interesting note that the decreasing incidence of *H. pylori* over time parallels the increasing incidence of GEJ tumours.

Smoking has been found to have a strong association with GEJ tumours. A pooled analysis of multiple primary studies from the Barrett's Esophagus and Esophageal Adenocarcinoma Consortium (BEACON)[19] found that smoking was positively associated with GEJ adenocarcinoma (OR = 2.18, 95%CI: 1.84-2.58), and also demonstrated a strong dose-response association.

The other factors found to be associated with GEJ tumours include alcohol intake, intake of highly processed meat diet while intake of high fibre diet and medications such as non-steroidal anti-inflammatory drugs are thought to confer a protective effect[18]. Further studies are required to provide more conclusive evidence.

MANAGEMENT

Management of GEJ tumours is challenging as they involve two contiguous organs and also straddle the thoracic cavity and abdominal cavity via hiatal opening.

Management of GEJ cancers depends on the stage of the tumour. For early tumours there is a role for endoscopic submucosal dissection (ESD) but advanced tumours require multimodality treatment including surgery.

Role of endoscopic treatment in early stage GEJ cancer

With the development of the Insulated-tip diathermic knife (IT-knife) in late 1990 and subsequent development of the ESD technique in 2003, the endoscopic management of early gastrointestinal tumours including early gastric cancer and early esophageal cancer became feasible and popular[20-23]. ESD has been accepted as the minimally invasive curative treatment option for superficial early gastrointestinal cancers including those of stomach, esophagus and colonic origins[24]. However, the indication of endoscopic treatment for early GEJ cancers including Barret's adenocarcinoma has not been clearly established due to unclear pattern of lymph node metastasis[25]. Meta-analysis of 6 retrospective studies have demonstrated the safety and feasibility of ESD on early superficial GEJ cancers[26]. Five studies used curative criteria for gastric cancer and one study used the criteria for esophageal cancer. 269 patients who met the curative resection criteria did not have any local or distant metastases. Out of 90 patients who underwent noncurative resection, 3 (3.3%) presented with local recurrence and 2 (2.2%) presented with distant metastasis. The study was limited by the small number of patients with short duration of follow-up. A group from Korea compared outcomes of 79 patients with Siewert II adenocarcinoma who underwent ESD compared to surgery. The 5-year overall survival rates were similar in both groups. There was no gastric cancer related death in each group and the incidence of treatment-related adverse events was similar in both groups leading the authors to conclude that ESD may be an effective alternative to surgery with comparable long-term oncologic outcomes[27]. ESD has a good safety profile with low number of adverse events reported by many centers[28,29]. According to one comparative study, ESD was associated with much less adverse events compared to surgery group (10% *vs.* 17.9%). ESD is a highly skilled procedure mainly performed in Asian centers and many authors have described a steep learning curve for those performing ESD especially for GEJ tumours, therefore appropriate training including simulation based practice within a training framework must be enforced to increase safety and efficacy[30-32]. Based on current evidence, ESD for superficial early EGJ cancers is feasible and safe with favorable long-term outcomes however further work is necessary to establish specific resection criteria for ESD of GEJ tumours.

Surgical management of GEJ tumours

There are various surgical strategies for management of GEJ cancers. They include esophagectomy with partial gastrectomy or extended total gastrectomy with or without thoracotomy. Individualization of the surgical strategy and adherence to sound oncological principles with aims of radical lymphadenectomy with negative margins for the resectable GEJ tumours is key in attaining good outcomes. Tumour location as per Siewert Classification and location of enlarged lymph nodes are critical factors in determining the surgical strategy.

The pattern and frequency of lymph node metastasis differ according to the epicenter of the tumour location and histology[33-36]. Matsuda *et al.*[37] carried out clinicopathological correlation of surgically resected GEJ tumours and found that the frequency of mediastinal lymph node metastasis was also found to be higher in squamous cell carcinoma than adenocarcinoma (46.7% *vs.* 7.5%).

Regardless of the Siewert classification, the majority of the junctional tumours metastasise to the perigastric/abdominal regional lymph nodes[36,37]. The frequency of mediastinal lymph node metastasis differs significantly depending on the Siewert types. The mediastinal lymph node metastasis was only 9% in Type III compared to 30% in Type II and 46% in Type I tumours while abdominal lymph nodes metastasis are found to be 51%, 71% and 91% respectively for Type I, II and III tumours[35]. Hence, choice of surgery and lymphadenectomy need to be tailored according to the epicentre and histology of the tumor.

Siewert type I tumours are considered as lower esophageal tumours with potential lymph node metastasis to mediastinal and abdominal lymph nodes. Subtotal esophagectomy with partial gastrectomy is considered to be a superior approach for type 1 tumours. Siewert type 3 tumours are considered proximal gastric cancer with potential lymph node metastasis to lower mediastinal and abdominal lymph nodes. Extended total gastrectomy with distal esophagectomy is considered more appropriate for type 3 tumour[15,38-40].

Siewert type II tumours are true junctional tumours and choice of surgical approach is controversial. In a retrospective study comparing transmediastinal esophagectomy with partial gastrectomy and extended total gastrectomy with transhiatal distal esophagectomy, it was demonstrated that the latter was associated with fewer post-operative morbidity and mortality without any difference in survival[38]. However, the subgroup analysis of those patients with R0 resection showed that extended total gastrectomy and not a transmediastinal oesophagogastrectomy was an independent predictor for long term survival.

There were two phase III randomized control trials which compared two operative strategies for GEJ cancers[41,42]. In the Dutch Trial, 220 patients with Siewert Type I and II tumours were randomly assigned to transhiatal esophagectomy (THE) *vs*. extended transthoracic esophagectomy and en-bloc lymphadenectomy (via right thoracic cavity) (TTE)[41]. THE was associated with lower morbidity such as pulmonary complications and chylothorax. Although median overall, disease-free, and quality-adjusted survival did not differ statistically between the groups, there was a trend toward improved long-term survival at five years with the extended transthoracic approach. In the follow-up study on 5 year survival, there was no significant overall survival benefit for either approach (36% in TTE *vs.* 34% in THE, P = 0.71[43]. However, extended TTE for type I esophageal adenocarcinoma showed a trend towards better 5-year survival (51% *vs.* 37%, P = 0.33). Moreover, patients with a limited number of positive lymph nodes in the resection specimen seem to benefit from an extended transthoracic esophagectomy.

In the Japanese JCOG 9502 trial, patients with Siewert II and III cancers were assigned to either transhiatal approach (TH) or left thoracoabdominal approach (LTA)[42]. TH consisted of a total gastrectomy with D2 lymphadenectomy (including splenectomy) via a laparotomy. Thoracotomy on either side was allowed to achieve a complete (R0) resection only when the proximal surgical margin was positive (determined either macroscopically or microscopically by frozen section) and no further transhiatal oesophageal resection was possible. In LTA group, a thorough mediastinal nodal dissection below the left inferior pulmonary vein was undertaken with oesophagectomy of sufficient length. The trial was closed prematurely as the planned interim analysis concluded that the LTA approach was associated with higher morbidity and mortality including postoperative complications such as pulmonary complications; 49% *vs.* 34%, P = 0.06) and in-hospital mortality (4% *vs.* 0%, P = 0.25). Although statistically insignificant, both 5 years (38% *vs.* 52%) and 10 years survival (24% *vs.* 37%) were found to be lower with LTA group[44].

Complete R0 resection of GEJ tumours is key to achieving good survival outcomes. Systematic review and meta-analysis of fourteen studies involving 2433 patients with oesophageal cancer who had undergone oesophagectomy showed that circumferential resection margin (CRM) involvement was associated with significantly higher 5-year mortality rate (OR 2.05, 95%CI: 1.41-2.99; P < 0.001)[45].

There are few options for reconstruction after resection of GEJ tumours. For Type II and Type III tumours, after extended total gastrectomy and distal esophagectomy the reconstruction is usually done with Roux-En-Y esophago-jejunostomy. For Type I tumours, combined transabdominal and transthroaic approach is required to perform enbloc eosophagectomy and proximal gastrectomy together with 2 field lymphadenectomy. The other available option is a left throacoabdominal approach with intrathoracic anastomosis know as Sweet esophagectomy. The stomach is used as a conduit to perform intrathoracic oesophagogastrostomy for reconstruction. In some patients, if gastric conduit is unsuitable, due to previous surgery, the jejunum and colon are both possible conduit options.

Open versus minimally invasive approach

Evidence suggests that transthoracic approach with radical lymphadenectomy may be an oncologically superior operation with better long-term survival with the downsides of increased operative morbidity and mortality especially pulmonary complications. Minimally invasive approaches may be a promising alternative with decreased post-operative complications without compromising the radicality of the surgery. The current evidence suggests the potential benefits for minimally invasive esophagectomy approach to GEJ tumours include smaller incisions, less intraoperative blood loss fewer postoperative complications, shorter admission to the intensive care unit and overall hospital stay, better preservation of postoperative pulmonary function and equivalent quality of lymph node dissections[46-49]. The evidence for minimally invasive surgeries for GEJ tumours is convincing, however more prospective studies are required to evaluate the long-term oncological outcomes.

Multimodality management of GEJ tumours

Multimodality treatment strategies in locally advanced GEJ tumours (T2 and higher or node positive) result in improved outcomes. These strategies include neoadjuvant and adjuvant chemotherapy with

 Oo et al. Mini-invasive Surg 2019;3:13 I http://dx.doi.org/10.20517/2574-1225.2019.02

or without radiation therapy in addition to surgery. The multimodality treatment has now become the standard of care for advanced GEJ cancers. However, the best approach to multimodality treatment for GEJ cancers is not established yet as GEJ tumours represent only a small subset of cohort in most of clinical trials[50-53]. Even though adjuvant chemotherapy has been proven to be beneficial and improve survival outcomes compared to surgery alone in gastric cancers, the role of adjuvant chemotherapy in GEJ tumours is still unclear as there are no large trials conducted for GEJ cancers specifically and are often categorised under the subset of gastric cancers[54,55].

Adjuvant chemoradiotherapy is one possible option for patients with GEJ tumours who didn't receive the preoperative treatment with survival benefit demonstrated in US intergroup 0116 trial[53]. This regimen also known as the "Macdonald regimen" is the current standard of adjuvant treatment for patients with gastric cancer. Of the 559 patients recruited in this trial only 20% had GEJ cancers. Adjuvant chemoradiotherapy produced substantial reduction in both overall relapse and locoregional relapse as well improved overall survival, hazard ratio (HR) 1.32 (95%CI: 1.10-1.60; P = 0.0046)[53]. One major criticism of the study was that only 10% of patients had received D2 lymphadenectomy and therefore the improvement in relapse rates and survival could be due to potential compensation of an oncologically inadequate surgery.

Neoadjuvant or perioperative chemotherapy with or without radiation therapy have proven to be effective in improving survival. The MAGIC trial compared patients who underwent surgery alone to surgery plus perioperative chemotherapy (3 cycles of preoperative and 3 cycles of postoperative epirubicin, cisplatin and infusional flurouracil)[50]. Of the 503 patients recruited only 11% had GEJ tumours. Compared to surgery alone group, the perioperative chemotherapy group had higher overall survival (HR for death, 0.75; 95%CI: 0.60-0.93; P = 0.00936 percent *vs*. 23 percent) and progression-free survival (HR for progression, 0.66; 95%CI: 0.53-0.81; P < 0.001).

The Dutch Chemoradiotherapy for Esophageal Cancer Followed by Surgery Study (CROSS) trial included 22%of patients with GEJ cancers and compared the effectiveness of neoadjuvant chemoradiation over surgery alone[52]. Overall survival was significantly better in the neoadjuvant chemoradiotherapy group (HR, 0.657; 95%CI: 0.495-0.871; P = 0.003). The survival benefit in chemoradiation group was persistent in the long term with median follow up of 86.4 months[56].

The Preoperative therapy in Esophagogastric adenocarcinoma Trial (POET) was the only trial which compared neoadjuvant chemotherapy versus chemoradiotherapy in locally advanced GEJ adenocarcinoma[57]. Although the study ended prematurely due to lower accrual, there was a trend observed towards improved 3-year survival in the chemoradiation group (47.4% *vs*. 27.7%; P = 0.07). The long-term follow-up of the patients also showed a trend in improved overall 5-year survival in favor of preoperative chemoradiotherarpy (HR 0.65, 95%CI: 0.42-1.01, P = 0.055).

A meta-analysis including 24 studies concluded that there was strong evidence for survival benefit of neoadjuvant chemoradiotherapy or chemotherapy over surgery alone in patients with esophageal carcinoma including GEJ cancers[58]. However, there was no clear advantage of neoadjuvant chemoradiotherapy over neoadjuvant chemotherapy according to the study.

CONCLUSION

The management of GEJ junction tumours is challenging and there is no one-size-fit-all strategy. The endoscopic option can be considered for early tumours especially for those patients with high risk for surgery. The surgical approach for advanced GEJ cancers should be tailored according to the histological subtype, extent of oesophageal and/or gastric invasion, clinical and radiological lymph node involvement, achievement of negative resection margins with R0 resection as well as achievement of safe anastomosis for reconstruction. Minimally invasive approach is promising especially in experienced hands however more data on long-term oncological results is needed.

Multimodality treatment is superior to surgery alone in locally advanced resectable GEJ tumours. The advantages of neoadjuvant or perioperative treatment are downstaging of tumour, reducing the risk of recurrence, improving rates of R0 resection and improving outcomes after complete resection. At present, there is no global consensus on the optimal multimodality management of GEJ tumours. Further studies are needed to explore the optimal treatment strategy including surgical approach, sequence and regimen of multimodality management .

DECLARATIONS

Authors' contributions

Oo AM and Ahmed S contributed equally to literature search and writing of manuscript.

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

The authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Copyright

REFERENCES

1. Chai J, Jamal MM. Esophageal malignancy: a growing concern. World J Gastroenterol 2012;18:6521-6.
2. Lerut T. Carcinoma of the esophagus and gastro-esophageal junction. 2001.
3. Wu AW, Ji JF. Adenocarcinoma of esophagogastric junction requires a clearer definition. Transl Gastrointest Cancer 2013;2:5-9.
4. Siewert JR, Stein HJ. Classification of adenocarcinoma of the oesophagogastric junction. Br J Surg 1998;85:1457-9.
5. Wittekind Ch, Sobin LH, Gospodarowicz MK. TNM classification of malignant tumours. 7th ed. Blackwell Publishing Ltd; 2009.
6. Amin MB, Edge S, Greene F, Byrd DR, Brookland RK, et al. AJCC Cancer Staging Manual. 8th ed. Springer; 2017.
7. Kshivets O. Cardioesophageal cancer: best treatment strategies. Open Cardiovasc Thorac Surg J 2009;2:21-32.
8. Strong VE, Song KY, Park CH, Jacks LM, Gonen M, et al. Comparison of gastric cancer survival following R0 resection in the United States and Korea using an internationally validated nomogram. Ann Surg 2010;251:640-6.
9. Wu AW, Ji JF, Yang H, Li YN, Li SX, et al. Long-term outcome of a large series of gastric cancer patients in China, Chinese J Cancer Res 2010;22:167-75.
10. Cellini F, Morganti AG, Di Matteo FM, Mattiucci GC, Valentini V. Clinical management of gastroesophageal junction tumors: past and recent evidences for the role of radiotherapy in the multidisciplinary approach. Radiat Oncol 2014;9:45.
11. Ekström AM, Signorello LB, Hansson LE, Bergström R, Lindgren A, et al. Evaluating gastric cancer misclassification: a potential explanation for the rise in cardia cancer incidence. J Natl Cancer Inst 1999;91:786-90.
12. Kauer WK, Peters JH, DeMeester TR, Feussner H, Ireland AP, et al. Composition and concentration of bile acid reflux into the esophagus of patients with gastroesophageal reflux disease. Surgery 1997;122:874-81.
13. Miwa K, Sahara H, Segawa M, Kinami S, Sato T, et al. Reflux of duodenal or gastro-duodenal contents induces esophageal carcinoma in rats. Int J Cancer 1996;67:269-74.
14. T. Miyashita, T. Ohta, T. Fujimura, I. Ninomiya, S. Fushida, et al. Duodenal juice stimulates oesophageal stem cells to induce Barrett's oesophagus and oesophageal adenocarcinoma in rats. Oncol Rep 2006;1469-75.

15. Siewert JR, Feith M, Werner M, Stein HJ. Adenocarcinoma of the esophagogastric junction: results of surgical therapy based on anatomical/topographic classification in 1,002 consecutive patients. Ann Surg 2000;232:353-61.
16. Whiteman DC, Sadeghi S, Pandeya N, Smithers BM, Gotley DC, et al. Combined effects of obesity, acid reflux and smoking on the risk of adenocarcinomas of the oesophagus. Gut 2008;57:173-80.
17. Whiteman DC, Parmar P, Fahey P, Moore SP, Stark M, et al. Association of helicobacter pylori infection with reduced risk for esophageal cancer is independent of environmental and genetic modifiers. Gastroenterology 2010;139:73-83.
18. Buas MF, Vaughan TL. Epidemiology and risk factors for gastroesophageal junction tumors: understanding the rising incidence of this disease. Semin Radiat Oncol 2013;23:3-9.
19. Cook MB, Kamangar F, Whiteman DC, Freedman ND, Gammon MD, Bernstein L, et al. Cigarette smoking and adenocarcinomas of the esophagus and esophagogastric junction: a pooled analysis from the international BEACON consortium. J Natl Cancer Inst 2010;102:1344-53.
20. Fukuzawa M, Gotoda T. History of endoscopic submucosal dissection and role for colorectal endoscopic submucosal dissection: a Japanese perspective. Gastrointest Interv 2012;1:30-5.
21. Hosokawa K, Yoshida S. Recent advances in endoscopic mucosal resection for early gastric cancer. Gan To Kagaku Ryoho 1998;25:476-83.
22. Ono H, Kondo H, Gotoda T, Shirao K, Yamaguchi H, et al. Endoscopic mucosal resection for treatment of early gastric cancer. Gut 2001;48:225-9.
23. Gotoda T, Kondo H, Ono H, Saito Y, Yamaguchi H, et al. A new endoscopic mucosal resection procedure using an insulation-tipped electrosurgical knife for rectal flat lesions: report of two cases. Gastrointest Endosc 1999;560-3.
24. Toyonaga T, Man-i M, East JE, Nishino E, Ono W, et al. 1,635 Endoscopic submucosal dissection cases in the esophagus, stomach, and colorectum: complication rates and long-term outcomes. Surg Endosc 2013;1000-8.
25. Nagami Y, Ominami M, Otani K, Hosomi S, Tanaka F, et al. Endoscopic submucosal dissection for adenocarcinomas of the esophagogastric junction. Digestion 2018;38-44.
26. Park CH, Kim EH, Kim HY, Roh YH, Lee YC. Clinical outcomes of endoscopic submucosal dissection for early stage esophagogastric junction cancer: a systematic review and meta-analysis. Dig Liver Dis 2015;47:37-44.
27. Gong EJ, Kim DH, Ahn JY, Jung KW, Lee JH, Choi KD, et al. Comparison of long-term outcomes of endoscopic submucosal dissection and surgery for esophagogastric junction adenocarcinoma. Gastric Cancer 2017;20:84-91.
28. Osumi H, Fujisaki J, Omae M, Shimizu T, Yoshio T, et al. Clinicopathological features of Siewert type II adenocarcinoma: comparison of gastric cardia adenocarcinoma and Barrett's esophageal adenocarcinoma following endoscopic submucosal dissection, Gastric Cancer 2017;20:663-70.
29. Nagami Y, Machida H, Shiba M, Obayashi T, Ominami M, et al. Clinical efficacy of endoscopic submucosal dissection for adenocarcinomas of the esophagogastric junction. Endosc Int Open 2014;2:E15-E20.
30. Tanimoto MA, Villalobos GT, Fujita R, Doherty PS, Saavedra JA, et al. Learning curve in a western training center of the circumferential en bloc esophageal endoscopic submucosal dissection in an in vivo animal model. Diagn Ther Endosc 2011;2011:847831.
31. Oda I, Odagaki T, Suzuki H, Nonaka S, Yoshinaga S. Learning curve for endoscopic submucosal dissection of early gastric cancer based on trainee experience. Dig Endosc 2012;24 Suppl 1:129-32.
32. Kato M, Gromski M, Jung Y, Chuttani R, Matthes K. The learning curve for endoscopic submucosal dissection in an established experimental setting. Surg Endosc 2013;27:154-61.
33. Dresner SM, Lamb PJ, Bennett MK, Hayes N, Griffin SM. The pattern of metastatic lymph node dissemination from adenocarcinoma of the esophagogastric junction. Surgery 2001;129:103-9.
34. Kakeji Y, Yamamoto M, Ito S, Sugiyama M, Egashira A, et al. Lymph node metastasis from cancer of the esophagogastric junction, and determination of the appropriate nodal dissection. Surg Today 2012;42:351-8.
35. Pedrazzani C, De Manzoni G, Marrelli D, Giacopuzzi S, Corso G, et al. Lymph node involvement in advanced gastroesophageal junction adenocarcinoma. J Thorac Cardiovasc Surg 2007;134:378-85.
36. Siewert JR, Stein HJ, Feith M. Adenocarcinoma of the Esophago-Gastric Junction. Scand J Surg 2006;95:260-9.
37. Matsuda T, Takeuchi H, Tsuwano S, Nakamura R, Takahashi T, et al. Optimal surgical management for esophagogastric junction carcinoma. Gen Thorac Cardiovasc Surg 2014;62:560-6.
38. Feith M, Stein HJ, Siewert JR. Adenocarcinoma of the esophagogastric junction: surgical therapy based on 1602 consecutive resected patients. Surg Oncol Clin N Am 2006;15:751-64.
39. von Rahden BH, Stein HJ, Siewert JR. Surgical management of esophagogastric junction tumors. World J Gastroenterol 2006;12:6608-13.
40. Gertler R, Stein HJ, Langer R, Nettelmann M, Schuster T, et al. Long-term outcome of 2920 patients with cancers of the esophagus and esophagogastric junction. Ann Surg 2011;253:689-98.
41. Hulscher JB, van Sandick JW, A.G. de Boer, B.P. Wijnhoven, J.G.Tijssen, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus. N Engl J Med 2002;347:1662-9.
42. Sasako M, Sano T, Yamamoto S, Sairenji M, Arai K, et al. Left thoracoabdominal approach versus abdominal-transhiatal approach for gastric cancer of the cardia or subcardia: a randomised controlled trial. Lancet Oncol 2006;7:644-51.
43. Omloo JM, Lagarde SM, Hulscher JB, Reitsma JB, Fockens P, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the mid/distal esophagus. Ann Surg 2007;246:992-1000, discussion 1000-1.
44. Kurokawa Y, Sasako M, Sano T, Yoshikawa T, Iwasaki Y, et al. Ten-year follow-up results of a randomized clinical trial comparing left thoracoabdominal and abdominal transhiatal approaches to total gastrectomy for adenocarcinoma of the oesophagogastric junction or gastric cardia. Br J Surg 2015;102:341-8.
45. Chan DSY, Reid TD, Howell I, Lewis WG. Systematic review and meta-analysis of the influence of circumferential resection margin involvement on survival in patients with operable oesophageal cancer, Br J Surg 2013:100:456-64.

46. Biere SS, van Berge Henegouwen MI, Maas KW, Bonavina L, Rosman C, et al. Minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomised controlled trial. Lancet 2012;379:1887-92.
47. Biere SSAY, Cuesta MA, van der Peet DL. Minimally invasive versus open esophagectomy for cancer: a systematic review and meta-analysis. Minerva Chir 2009;121-33.
48. Verhage RJJ, Hazebroek EJ, Boone J, Van Hillegersberg R. Minimally invasive surgery compared to open procedures in esophagectomy for cancer: a systematic review of the literature. Minerva Chir 2009;64:135-46.
49. Santillan AA, Farma JM, Meredith KL, Shah NR, Kelley ST. Minimally invasive surgery for esophageal cancer. J Natl Compr Canc Netw 2008:879-84.
50. Cunningham D, Allum WH, Stenning SP, Thompson GN, Van de Velde CJ, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med 2006;355:11-20.
51. Medical Research Council Oesophageal Cancer Working Group. Surgical resection with or without preoperative chemotherapy in oesophageal cancer: a randomised controlled trial. Lancet 2002;359:1727-33.
52. van Hagen P, Hulshof MC, van Lanschot JJ, Steyerberg EW, van Berge Henegouwen MI, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. N Engl J Med 2012;366:2074-84.
53. Macdonald JS, Smalley SR, Benedetti J, Hundahl SA, Estes NC, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med 2001;345:725-30.
54. Bang YJ, Kim YW, Yang HK, Chung HC, Park YK, et al. Adjuvant capecitabine and oxaliplatin for gastric cancer after D2 gastrectomy (CLASSIC): a phase 3 open-label, randomised controlled trial. Lancet 2012;379:315-21.
55. Sakuramoto S, Sasako M, Yamaguchi T, Kinoshita T, Fujii M, et al. Adjuvant chemotherapy for gastric cancer with S-1, an oral fluoropyrimidine. N Engl J Med 2007;357:1810-20.
56. Shapiro J, van Lanschot JJB, Hulshof MCCM, van Hagen P, van Berge Henegouwen MI, et al. Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long-term results of a randomised controlled trial. Lancet Oncol 2015;16:1090-8.
57. Stahl M, Walz MK, Stuschke M, Lehmann N, Meyer HJ, et al. Phase III comparison of preoperative chemotherapy compared with chemoradiotherapy in patients with locally advanced adenocarcinoma of the esophagogastric junction. J Clin Oncol 2009;27:851-6.
58. Sjoquist KM, Burmeister BH, Smithers BM, Zalcberg JR, Simes RJ, et al. Survival after neoadjuvant chemotherapy or chemoradiotherapy for resectable oesophageal carcinoma: an updated meta-analysis. Lancet Oncol 2011;12:681-92.

Mini-invasive Surgery

Editorial

Open Access

Check for updates

New trends in minimally invasive management of liver tumors

Fernando Andrés Alvarez[1,2]

[1]Hepato-pancreato-biliary Surgery Section, General Surgery Service, Clínica Universitaria Reina Fabiola, Córdoba 14014, Argentina.
[2]General Surgery Service, Hospital Italiano de Buenos Aires, Buenos Aires C1199ABB, Argentina.

Correspondence to: Dr. Fernando Andrés Alvarez, Hepato-pancreato-biliary Surgery Section, General Surgery Service, Clínica, Universitaria Reina Fabiola, Córdoba 14014, Argentina. E-mail: fernandoalvarez@curf.ucc.edu.ar

How to cite this article: Alvarez FA. New trends in minimally invasive management of liver tumors. *Mini-invasive Surg* 2019;3:14. http://dx.doi.org/10.20517/2574-1225.2019.11

Received: 10 Apr 2019 **Accepted:** 10 Apr 2019 **Published:** 14 May 2019

Science Editor: Fernando Andrés Alvarez **Copy Editor:** Cai-Hong Wang **Production Editor:** Huan-Liang Wu

Surgery has evolved greatly in the last decades, being the development and widespread application of minimally invasive surgery for a critical protagonist such evolution for nearly all surgical fields. In the field of hepatobiliary surgery, the introduction of new technological devices along with several improvements in anesthetic management and surgical techniques have brought us nowadays to a reality in which most patients suffering from liver tumors can safely benefit from a minimally invasive approach at some point of their treatment pathway[1-3]. For those patients who are candidates to curative intent liver resection, laparoscopic approach has gained increasing importance within modern oncological liver surgery, with recent evidence showing a faster recovery and uncompromised long-term outcomes[4]. On the other hand, minimally invasive percutaneous, endovascular or endoscopic palliation has also evolved greatly in recent years, allowing chemotherapy treatment and a better quality of life for those patients who are not up-front candidates to surgical resection[1-3].

The aim of this Special Issue was to portray in full range the state-of-the-art minimally invasive surgical techniques that form the up-to-date armamentarium to manage patients with liver tumors. This special issue would not have been produced without the outstanding contributions of experts from Brazil, Germany, Italy and India, who present their experience and discuss topics such as minimally-invasive liver resection for liver tumors both in adults and children, quality-of-life evaluation after laparoscopic liver resections, enhanced recovery after surgery in liver resections and endoscopic ultrasound-guided drainage of the biliary tree in malignant obstructions[5-9].

I want to express my gratitude to these authors for their time and effort in producing high-quality original manuscripts that demonstrate the many benefits of minimally invasive management of liver tumors and confirm that these approaches will certainly keep developing in the years to come for the good of our patients. Finally I would like to thank the Mini-invasive Surgery Journal, its editorial Board and the Assistant Editor Ms. Anne Niu, for honoring me with the invitation to serve as Guest Editor for this Special Issue.

DECLARATIONS

Authors' contributions

Alvarez FA contributed solely to this preface.

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

The author declared that there are no conflicts of interest.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Copyright

REFERENCES

1. de Santibañes E, Ardiles V, Alvarez F, Busnelli VC, de santibañes M. Extreme hepatic surgery and other strategies: increasing resectability in colorectal liver metastases. Springer; 2017.
2. Yohanathan L, Cleary SP. Minimally invasive management of secondary liver cancer. Surg Oncol Clin N Am 2019;28:229-41.
3. Li D, Kang J, Golas BJ, Yeung VW, Madoff DC. Minimally invasive local therapies for liver cancer. Cancer Biol Med 2014;11:217-36.
4. Wakabayashi G, Cherqui D, Geller DA, Buell JF, Kaneko H, et al. Recommendations for laparoscopic liver resection: a report from the second international consensus conference held in Morioka. Ann Surg 2015;261:619-29.
5. Kumar N, Jha SK, Negi SS. Enhanced recovery after surgery in liver surgery. Mini-invasive Surg 2018;2:41.
6. Pais-Costa SR, Teixeira Lima OA, Costa GC, Martins SJ. Laparoscopic hepatectomy for benign hepatic lesions: short and long-term outcomes including quality-of-life evaluation. Mini-invasive Surg 2018;2:33.
7. Armellini E, Mazza F, Ballarè M, Donato G, Orsello M, et al. Endoscopic ultrasound-guided drainage of the biliary tree in malignant obstruction. Mini-invasive Surg 2018;2:23.
8. Cortes-Cerisuelo M, Berger M. Minimally-invasive liver resection for liver tumors in children: a snapshot of the current landscape. Mini-invasive Surg 2019;3:1.
9. Golhar A, Nikam V, Rao P, Mohanka R. Laparoscopic resection of liver tumors. Mini-invasive Surg 2019;3:9.

Mini-invasive Surgery

Commentary

Open Access

Siewert type II adenocarcinoma of esophagogastric junction: treatment status

Shu-Chun Li[1,2], Lu Zang[1,2]

[1]Department of Surgery, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, China.
[2]Shanghai Minimally Invasive Surgery Center, Shanghai 200025, China.

Correspondence to: Dr. Lu Zang, Department of Surgery, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, 197 Ruijin Er Road, Shanghai 200025, China. Shanghai Minimally Invasive Surgery Center, Shanghai 200025, China.
E-mail: zanglu@yeah.net

How to cite this article: Li SC, Zang L. Siewert type II adenocarcinoma of esophagogastric junction: treatment status. *Mini-invasive Surg* 2019;3:15. http://dx.doi.org/10.20517/2574-1225.2018.13

Received: 31 Dec 2018 **First Decision:** 25 Mar 2019 **Revised:** 8 Apr 2019 **Accepted:** 17 Apr 2019 **Published:** 15 May 2019

Science Editor: Tetsu Fukunaga **Copy Editor:** Cai-Hong Wang **Production Editor:** Huan-Liang Wu

Abstract

The incidence of adenocarcinoma of esophagogastric junction (AEG) has been increased continuously in the past decades, especially in western countries. Siewert type II is regard as the true AEG because of its location, however, the treatment for Siewert type II AEG has not reached a consensus in the academic. According to published studies nowadays, this commentary will introduce the surgical strategies and put forward suggestions for Siewert type II AEG in several aspects as follows: (1) optimal surgical approach; (2) optimal extent of lymph node dissection; (3) reconstruction methods. With the development of minimally invasive surgery, many experienced surgeons perform esophagogastrostomy via transhiatal approach. Moreover, many details during the surgery still need further research by cooperation between different departments and even countries.

Keywords: Esophagogastric junction, adenocarcinoma, surgical approach, reconstruction

INTRODUCTION

The incidence of adenocarcinoma of esophagogastric junction (AEG) has been increased continuously in the past decades, especially in western countries[1,2]. AEG refer to the adenocarcinoma which straddle the gastroesophageal junction (EGJ). EGJ is the region where the esophagus joins the stomach[3]. There are different methods to identify the EGJ including surgical, physiology, histology, endoscopy or upper gastrointestinal imaging[4,5]. In terms of conveniences, the surgeons usually regard the boundary of the tubular esophagus and the saccular stomach as EGJ in the surgery.

Siewert classification, one of the most widely used classifications today for AEG, was come up by Siewert in 1987[6]. In this classification, AEG was defined as the tumor whose epicenter located within 5 cm oral and aboral of the esophagogastric junction[7]. Siewert type I refers to the tumor whose epicenter located 1-5 cm above the EGJ, and it is usually regarded as esophagus cancer. Siewert type II tumor is considered as true AEG with a center within 1 cm above and 2 cm below EGJ. Siewert type III, with whose center located 2-5 cm below the EGJ, is treated as gastric cardia tumors. Because AEG has unusual oncology behavior and characteristics, the treatment for type II remains controversial. The aim of this commentary is to introduce the surgical strategies for type II AEG in recent years.

OPTIMAL SURGICAL APPROACH FOR SIEWERT TYPE II AEG

For advanced AEG, surgery remains predominant treatment because of the possibility of lymph node involvement. The appropriate surgical approach should take a lot into consideration including oncology safety, lymph node dissection and resection margin involvement. In Japan, no matter which type of AEG is treated by upper gastrointestinal surgeons. However, in China, gastric cancer belongs to abdominal surgery, and esophagus cancer belongs to thoracic surgery. For Siewert type II AEG, transthoracic and transhiatal are two major surgical approach. Different surgeons have different opinions on surgical approach.

The Japan Clinical Oncology Group (JCOG) conducted a randomized controlled multicenter clinical trial in Japan (JCOG9502). 167 patients with cancer of Siewert type II or III were enrolled from 27 hospitals in japan and randomly assigned to abdominal transhiatal approach (TH) or left thoracoabdominal (LTA). The aim of this trial was to explore whether LTA, compared with TH, could prolong the overall survival. The 5-year overall survival was 52.3% and 37.9% in the TH group and LTA group, respectively, but the morbidity was worse in LTA than TH[8]. Subgroup analyses showed no survival benefit for Siewert II patients in LTA group. Moreover, with respect of six selected major complications (pancreatic fistula, abdominal abscess, pneumonia, anastomotic leak, empyema thoracis and mediastinitis), the incidence was significantly higher following the LTA than the TH group: 41% *vs.* 22% (P = 0.008). And there were two treatment-related death in LTA group[9]. Therefore, LTA approach is not recommended for Siewert type II AEG with the length of esophagus invasion ≤ 3 cm.

Another trial focused on the best approach for esophageal carcinoma. It randomly assigned 220 patients with adenocarcinoma of mid-to-distant esophagus or adenocarcinoma of the gastric cardia involving the distal esophagus to transhiatal esophagectomy (THE) or right transthoracic esophagectomy (TTE, Ivor-Lewis) with extended lymphadenectomy. Ivor-Lewis is a right transthoracic surgical approach for distal esophagus cancer, which was introduced by Lewis in 1946[10]. And this approach was widely used in western countries. This approach has two procedure which includes gastrectomy and abdominal lymphadenectomy for stage I, then a right thoracotomy with esophageal resection and peri-esophageal lymphadenectomy for stage II. Ivor-Lewis was associated with more in-hospital morbidity than transhital. After transhiatal and transthoracic resection, 5-year survival was 34% and 36% (P = 0.71), respectively. Although no statistically difference founded among groups, there was a trend toward improving long-term survival at five years with Ivor-Lewis approach. In subgroup analysis based on Siewert classification, a 5-year survival benefit of 14% was found in transthoracic group for Siewert type I (51% *vs.* 37%, P = 0.33) than transhital group[11,12], which indicated that Ivor-Lewis may have no benefits for type II AEG. It may be related to TTE could gain more involved lymph nodes than THE in type I AEG. Recently a single center reviewed 242 Siewert type II AEG retrospectively, of whom 56 (23.1%) underwent thoracoabdominal esophagectomy (TAE) and 186 (76.9%) had a transhiatal extended gastrectomy (THG). No difference in morbidity (P = 0.197) and mortality (P = 0.711) were observed, including anastomotic leakages (P = 0.625) and pulmonary complications (P = 0.494). And the number of resected lymph node and rate of R0 resection have no difference as well. Overall survival after TAE was significantly longer than after THG (33.6 months *vs.* not reached, $P = 0.02$)[13]. It suggested TAE isn't worse than THG for Siewert type II AEG, especially for advanced patients who had neoadjuvant chemotherapy. But this study didn't report the length of esophagus invasion, which may influence the surgical approach chosen.

In terms of surgical extent of type II AEG, it is related to surgical approach. In order to evaluate the worldwide trends in surgical techniques for esophageal cancer surgery, a worldwide survey was performed among surgeons. In Asia gastrectomy was more popular, whereas in North America the majority procedure was esophagectomy[14]. And thoracic surgeons may prefer distal esophagectomy, while abdominal surgeons prefer proximal or total gastrectomy via transhital approach. And a sufficient resection margin is another prognostic factor for oncology safety. Mine *et al*.[15] demonstrated that proximal margin length of more than 20 mm in resected specimens seem satisfactory for patients with type II AEG by transhital approach. Frozen section examination of the resection line is recommended by the Japanese gastric cancer treatment guidelines to ensure an R0 resection[16].

On the basis of the best evidence so far, JCOG 9502, for Siewert type II AEG with esophagus invasion of 3 cm or less, transhiatal approach is safety and effective. It is necessary to conduct well-designed multicenter clinical trials to investigate appropriate approach for type II AEG with a larger lesion.

OPTIMAL EXTENT OF LYMPH NODE DISSECTION FOR SIEWERT TYPE II AEG

Siewert type II AEG is located in the boundary of distal esophagus and gastric cardia, the pathway of lymph metastasis is not same as esophagus or gastric cancer alone. In previous retrospective study, mediastinal lymph node involvement rate was 46.2%-65.0% for type I, 12.0%-29.5% for type II, and 6.0%-9.3% for type III tumors[17,18]. Nunobe *et al*.[19] claimed that the more esophagus invaded, the higher lymph node metastasis rate is.

The optimal extent of lymph node dissection for Siewert type II AEG remain uncertain. A nation-wide retrospective study of lymphadenectomy for EGJ cancer was conducted in 2012 in Japan[20]. 2807 patients without preoperative therapy were included in the analysis. The frequency of dissection for mediastinal lymph node was higher in esophagus-predominant cancer than stomach-predominant cancer. With respect to esophagus-predominant cancer, the lymph node dissection rate is higher in lower mediastinal lymph node than upper or middle mediastinal (40% *vs.* 15%). For stomach-predominant cancer, the mediastinal lymph node dissection focuses mainly on lower mediastinal, and advanced cancer especially. The possibolity of metastasis rose as the pT stage increased, and rates of metastasis is high in No. 1, 2, 3, 7. Mediastinal lymph node metastasis could be found in esophagus-predominant cancer, especially in lower mediastinal. On the contrast, it is rare in stomach-predominant. And rates of metastasis at No. 4sa, 4sb, 4d, 5 and 6 were very low, despite their high dissection rates especially in stomach-predominant cancer cases. Therefore, lymph node metastasis is mainly in the abdominal and lower mediastinal for Siewert type II AEG. Another study has similar result. It reviewed 381 Siewert type II AEG retrospectively. The nodal metastasis mainly founded in No. 1, 2, 3, 7, 11p and lower mediastinal. The middle and upper mediastinal metastasis rate is low, but related to extremely poor prognosis[21].

It still doesn't have a standard lymph node dissection extent. The Japanese Gastric Cancer Association published a temporary lymphadenectomy guideline for junctional cancer ≤ 4 cm. It is based on the tumor location, histology and T-categories[16]. Abdominal lymph node dissection can refer to gastric cancer, and No 4, 5, 6 can be omitted in early stage cases, because of low metastasis rate. Lower mediastinal should dissect routinely, but upper and middle mediastinal not. According to personal experience, lower thoracic paraesophageal lymph nodes (No. 110) and supradiaphragmatic lymph nodes (No. 111) can be resected via transhital approach, but it's difficult to resect posterior mediastinal lymph nodes (No. 112) because of limited space. In terms of peri-esophageal lymphadenectomy, transthoracic approach may have superiority for *en bloc* lymphadenectomy[22].

RECONSTRUCTION METHODS FOR SIEWERT TYPE II AEG

Reconstruction is one of the most difficult steps during the surgery. For early type II AEG, lower esophagectomy plus proximal gastrectomy seems enough, because of low para-stomach nodal metastasis rate in No. 4, 5 and 6. While as for advanced type II AEG, lower esophagectomy plus total gastrectomy is essential[23]. There are many reconstruction methods for proximal gastrectomy, including esophagogastrostomy, gastric tube reconstruction[24,25], double tract[26], different kinds of jejunal interposition and double flap method[27,28]. The major concern for proximal gastrectomy is the high incidence of postoperative complications, reflux esophagitis especially, which is a negative factor for quality of life. Many reconstruction methods are meant to resist reflux, while it remains lacking consensus. A retrospective study demonstrated that double tract reconstruction is a simple and effective method in decreasing reflux esophagitis compared with Roux-en-Y[29]. It still needs RCT to provide high-grade evidence for the method.

Compared with open surgery, minimally invasive surgery has unique advantages, such as acceptable lymph node retrieval, good postoperative outcomes, and low mortality[30]. Many experienced surgeons choose minimally invasive surgery for type II AEG[31]. Laparoscopic-assisted proximal gastrectomy is prevalent for type II AEG. Because circular stapler can finish a higher anastomosis level, it is easier for type II AEG with R0 resection. And the key procedure of using circular stapler in totally laparoscopic procedure is placing the anvil to the stump of esophagus. Transorally inserted anvil (OrVil)[31,32] and hemidouble stapling technique[33] are two easy methods to accomplish that. Recently, it has become more and more popular for totally laparoscopic technique. Liner stapler is a good choice for totally laparoscopic anastomosis, such as Overlap method[34]. But compared with laparoscopic-assisted gastrectomy, which could provide some reference for the border of tumor through a sense of touch, it is harder to ensure R0 resection, especially in advanced type II AEG. In addition, there is little space to use such devices, especially for type II AEG which needs a high anastomosis level. Takiguchi *et al*.[35] introduce laparoscopic mediastinal dissection via an open left diaphragm approach for advanced type II AEG. Firstly, divide phrenicoesophageal ligament around the esophagus along the esophageal hiatus. Then, open the left side of mediastinal pleura and incise the left diaphragm with a 60-mm linear stapler. So that, it creates a clear space and a good view for the further mediastinal lymph node dissection and reconstruction. Although no severe complication was seen in this study, it is still unknown whether this method is more harmful compared with transthoracic approach like Ivor-Lewis. The method may lead to a larger trauma which needs to place an intrathoracic drainage tube. And a larger sample size was needed to provide more evidence.

The incidence rate of AEG has been on the rise for decades. Siewert classification has become the standard classification for AEG. Siewert type I AEG should be treated as esophagus cancer, while type III should be regarded as gastric cancer. Because of the unique location of Siewert type II AEG, the treatment still doesn't reach consensus. Surgery remains the fundamental treatment, a lot of detail during surgery are needed to research in the future.

DECLARATIONS

Authors' contributions

Concept and design: Zang L
Manuscript preparation: Li SC
Manuscript review: Zang L

Availability of data and materials

Not applicable.

Financial support and sponsorship
None.

Conflicts of interest
Both authors declared that there are no conflicts of interest.

Ethical approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

REFERENCES

1. Dubecz A, Solymosi N, Stadlhuber RJ, Schweigert M, Stein HJ, et al. Does the incidence of adenocarcinoma of the esophagus and gastric cardia continue to rise in the twenty-first century?-a SEER database analysis. J Gastrointest Surg 2013.
2. Zhou Y, Zhang Z, Zhang Z, Wu J, Ren D, et al. A rising trend of gastric cardia cancer in Gansu Province of China. Cancer Lett 2008;269:18-25.
3. Oezcelik A, DeMeester SR. General anatomy of the esophagus. Thorac Surg Clin 2011;21:289-97.
4. Odze RD. Pathology of the gastroesophageal junction. Semin Diagn Pathol 2005;22:256-65.
5. Wallner B. Endoscopically defined gastroesophageal junction coincides with the anatomical gastroesophageal junction. Surg Endosc 2009;23:2155-8.
6. Siewert JR, Holscher AH, Becker K, Gossner W. Cardia cancer: attempt at a therapeutically relevant classification. Chirurg 1987;58:25-32.
7. Siewert JR, Stein HJ. Carcinoma of the gastroesophageal junction - classification, pathology and extent of resection. Dis Esophagus 1996;9:173-82.
8. Sasako M, Sano T, Yamamoto S, Sairenji M, Arai K, et al. Left thoracoabdominal approach versus abdominal-transhiatal approach for gastric cancer of the cardia or subcardia: a randomised controlled trial. Lancet Oncol 2006;7:644-51.
9. Kurokawa Y, Sasako M, Sano T, Yoshikawa T, Iwasaki Y, et al. Ten-year follow-up results of a randomized clinical trial comparing left thoracoabdominal and abdominal transhiatal approaches to total gastrectomy for adenocarcinoma of the oesophagogastric junction or gastric cardia. Br J Surg 2015;102:341-8.
10. Lewis I. The surgical treatment of carcinoma of the oesophagus; with special reference to a new operation for growths of the middle third. Br J Surg 1946;34:18-31.
11. Omloo JM, Lagarde SM, Hulscher JB, Reitsma JB, Fockens P, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the mid/distal esophagus: five-year survival of a randomized clinical trial. Ann Surg 2007;246:992-1000; discussion 1000-1.
12. Hulscher JB, van Sandick JW, de Boer AG, Wijnhoven BP, Tijssen JG, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus. N Engl J Med 2002;347:1662-9.
13. Blank S, Schmidt T, Heger P, Strowitzki MJ, Sisic L, et al. Surgical strategies in true adenocarcinoma of the esophagogastric junction (AEG II): thoracoabdominal or abdominal approach? Gastric Cancer 2018;21:303-14.
14. Haverkamp L, Seesing MF, Ruurda JP, Boone J, R VH. Worldwide trends in surgical techniques in the treatment of esophageal and gastroesophageal junction cancer. Dis Esophagus 2017;30:1-7.
15. Mine S, Sano T, Hiki N, Yamada K, Kosuga T, et al. Proximal margin length with transhiatal gastrectomy for Siewert type II and III adenocarcinomas of the oesophagogastric junction. Br J Surg 2013;100:1050-4.
16. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2014 (ver. 4). Gastric Cancer 2017;20:1-19.
17. Pedrazzani C, de Manzoni G, Marrelli D, Giacopuzzi S, Corso G, et al. Lymph node involvement in advanced gastroesophageal junction adenocarcinoma. J Thorac Cardiovasc Surg 2007;134:378-85.
18. Siewert JR, Stein HJ, Feith M. Adenocarcinoma of the esophago-gastric junction. Scand J Surg 2006;95:260-9.
19. Nunobe S, Ohyama S, Sonoo H, Hiki N, Fukunaga T, et al. Benefit of mediastinal and para-aortic lymph-node dissection for advanced gastric cancer with esophageal invasion. J Surg Oncol 2008;97:392-5.
20. Yamashita H, Seto Y, Sano T, Makuuchi H, Ando N, et al. Results of a nation-wide retrospective study of lymphadenectomy for esophagogastric junction carcinoma. Gastric Cancer 2017;20:69-83.
21. Yoshikawa T, Takeuchi H, Hasegawa S, Nozaki I, Kishi K, et al. Theoretical therapeutic impact of lymph node dissection on adenocarcinoma and squamous cell carcinoma of the esophagogastric junction. Gastric Cancer 2016;19:143-9.
22. Barreto JC, Posner MC. Transhiatal versus transthoracic esophagectomy for esophageal cancer. World J Gastroenterol 2010;16:3804-10.
23. Mariette C, Piessen G, Briez N, Gronnier C, Triboulet JP. Oesophagogastric junction adenocarcinoma: which therapeutic approach? Lancet Oncol 2011;12:296-305.

24. Shiraishi N, Hirose R, Morimoto A, Kawano K, Adachi Y, et al. Gastric tube reconstruction prevented esophageal reflux after proximal gastrectomy. Gastric Cancer 1998;1:78-9.
25. Chen XF, Zhang B, Chen ZX, Hu JK, Dai B, et al. Gastric tube reconstruction reduces postoperative gastroesophageal reflux in adenocarcinoma of esophagogastric junction. Dig Dis Sci 2012;57:738-45.
26. Aikou T, Natsugoe S, Shimazu H, Nishi M. Antrum preserving double tract method for reconstruction following proximal gastrectomy. Jpn J Surg 1988;18:114-5.
27. Mine S, Nunobe S, Watanabe M. A novel technique of anti-reflux esophagogastrostomy following left thoracoabdominal esophagectomy for carcinoma of the esophagogastric junction. World J Surg 2015;39:2359-61.
28. Muraoka A, Kobayashi M, Kokudo Y. Laparoscopy-assisted proximal gastrectomy with the hinged double flap method. World J Surg 2016;40:2419-24.
29. Xiao JW, Liu ZL, Ye PC, Luo YJ, Fu ZM, et al. Clinical comparison of antrum-preserving double tract reconstruction vs roux-en-Y reconstruction after gastrectomy for Siewert types II and III adenocarcinoma of the esophagogastric junction. World J Gastroenterol 2015;21:9999-10007.
30. Wiesel O, Whang B, Cohen D, Fisichella PM. Minimally invasive esophagectomy for adenocarcinomas of the gastroesophageal junction and distal esophagus: notes on technique. J Laparoendosc Adv Surg Tech A 2017;27:162-9.
31. Kinoshita T, Gotohda N, Kato Y, Takahashi S, Konishi M, et al. Laparoscopic transhiatal resection for Siewert type II adenocarcinoma of the esophagogastric junction: operative technique and initial results. Surg Laparosc Endosc Percutan Tech 2012;22:e199-203.
32. Jeong O, Park YK. Intracorporeal circular stapling esophagojejunostomy using the transorally inserted anvil (OrVil) after laparoscopic total gastrectomy. Surg Endosc 2009;23:2624-30.
33. Omori T, Oyama T, Mizutani S, Tori M, Nakajima K, et al. A simple and safe technique for esophagojejunostomy using the hemidouble stapling technique in laparoscopy-assisted total gastrectomy. Am J Surg 2009;197:e13-7.
34. Inaba K, Satoh S, Ishida Y, Taniguchi K, Isogaki J, et al. Overlap method: novel intracorporeal esophagojejunostomy after laparoscopic total gastrectomy. J Am Coll Surg 2010;211:e25-9.
35. Takiguchi S, Miyazaki Y, Shinno N, Makino T, Takahashi T, et al. Laparoscopic mediastinal dissection via an open left diaphragm approach for advanced Siewert type II adenocarcinoma. Surg Today 2016;46:129-34.

Shibao *et al*. *Mini-invasive Surg* 2019;3:16
DOI: 10.20517/2574-1225.2019.01

Mini-invasive Surgery

Review

Open Access

Minimally invasive approach for cancer of the esophagogastric junction

Kazunori Shibao, Masahiro Mitsuyoshi, Nobutaka Matayoshi, Yuzuru Inoue, Takefumi Katsuki, Nagahiro Sato, Keiji Hirata

Department of Surgery I, School of Medicine, University of Occupational and Environmental Health Japan, 1-1 Iseigaoka, Yahatanishi-ward, Kitakyushun 807-8555, Japan.

Correspondence to: Dr. Kazunori Shibao, Department of Surgery I, School of Medicine, University of Occupational and Environmental Health Japan 1-1 Iseigaoka, Yahatanishi-ward, Kitakyushu 807-8555, Japan. E-mail: shibao@med.uoeh-u.ac.jp

How to cite this article: Shibao K, Mitsuyoshi M, Matayoshi N, Inoue Y, Katsuki T, Sato N, Hirata K. Minimally invasive approach for cancer of the esophagogastric junction. *Mini-invasive Surg* 2019;3:16. http://dx.doi.org/10.20517/2574-1225.2019.01

Received: 11 Jan 2019 **First Decision**: 26 Apr 2019 **Revised**: 10 May 2019 **Accepted**: 28 May 2019 **Published**: 18 Jun 2019

Science Editor: Tetsu Fukunaga **Copy Editor**: Cai-Hong Wang **Production Editor**: Jing Yu

Abstract

The incidence of esophagogastric junction (EGJ) cancer is increasing in the world. EGJ cancer is traditionally classified by the Siewert classification, despite its limitations. The definition and classification of EGJ cancer is a controversial topic. Thus, the best available strategy for the surgical treatment of EGJ cancer remains controversial. This chapter reviews a minimally invasive approaches for EGJ cancer. Most operations for EGJ cancer that are performed by open surgery can be performed minimally invasively. A minimally invasive transthoracic approach (Ivor-Lewis or McKeown esophagectomy) is the optimal surgical approach for Siewert type I cancer. Mediastinoscope-assisted transhiatal esophagectomy, which was recently reported, may be a suitable surgical option, especially for frail patients with Siewert type I cancer. Generally, laparoscopic total or proximal gastrectomy is regarded as the standard for surgerical method for Siewert type III cancer, while both laparoscopic gastrectomy (with lower esophagectomy) or a minimally invasive Ivor-Lewis approach are recommended for Siewert type II cancer. Minimally invasive surgery (MIS) has the potential to shorten the length of hospitalization, reduce the risk of postoperative pulmonary complications, and improve quality of life with a similar margin status, nodal harvest, and survival rate to open techniques. However, as the existing literature is still limited, the choice of surgical method should be judged by the experienced surgeons, especially in MIS. This review reveals that further large clinical stuidies are need to deepen our understanding of MIS for EGJ cancer.

Keywords: Esophagogastric junction cancer, thoraco-abdominal approach, transhiatal approach, minimally invasive esophagectomy

INTRODUCTION

Esophageal cancer and gastric cancer are among the most common malignancies worldwide, and are a main causes of cancer-related mortality[1]. The term "esophagogastric junction (EGJ) tumor" refers to a tumor that arises close to the esophagogastric junction. The incidence of EGJ cancer has dramatically increased in the last decade[2]. In Eastern countries, westernized lifestyle habits, *Helicobacter pylori* infection, obesity, a combination of alcohol and smoking, and the increased incidence of gastroesophageal reflux disease are thought to be possible reasons[3].

EGJ cancers are traditionally classified into one of the three categories of the Siewert system, which is the most commonly used classification system, based on the location of the epicenter of the given tumor.

Type I: Adenocarcinoma of the distal esophagus with the center located within 1 to 5 cm above the anatomic EGJ. Type II: True carcinoma of the cardia infiltrating from 1 cm on the side of the esophagus up to 2 cm below the GEJ in the stomach. Type III: Subcardial gastric carcinoma with the tumor center between 2 and 5 cm below the GEJ.

Meanwhile, in the Japanese Classification of Gastric Carcinoma, EGJ cancer has been defined as cancer with its center located within 2 cm of the EGJ since 1972. In 2012, the Japanese Gastric Cancer Association and Japan Esophageal Society joint force conducted a nationwide surveillance of EGJ cancer of < 4 cm in diameter, which included the retrospective data of 3,177 patients from 273 institutions[4]. The joint force presented an algorithm showing the tentative standard in the extent of lymphadenectomy, based on this surveillance, in Japanese Gastric Cancer Treatment Guidelines, 2014 (ver. 4). Similarly, the American Joint Committee on Cancer (AJCC) has changed the definition of EGJ cancer to a cancer whose epicenter is within the proximal 2 cm of the cardia (Siewert I/II) in the eighth edition of the TNM classification[5]. However, they categorized EGJ cancer as an esophageal cancer and staged it accordingly. Meanwhile, The National Comprehensive Cancer Network, recommends that Siewert type III tumors should be treated as gastric cancers, since their lymph nodal flow and prognosis are different from Siewert type I and type II cancers[6]. Thus, a current concern of surgeons is whether Siewert type II and III cancer should be regarded-and thus surgically approached-as the same tumor. The lack of consensus regarding the definition of EGJ cancer and the classification scheme that could affect the standard of care for this category contribute to this controversy[7].

Minimally invasive surgery have been gaining popularity in recent years. Cuschieri *et al*.[8] first described the successful performance of thoracoscopic esophagectomy for esophageal cancer in 1992, and several authors have reported their experience with good results[9,10]. The first laparoscopy-assisted distal gastrectomy was reported by Kitano *et al*.[11] Thereafter, many clinical trials have unveiled the benefits of this technique, generally revealing surgical and oncological outcomes that are equal to those of open surgery[12,13]. Minimally invasive surgeries have evolved for the purpose of further reducing postoperative complications and enhanced recovery. Intrducing minimally invasive esophagectomy (MIE) for esophageal cancer has some potential benefits over conventional open esophagectomy (OE)[14]. In this article, we reviewed the existing evidence and rationale for minimally invasive surgeries of EGJ cancer.

SURGICAL APPROACH FOR THE EGJ CANCER

Although, the optimal surgical approach for these tumors remains under debate, three main surgical approaches are applied in the resection of EGJ tumors: transthoracic esophagectomy (the right transthoracic approach and the left transthoracic approach), transhiatal esophagectomy, and total gastrectomy. All three approaches enable a minimally invasive approach to be pursued. Irrespective of the surgical method and tumor stage, complete removal of the primary tumor is most relevant to prognosis[15].

The right transthorathic approach is possible to ensure a sufficient proximal margin even in EGJ cancer with long esophageal invasion. The upper mediastinal LNs can be removed by this approach. However, because of the surgical stress associated with thoracotomy, careful management is required to avoid postoperative pneumonia. There are two types of left transthorathic approaches in open surgery: the left thoracoabdominal approach, with an oblique incision from the left thorax to the abdomen, and left thoracophrenolaparotomy, which includes laparotomy and transdiaphragmatic thoracotomy. The one of the merit of these techniques is no requirement of repositioning during surgery. However, it is not possible to dissect the upper and middle mediastinal LNs with these approach.

The transhiatal approach, consists of transhiatal surgery on the abdomen and lower mediastinum and does not require thoracotomy. The procedures in the lower mediastinum include lower esophagectomy and only peri-esophageal LN dissection. Respiratory damage appears to be less than with the other approaches. Although *en bloc* dissection of the lower mediastinal LNs is possible, the surgical view of the mediastinum of this approach in open surgery is worse compared with the other approaches.

In general, Siewert type I cancer should be treated with *en bloc* transthoracic or transhiatal resection. The transthoracic approach is most beneficial, especially in advanced Siewert type I cancer, and the appropriate extent of lymphadenectomy (two-field Ivor-Lewis esophagectomy or three-field McKeown esophagectomy) remains a focus of discussion[16,17]. Generally, transhiatal esophagectomy has limitations due to the inability of mediastinal lymphadenectomy and should therefore be applied for frail patients.

The standard surgical approach for Siewert type II and type III cancers involves total gastrectomy with D2 lymphadenectomy. In Siewert type II, it involves the transhiatal resection of the distal esophagus with lower mediastinal lymphadenectomy. Splenectomy and pancreatectomy are not essential if the tumor is not located along the greater curvature and harbors metastasis of the no. 4sb lymph nodes[18]. Furthermore, in Siewert type II and III early cancers, recent evidence suggests that proximal gastric resection with D1 + lymphadenectomy may contribute to avoid postgastrectomy syndrome without a detrimental effect on complete oncologic clearance[19].

Finally, minimally invasive approaches have been developed as a safe and feasible alternative to traditional open surgery for the treatment of esophageal cancer[20,21]. Efforts have been made by surgeons to establish all types of minimally invasive surgery (MIS), including minimally invasive Ivor-Lewis, McKeown esophagectomy, and transhiatal esophagectomy. An *en bloc* lymphadenectomy method in the upper and middle mediastinum with a single-port mediastinoscopic cervical approach that was recently developed by a Japanese surgeon is a hot topic in the treatment of EGJ cancer [22]. In combination with lower mediastinal lymph nodes dissection using laparoscopic trans hiatal approach, they perform total mediastinal lymphadenectomy under pneumomediastinum assistance without thoracotomy. This technique achieves minimum invasiveness and has curative potential. Further investigation is needed to evaluate its safety and feasibility.

EVIDENCE FOR VARIOUS SURGICAL STRATEGIES IN THE MINIMALLY INVASIVE APPROACH FOR CANCER OF THE EGJ

Table 1 summarized the cited results in this manuscript. Schoppmann *et al.*[23] described a case controlled study (n = 31) that demonstrated higher rates of morbidity, transfusion rate, and postoperative respiratory complications in MIE comparing to OE. Briez *et al.*[24] evaluated the impact of a hybrid MIE (HMIE, laparoscopic gastric mobilization and open thoracotomy, n = 140) to OE (n = 140) on respiratory complications. They found that the incidence of respiratory complications at 30 days after HMIE was significantly lower in comparison to OE. Moreover, the in-hospital mortality and overall morbidity rates were significantly

Table 1. Summary of the cited results

author	reference#	case	location	procedure	methods	conclusions
Schoppmann	23	62	esophagus or EGJ	MIE, HMIE (I, M)	RS	higher rates of morbidity, transfusion, and respiratory complications in MIE
Briez	24	280	mid- or distal esophagus	HMIE (I)	RS	lower rates of respiratory complications, in-hospital mortality, and overall morbidity rates after HMIE
Luketich	9	1,011	esophagus or EGJ	MIE (I, M)	RS	reduced blood loss and post-operative complications, and a shorter LOS in MIE
Seeing	25	866	esophagus or EGJ	MIE (I, M)	PMA	shorter LOS, but higer rates of anastomotic leakage and reintervention in MIE.
Maas	28	100	distal esophagus or EGJ	MIE (T)	RS	shorter hospital and intensive care unit stay with a similar operation time in MIE
Dantoc	34	1,598	esophagus or EGJ	MIE, HMIE (I, M)	SR	higher number of dissected lymph nodes in MIE with no difference in 5-year survival rates
Mamidanna	35	7,502	esophagus or EGJ	MIE, HMIE (I, M)	RS	higher reintervention rate in MIE, but no difference in 30-day mortality and overall medical morbidity
Zhou	36	14,311	esophagus or EGJ	MIE, HMIE (I, M)	MA	lower rate of in-hospital mortality, pulmonary complications, and arrhythmia in MIE
Luketich	14	95	mid- or distal esophagus	MIE (I, M)	PS	low peri-operative morbidity and mortality in MIE
Biere	37	115	esophagus or EGJ	MIE (I, M)	RCT	lower rates of respiratory complications, a shorter LOS and better QOL scores in MIE
Mariette	38	207	mid- or distal esophagus	HMIE (I)	RCT	reduced the rate of postoperative complications and improved morbidity with better global health in MIE
Sihag	40	3,780	esophagus	MIE (I, T)	PMA	longer operation times, higher rates of reoperation, but a shorter LOS in MIE
Yerokun	41	4,574	mid- or distal esophagus	MIE (I, M)	RS	higher number of exracted lymph nodes and shorter LOS in MIE
Shanmugasundaram	42	573	esophagus or EGJ	MIE (M)	MA	reduced incidence of respiratory complication, bleeding, LOS, but a longer operating time in MIE

E esophageal cancer, EGJ Esophagogastoric junctional cancer, I Ivor-Lewis, M McKeown, T Transhiatal, LOS length of hospital stay RCT randomized controlled trial, RS retrospective study, PS prospective study, PMA Propensity-matched analysis, SR systematic review, MA meta-analysis

lower in the HMIE group. Luketich *et al.*[9] reviewed 1,033 consecutive patients undergoing MIE and revealed reduced blood loss, reduced post-operative complications and a shorter hospital stay, with same oncological outcomes. Seeing *et al.*[25] compared the short-term surgical results of OE (n = 433) with MIE (n = 433) after propensity score matching. Although OE and MIE showed similar rates of mortality and pulmonary complications, anastomotic leakage and reintervention was more frequently observed after MIE. However, MIE was associated with a shorter length of hospitalization . The problem of their study was that the complication rates in both groups (62.6% after OE and 60.2% after MIE) were relatively high in comparison to historical studies[25,26,27]. Maas *et al.*[28] also demonstrated that minimally invasive transhiatal esophagectomy by a laparoscopic approach (n = 50) is feasible and has the comparable oncologic outcome as open transhiatal esophagectomy (n = 50), and a shorter hospital and intensive care unit stay with a similar operation time (300 *vs.* 280 min, P = 0.110). Other retrospective reviews have also revealed that MIE is safe without compromising oncologic outcomes in comparison to the OE[29-33].

Dantoc *et al.*[34] reported a systematic review of 17 case-control studies that compared total minimally invasive (thoracoscopy "and" laparoscopy, n = 494) or hybrid MIE (thoracoscopy "or" laparoscopy, n = 386) to OE (n = 718) for esophageal or EGJ cancer. In comparison to OE, MIE and HMIE had a higher number of dissected lymph nodes, while the overall 5-year survival rates of the OE and MIE/HMIE groups did not differ to a statistically significant extent. Mamidanna *et al.*[35] investigated a population-based national study evaluating the short-term outcomes following OE (n = 6347) *vs*. MIE (n = 1155) for cancer in England. No differences were observed between the OE and MIE groups with regard to 30-day mortality and overall medical morbidity. The reintervention rate of the MIE group was higher than that of the OE group. Zhou *et al.*[36] reported a meta-analysis of 48 studies involving 14,311 cases of resectable esophageal or EGJ cancer. In comparison to patients undergoing OE (n = 9,973), those undergoing MIE/HMIE (n = 4,509) had a significantly lower rate of in-hospital mortality. Patients undergoing MIE also had significantly lower rates of pulmonary complications and arrhythmia. The limitation of this study was that almost all of the included studies were non-randomized case-control studies (RCTs, n = 1; observational studies, n = 47), with a diversity of study designs and surgical interventions. They concluded that MIE should be the first-choice surgery for esophageal cancer patients. However, these findings must be interpreted cautiously due to the selection bias, as the patients selected for MIE had early-stage cancer with better physical status.

Luketich *et al.*[14] conducted a multi-center, phase II, prospective study that revealed that MIE (n = 95) is feasible with low peri-operative morbidity (49.5%) and mortality (2.1%), and a 3-year overall survival rate of 58.4% Biere *et al.*[37] conducted a randomized trials of MIE *vs*. OE for patients with esophageal or EGJ cancer. In this study, 59 patients were randomized to the MIE group and 56 patients were randomized to the OE group. They revealed the advantages of MIE over OE, including a reduced incidence of postoperative pulmonary infections, a shorter length of hospitalization and better quality of life scores, indicating improved patient recovery. Mariette *et al.*[38] conducted a multicenter, randomized controlled trial that included 207 patients (MIRO trial). They investigated a HMIE using thoracotoic chest access with laparoscopy for abdominal access. In comparison to Ivor-Lewis resection, HMIE reduced the rate of postoperative complications and improved morbidity with an equivalent number of dissected lymph nodes, and no difference in resectability and curability. In the OE group, 64.4% of the patients had major postoperative morbidity in comparison to 35.9% in the HMIE group (P < 0.01). The incidence of pulmonary complications was 30.1% in the OE group and 17.7% in the HMIE group (P < 0.05). The 30-day mortality rate was 4.9% in both arms. They also reported a one-year follow-up results of the quality of life with their RCT participants and demonstrated that the MIE group had a better physical component, global health, and postoperative pain[39]. A propensity score matched analysis of 3,780 patients who underwent OE or MIE for esophageal cancer by both transhiatal and Ivor-Lewis approaches demonstrated that OE and MIE had similar rates of morbidity and mortality. MIE was associated with longer operation times, higher rates of reoperation, and empyema, but a shorter median length of hospitalization. OE was associated with higher rates of wound infection, postoperative transfusion, and ileus[40].

Yerokun *et al.*[41] investigated the predictive factors associated with the use of minimally invasive approaches (n = 1,308) for patients in the National Cancer Database who underwent resection of middle and distal esophageal cancers (n = 4,266). In the MIE group, the number of lymph nodes examined was significantly higher (15 *vs.* 13; P = 0.016) and the hospital stay was significantly shorter (10 days *vs.* 11 days; P = 0.046), however the rates of resection margin positivity, readmission, postoperative mortality, and, 3-year survival were comparable. With regard to oncological safety, no differences were found in OS or disease-free survival after 1 and 3 years of follow-up, with a better quality of life of physical components at 1 and 3 years of follow-up[33,39]. Thus, they concluded that MIE is considered to be a safe surgical approach and the majority of patients with a resectable cancer of esophagus or EGJ should be treated with MIE.

Shanmugasundaram *et al.*[42] reported a meta-analysis of 4 studies involving 573 cases of resectable esophageal or EGJ cancer. In comparison to patients undergoing OE (n = 9,973), those undergoing McKeown's-MIE (n = 4,509) had a significantly lower rates of pulmonary complications, less blood loss, and a shorter duration of hospital stay but a longer operating time.

However, since the current literatures are still limited, further large scale RCTs are needed. Thus, at present, the surgical method should be decided is at the surgeon's discretion.

ROBOTIC APPROACHES FOR EGJ CANCER

The introduction of surgical robots has shown the potential to expand the capabilities of performing complex operations through improved visualization and maneuverability. Recently, many surgeons have found robot-assisted thoracoscopic and transhiatal esophagectomy to be safe and acceptable for the treatment of esophageal and gastric cancer[43]. Future randomized trials are expected to establish this procedure as one of the best approaches for esophageal and gastric cancer. Robotic surgery will be described in greater detail in another chapter.

CONCLUSION

The incidence of cancer of EGJ has increased in worldwide. This article reviews MIE for cancer of EGJ. All major approaches for the resection of EGJ cancer can be pursued by MIS. EGJ adenocarcinoma is traditionally classified by the Siewert classification system, although which has some limitations. The definition and classification of EGJ cancer remains controversial. MIE has emerged as a promising approach that might reduce the postoperative complications in comparison to open techniques. The advantages of MIE as a treatment for EGJ cancer in comparison to OE included a reduced hospitalization, and rate of pulmonary complications, and an improved quality of life with a similar nodal harvest, margin status, and 1- and 3-year survival rates. However, since the current literature is still limited, the selection of surgical method should be judged by the experienced surgeons. In any type of EGJ cancer, R0 radical resection is mandatory for improving the patient's prognosis. Minimally invasive Ivor-Lewis or McKeown esophagectomy are the treatments of choice for Siewert type I cancer. Transhiatal esophagectomy is a surgical option for frail patients, which is limited because the operator cannot perform mediastinal lymphadenectomy. Single-port mediastinoscope-assisted transhiatal esophagectomy with mediastinal lymphadenectomy is an emerging minimally invasive approach that also has curative potential. Laparoscopic total (or proximal) gastrectomy is the optimal surgery for Siewert type III cancer, whereas both laparoscopic gastrectomy (with lower esophagectomy) and a minimally invasive Ivor-Lewis approach are the optimal minimally invasive choices for Siewert type II cancer. With the introduction of robotic surgery, esophagectomy is expected to evolve even further.

In conclusion, since the current literature is still limited, further well-desined RCTs are needed to clarify the optimal minimally invasive surgery for EGJ cancer.

DECLARATIONS

Authors' contributions

Made substantial contributions to conception and design of the study and performed data analysis and interpretation: Shibao K, Hirata K

Performed data acquisition, as well as provided administrative, technical, and material support: Mitsuyoshi M, Matayoshi N, Inoue Y, Katsuki T, Sato N

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest
All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Copyright

REFERENCES

1. Zhang Y. Epidemiology of esophageal cancer. World J Gastroenterol 2013;19:5598-606.
2. Buas M, Vaughan T. Epidemiology and risk factors for gastroesophageal junction tumors: understanding the rising incidence of this disease. Semin Radiat Oncol 2013;23:3-9.
3. Abbas G, Krasna M. Overview of esophageal cancer. Ann Cardiothorac Surg 2017;6:131-6.
4. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2014 (ver. 4). Gastric Cancer 2017;20:1-19.
5. Brierley JD, Gospodarowicz MK, Wittekind C (eds.). TNM Classification of Malignant Tumours, 8th ed. JOHN WILEY & SONS, LTD; 2017.
6. Kulig P, Sierzega M, Pach R, Kolodziejczyk P, Kulig J, et al. Differences in prognosis of Siewert II and III oesophagogastric junction cancers are determined by the baseline tumour staging but not its anatomical location. Eur J Surg Oncol 2016;42:1215-21.
7. de Manzoni G, Pedrazzani C, Pasini F. Results of surgical treatment of adenocarcinoma of the gastric cardia. Ann Thorac Surg 2002;73:1035-40.
8. Cuschieri A, Shimi S, Banting S. Endoscopic oesophagectomy through a right thoracoscopic approach. J R Coll Surg Edinb 1992;37:7-11.
9. Luketich JD, Pennathur A, Awais O, Levy RM, Keeley S, et al. Outcomes After Minimally Invasive Esophagectomy Review of Over 1000 Patients. Ann Surg 2012;256:95-103.
10. Levy RM, Trivedi D, Luketich JD. Minimally invasive esophagectomy. Surg Clin North Am 2012;92:1265-85.
11. Kitano S, Iso Y, Moriyama M. Laparoscopy-assisted Billroth I gastrectomy. Surg Laparosc Endosc 1994;4:146-8.
12. Lee JH, Han HS, Lee JH. A prospective randomized study comparing open vs laparoscopy-assisted distal gastrectomy in early gastric cancer: early results. Surg Endosc 2005;19:168-73.
13. Kim HH, Hyung WJ, Cho GS. Morbidity and mortality of laparoscopic gastrectomy versus open gastrectomy for gastric cancer: an interim report--a phase III multicenter, prospective, randomized Trial (KLASS Trial). Ann Surg 2010;251:417-20.
14. Luketich JD, Pennathur A, Franchetti Y, Catalano PJ, Swanson S, et al. Minimally invasive esophagectomy: results of a prospective phase II multicenter trial- the Eastern cooperative oncology group (E2202) study. Ann Surg 2015;261:702-7.
15. Feith M, Stein HJ, Siewert JR. Adenocarcinoma of the esophagogastric junction: surgical therapy based on 1602 consecutive resected patients. Surg Oncol Clin N Am 2006;15:751-64.
16. Hulscher JB, van Sandick JW, de Boer AG, Wijnhoven BP, Tijssen JG, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus. N Engl J Med 2002;347:1662-9.
17. Omloo JM, Lagarde SM, Hulscher JB, Reitsma JB, Fockens P, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the mid/distal esophagus: five-year survival of a randomized clinical trial. Ann Surg 2007;246:992-1000.
18. Sano T, Sasako M, Mizusawa J, Yamamoto S, Katai H, et al. Randomized controlled trial to evaluate splenectomy in total gastrectomy for proximal gastric carcinoma. Ann Surg 2017;265:277-83.
19. Zhao P, Xiao SM, Tang LC, Ding Z, Zhou X, et al. Proximal gastrectomy with jejunal interposition and TGRY anastomosis for proximal gastric cancer. World J Gastroenterol 2014;20:8268-73.
20. Wei MT, Zhang YC, Deng XB, Yang TH, He YZ, et al. Transthoracic vs transhiatal surgery for cancer of the esophagogastric junction: a meta-analysis. World J Gastroenterol 2014;20:10183-92.
21. Guo W, Ma L, Zhang Y, Ma X, Yang S, et al. Totally minimally invasive Ivor-Lewis esophagectomy with single-utility incision video-assisted thoracoscopic surgery for treatment of mid-lower esophageal cancer. Dis Esophagus 2016;29:139-45.
22. Fujiwara H, Shiozaki A, Konishi H, Kosuga T, Komatsu S, et al. Perioperative outcomes of single-port mediastinoscope-assisted transhiatal esophagectomy for thoracic esophageal cancer. Dis Esophagus 2017;30:1-8.
23. Schoppmann SF, Prager G, Langer FB, Riegler FM, Kabon B, et al. Open versus minimally invasive esophagectomy: a single-center case controlled study. Surg Endosc 2010;24:3044-53.
24. Briez N, Piessen G, Torres F, Lebuffe G, Triboulet JP, et al. Effects of hybrid minimally invasive oesophagectomy on major postoperative pulmonary complications. Br J Surg 2012;99:1547-53.

25. Seesing MFJ, Gisbertz SS, Goense L, van Hillegersberg R, Kroon HM, et al. A propensity score matched analysis of open versus minimally invasive transthoracic esophagectomy in the netherlands. Ann Surg 2017;266:839-46.
26. Stark SP, Romberg MS, Pierce GE, Hermreck AS, Jewell WR, et al. Transhiatal versus transthoracic esophagectomy for adenocarcinoma of the distal esophagus and cardia. Am J Surg 1996;172:478-81; discussion 481-2.
27. Yamamoto M, Weber JM, Karl RC, Meredith KL. Minimally invasive surgery for esophageal cancer: review of the literature and institutional experience. Cancer Control 2013;20:130-7.
28. Maas KW, Biere SS, Scheepers JJ, Gisbertz SS, van-der-Peet DL, et al. Laparoscopic versus open transhiatal esophagectomy for distal and junction cancer. Rev Esp Enferm Dig 2012;104:197-202.
29. Santillan AA, Farma JM, Meredith KL, Shah NR, Kelley ST., Minimally invasive surgery for esophageal cancer. J Natl Compr Canc Netw. 2008;6:879-84.
30. Verhage RJ, Hazebroek EJ, Boone J, Van Hillegersberg R. Minimally invasive surgery compared to open procedures in esophagectomy for cancer: a systematic review of the literature. Minerva Chir 2009;64:135-46.
31. Safranek PM, Cubitt J, Booth MI, Dehn TC. Review of open and minimal access approaches to oesophagectomy for cancer. Br J Surg 2010;97:1845-53.
32. Singh RK, Pham TH, Diggs BS, Perkins S, Hunter JG. Minimally invasive esophagectomy provides equivalent oncologic outcomes to open esophagectomy for locally advanced (stage II or III) esophageal carcinoma. Arch Surg 2011;146:711-4.
33. Straatman J, van der Wielen N, Cuesta MA, Daams F, Roig Garcia J, et al. Minimally invasive versus open esophageal resection: three-year follow-up of the previously reported randomized controlled trial: the TIME trial. Ann Surg 2017;266:232-36.
34. Dantoc MM, Cox MR, Eslick GD. Does minimally invasive esophagectomy (MIE) provide for comparable oncologic outcomes to open techniques? A systematic review. J Gastrointest Surg 2012;16:486-94.
35. Mamidanna R, Bottle A, Aylin P, Faiz O, Hanna GB. Short-term outcomes following open versus minimally invasive esophagectomy for cancer in England: a population-based national study. Ann Surg 2012;255:197-203.
36. Zhou C, Zhang L, Wang H, Ma X, Shi B, et al. Superiority of minimally invasive oesophagectomy in reducing in-hospital mortality of patients with resectable oesophageal cancer: a meta-analysis. PLoS one 2015;10:e0132889.
37. Biere SS, van Berge Henegouwen MI, Maas KW, Bonavina L, Rosman C, et al. Minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomised controlled trial. Lancet 2012;379:1887-92.
38. Mariette C, Meunier B, Pezet D, Dalban C, Collet D, et al. Hybrid minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicenter, open- label, randomized phase III controlled trial, the MIRO trial. J Clinic Oncol 2015;33:suppl 5.
39. Maas KW, Cuesta MA, van Berge Henegouwen MI, Roig J, Bonavina L, et al. Quality of life and late complications after minimally invasive compared to open esophagectomy: results of a randomized trial. World J Surg 2015;39:1986-993.
40. Sihag S, Kosinski AS, Gaissert HA, Wright CD, Schipper PH. Minimally invasive versus open esophagectomy for esophageal cancer: a comparison of early surgical outcomes from the society of thoracic surgeons national database. Ann Thorac Surg 2016;101:1281-8.
41. Yerokun BA, Sun Z, Yang CJ, Gulack BC, Speicher PJ, et al. Minimally invasive versus open esophagectomy for esophageal cancer: a population-based analysis. Ann Thorac Surg 2016;102:416-23.
42. Shanmugasundaram R, Hopkins R, Neeman T, Beenen E, Fergusson J, et al. Minimally invasive McKeown's vs open oesophagectomy for cancer: a meta-analysis. Eur J Surg Oncol 2019;45:941-9.
43. Seto Y, Mori K, Aikou S. Robotic surgery for esophageal cancer: merits and demerits. Ann Gastroenterol Surg 2017;14:193-8.

Mini-invasive Surgery

Case Report

Open Access

Check for updates

A rare cause of ureteric stricture and hydronephrosis: metastatic esophageal cancer to the urinary bladder

Darren Goh, Xin Ling Teo, Sey Kiat Terence Lim

Department of Urology, Changi General Hospital, Singapore 529889, Singapore.

Correspondence to: Dr. Darren Goh, Department of Urology, Changi General Hospital, 2 Simei Street 3, Singapore 529889, Singapore. E-mail: darren.goh.w.y@singhealth.com

How to cite this article: Goh D, Teo XL, Lim SKT. A rare cause of ureteric stricture and hydronephrosis: metastatic esophageal cancer to the urinary bladder. *Mini-invasive Surg* 2019;3:17. http://dx.doi.org/10.20517/2574-1225.2019.06

Received: 12 Feb 2019 **First Decision**: 4 May 2019 **Revised**: 15 May 2019 **Accepted**: 17 May 2019 **Published**: 18 Jun 2019

Science Editor: Giulio Belli **Copy Editor**: Cai-Hong Wang **Production Editor**: Huan-Liang Wu

Abstract

The presence of hydronephrosis usually signifies the presence of significant urinary tract obstruction, more commonly at the level of the ureter, and occasionally at the bladder outlet in cases of bilateral hydronephrosis. Unilateral hydronephrosis is most commonly caused by a ureteric stone or stricture, and rarely caused by neoplasm. Metastatic disease to the urinary bladder is rare and usually presents with hematuria, and we report the first case of hydronephrosis resulting from a metastatic esophageal cancer to the bladder.

Keywords: Hydronephrosis, metastatic esophageal cancer, ureteric stricture

INTRODUCTION

Unilateral hydronephrosis is most commonly caused by obstruction of the ureter due to the presence of a ureteric stone or stricture, and rarely secondary to a primary ureteric or bladder neoplasm or from direct invasion or external compression by locally advanced cancers from adjacent organs such as the lower gastrointestinal and female genitourinary tract. We report the first case of a patient presenting with a ureteric stricture with hydronephrosis and acute kidney injury secondary to a metastatic esophageal cancer to the urinary bladder.

CASE REPORT

This is a 72-year-old Chinese male who was diagnosed with cardio-esophageal cancer on esophago-gastro-duodenoscopy for work up of dyspepsia. Biopsies revealed poorly differentiated adenocarcinoma. Staging computed tomography (CT) scan of the chest, abdomen and pelvis showed a heterogeneously enhancing mural thickening of the lower esophagus, with no enlarged regional lymph nodes and a fluorodeoxyglucose positron emission tomography (FDG PET) scan did not show any nodal or distant metastasis. He underwent neoadjuvant chemotherapy and radiotherapy, followed by Ivor Lewis esophagectomy, total gastrectomy and colonic interposition. Final histology showed invasive poorly differentiated adenocarcinoma at the gastro-esophageal junction, arising in the background of Barrett's esophagus. The tumor invaded the peri-esophageal adventitia and involved the serosa of stomach with extensive peri-neural invasion seen. All 45 lymph nodes were negative for malignancy and the final staging was pT4aN0M0 with clear resection margins. His case was discussed at the gastrointestinal tumor board and decision was for surveillance alone, without a need for adjuvant chemotherapy or radiotherapy. He was followed up with surveillance CT scan of the abdomen and pelvis and was noted to have new onset moderate left hydronephrosis 9 months after the operation. The left hydronephrosis extended all the way down to the urinary bladder with no obvious cause of obstruction or lesions noted. He underwent a ureteroscopy and was noted to have a 4-cm tight distal ureteric stricture with unhealthy looking ureteric mucosa, but no obvious bladder or ureteric lesion [Figure 1A]. Balloon dilatation of the ureteric stricture was performed and a double-J stent was inserted, which was removed 2 weeks later. He was planned for follow up CT intravenous pyelogram to evaluate the ureteric stricture but was subsequently noted to develop acute kidney injury with a rise in serum creatinine. A non-contrast CT scan of the abdomen and pelvis now showed an area of bladder wall thickening in the region of the left ureteric orifice with worsening hydronephrosis [Figure 1B]. He underwent a rigid cystoscopy and was noted to have edematous bladder wall mucosa with solid looking areas and had a transurethral resection of bladder tumor performed; histology showed normal urothelium with submucosal infiltration by metastatic adenocarcinoma with signet cell morphology. Immunostains show the carcinoma cells staining positively with CK7 and CK20, and negatively with CDX2, TTF1, Napsin A, S100, GATA3, PSA and PSAP. These findings were in keeping with metastatic poorly differentiated adenocarcinoma of esophagus/gastric origin. A re-staging FDG PET CT scan was performed and did not show any obvious nodal or distant metastasis. He was referred to the medical oncologist for palliative treatment of the metastatic esophageal cancer.

DISCUSSION

Esophageal cancer is the eighth most common cancer worldwide and esophageal cancer most commonly metastasize to the liver and peritoneum, regional lymph nodes, lung, stomach, kidney, adrenals and bone[1]. Esophageal cancer can metastasize via several different routes; with direct invasion, lymphatic and hematogenous spread being the more common routes of spread. Other mechanisms of metastasis include trans-peritoneal and intra-luminal implantation. The most common sites of esophageal metastases include liver, regional lymph nodes and lung, but unexpected sites of metastasis have increasingly been reported. It is unclear how esophageal cancer can spread to the urinary bladder, but one possibility may be via the hematogenous route.

Shaheen *et al*.[2] performed a systematic review on esophageal cancer metastases to unexpected sites and found 164 cases reported, of which there were 14 cases of metastatic spread to the urinary tract (10 to kidney, 2 to penis and 2 to testis/spermatic cord), but none was found to have spread to the urinary bladder.

Metastatic spread to the bladder constitutes 2% of all bladder neoplasms, and most commonly they occur by direct invasion rather than from distant spread[3]. Velcheti and Govindan[4] reviewed 264 cases of metastatic disease to the bladder and found the most common primary site to be genitourinary and colorectal; and melanoma, breast and stomach are the commonest primary foci for distant spread.

The urinary bladder is an extremely rare site of metastasis from the esophagus with less than 5 cases reported worldwide. An extensive literature search found only four reported cases of metastatic disease to

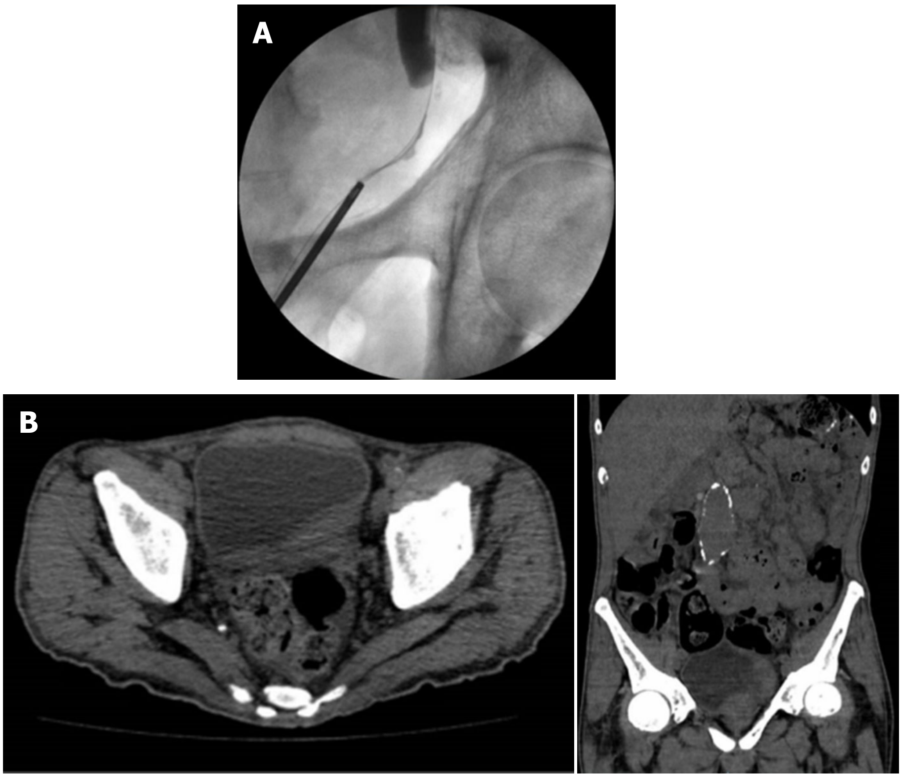


Figure 1. This (A) shows the initial intra-operative contrast study which demonstrates the left ureteric stricture with hydronephrosis. Follow up non contrast scan (B) of the abdomen and pelvis which shows left bladder wall thickening with worsening hydronephrosis

the bladder originating from the esophagus, with gross hematuria being the main presenting symptom. This is the first known reported case of a metastatic esophageal cancer to the bladder presenting with hydronephrosis and acute kidney injury.

Matsumoto *et al.*[5] in 2004 described a patient who presented with hematuria and was found to have metastatic intra-pelvic tumour from oesophageal cancer which invaded the bladder, rectum and sigmoid colon. Hargunani *et al.*[6] in 2005 reported a patient with esophageal cancer who underwent curative resection after neoadjuvant chemotherapy; but was subsequently found to have metastasis to the bladder after he presented with gross hematuria. Schuurman *et al.*[7] reported another case of metastatic esophageal cancer to the bladder in 2009. This was diagnosed as part of staging of the esophageal cancer and was treated with palliative radiotherapy. Katz *et al.*[8] in 2017 reported a patient with esophageal cancer and staging scan showed metastatic liver lesions with retroperitoneal adenopathy. She completed chemotherapy, but developed anaemia with hematuria and was subsequently found to have metastatic esophageal cancer to the bladder. Two of these cases were diagnosed at presentation to have synchronous metastasis to the bladder while the other 2 cases developed metachronous metastasis to the bladder on follow up. Most of the cases were treated with palliative intent, and only one case underwent operation with curative intent, only to develop metachronous metastasis to the bladder subsequently. Our case is the second reported case to be diagnosed with metachronous metastasis to the bladder after treatment of esophageal cancer with curative intent.

The two main subtypes of esophageal carcinoma are adenocarcinoma and squamous cell carcinoma (SCC). There have been studies that looked at patterns of metastasis based on the histological subtype, and it has been found that esophageal adenocarcinoma is more likely to develop liver and brain metastasis; while SCC tend to develop lung metastasis, with no difference found for lymph node and bone metastases. Esophageal metastasis to the urinary bladder and its association with the histological subtype has not been reported in view of its rare occurrence, and will not make for a meaningful analysis in view of its small numbers.

This is the first reported case of a ureteric stricture with hydronephrosis and acute kidney injury resulting from a metachronous esophageal cancer to the bladder. An accurate diagnosis of the cause of hydronephrosis is crucial in all cases as it can affect the management of patients. In this case, the metastatic disease had infiltrated the bladder submucosa and initial cystoscopy and ureteroscopy did not show any obvious bladder mucosal or ureteric lesion, and he was treated as for a benign ureteric stricture. The initial CT scan did not show any other abnormality such as local recurrence, metastatic spread to other organs or enlarged lymph nodes to suggest metastatic disease. This case illustrates the importance of taking into consideration patient's past medical history and to consider the various differentials for hydronephrosis, regardless of how unlikely or rare the possibility is. Ureteric re-implantation would be one of the treatment options for a long segment tight ureteric stricture or if the stricture had recurred after balloon dilatation. A decision was made to follow up with imaging first, which demonstrated the development of bladder wall thickening which eventually led to the diagnosis of a metastatic esophageal cancer. Treatment will now be with palliative intent and a percutaneous nephrostomy has been inserted to relieve the hydronephrosis, and the patient will be planned for palliative chemotherapy. His baseline renal function was initially normal, but he subsequently developed acute kidney injury due to obstructive uropathy. The percutaneous left nephrostomy relieved the obstruction and his renal function returned to normal. A normal renal function is important as many chemotherapeutic agents may cause nephrotoxicity and cannot be given in patients with renal impairment, or may need renal dose adjustment. For this patient, he was treated with capecitabine (Xeloda).

DECLARATIONS

Authors' contributions

Literature review: Goh D
Creation of manuscript: Goh D, Teo XL, Lim SKT

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Informed consent to participate in the study was obtained from the patient.

Consent for publication

Written informed consent was obtained from the patient for publication.

REFERENCES

1. Napier KJ, Scheerer M, Misra S. Esophageal cancer: a review of epidemiology, pathogenesis, staging workup and treatment modalities. World J Gastrointest Oncol 2014;6:12-20.

2. Shaheen O, Ghibour A, Alsaid B. Esophageal cancer metastases to unexpected sites: a systematic review. Gastroenterol Res Pract 2017;2017:1657310.
3. Bates AW, Baithun SI. Secondary neoplasms of the bladder are histological mimics of nontransitional cell primary tumours: clinicopathological and histological features of 282 cases. Histopathology 2000;36:32-40.
4. Velcheti V, Govindan R. Metastatic cancer involving bladder: a review. Can J Urol 2007;14:3443-8.
5. Matsumoto Y, Mibu H, Kagebayashi Y, and Miyasaka Y. Metastatic intrapelvic tumor from esophageal cancer: a case report. Hinyokika Kiyo 2004;50:725-7.
6. Hargunani R, Al-Dujaily S, Abdulla AKS, Osborne DR. Haematuria as a presentation of metastatic oesophageal carcinoma. Int Semin Surg Oncol 2005;2:4.
7. Schuurman JP, De Vries Reilingh TS, Roothaan SM, Bijleveld RT, Wiezer MJ. Urinary bladder metastasis from an esophageal adenocarcinoma: a case report. Am J Gastroenterol 2009;104:1603-4.
8. Katz H, Saad RE, Denning K, Pacioles TO. A rare case of oesophageal adenocarcinoma with urinary bladder metastasis. Case Rep Gastrointest Med 2017;2017:9343896.

de Pascale *et al*. *Mini-invasive Surg* 2019;3:18
DOI: 10.20517/2574-1225.2019.04

Mini-invasive Surgery

Original Article

Open Access

Check for updates

Totally minimally invasive Ivor-Lewis esophagectomy: initial single center experience

Stefano de Pascale[1], Federico Ghidinelli[2], Alessandra Nella Piccioli[1], Simona Borin[1], Uberto Fumagalli Romario[1]

[1]European Institute of Oncology IRCCS, Milan 20141, Italy.
[2]Spedali Civili di Brescia, Brescia 25123, Italy.

Correspondence to: Dr. Stefano de Pascale, European Institute of Oncology IRCCS, Milan 20141, Italy.
E-mail: stefano.depascale@gmail.com

How to cite this article: de Pascale S, Ghidinelli F, Piccioli AN, Borin S, Fumagalli Romario U. Totally minimally invasive Ivor-Lewis esophagectomy: initial single center experience. *Mini-invasive Surg* 2019;3:18. http://dx.doi.org/10.20517/2574-1225.2019.04

Received: 18 Jan 2019 **First Decision**: 18 Mar 2019 **Revised**: 1 Apr 2019 **Accepted**: 30 Apr 2019 **Published**: 26 Jun 2019

Science Editor: Tetsu Fukunaga **Copy Editor**: Cai-Hong Wang **Production Editor**: Jing Yu

Abstract

Aim: Minimally invasive techniques for esophagectomy decrease cardiopulmonary complications and guarantee better quality of life (QoL) compared to open techniques, without compromising oncological radicality. This retrospective study compares the short-term and QoL outcomes of hybrid Ivor Lewis (HIL) and totally minimally invasive Ivor Lewis (TMIIL).

Methods: Patients with cancer of the distal esophagus and esophagogastric junction were included into (HIL) and (TMIIL) groups in the period January 2017-July 2018. General features, intraoperative and postoperative results were analyzed. The surgical radicality and number of resected nodes were also evaluated. QoL was determined preoperatively and at 7 and 90 days postoperatively with EORTC QLQ-C30 questionnaire.

Results: General features were similar in the TMIIL and HIL groups, which contained 13 and 14 patients, respectively. Median intervention duration was 360 min (range: 240-420) for TMIIL and 330 min (range: 240-400) for HIL (P = 0.0647). Median blood losses were similar for TMIIL and HIL at 100 mL (range: 50-400) and 175 mL (range: 50-350), respectively (P = 0.0831); pulmonary complications were 15% and 14% (P = 1) and leaks were 7% and 14% (P = 1) for TMIIL and HIL, respectively.

Conclusion: Our experience suggests that TMIIL esophagectomy appears to give results similar to HIL and positively influences the QoL within 90 days after surgery. Duration of surgery and anastomotic leaks are the key elements influencing the learning curve. Randomized controlled trials are necessary to confirm the good results obtained and to give recommendations to avoid a high rate of complications during the learning curve for this difficult technique.

Keywords: Minimally invasive esophagectomy, Ivor Lewis, esophageal cancer, thoracoscopic esophagectomy

INTRODUCTION

Esophagectomy is a complex surgical procedure that requires two- or three-field access depending on tumor location, histology, preoperative clinical staging, comorbidities, anatomy, and physiological status. Despite considerable improvements in cancer staging, patient selection and surgical results in recent decades, overall and pulmonary complication (PC) rates have remained high enough to encourage the search for alternative operative techniques that could achieve similar cure rates with less morbidity and probable better postoperative quality of life (QoL).

Many different techniques have been adopted worldwide to achieve complete tumor resection and appropriate lymphadenectomy; a minimally invasive (MI) approach is used either for the abdominal or thoracic portion of surgery time or for both[1,2]. The Ivor-Lewis (IL) esophagectomy is the universally accepted technique to resect cancers situated in the middle and distal esophagus and esophagogastric junction (EGJ).

A minimally invasive approach was considered elective by 14% of surgeons involved in a National survey on treatment of esophageal and EGJ cancer in 2007; the same survey reported an increase to 43% of surgeons in 2014. This indicates a shift towards more diffuse application of this technique for such a complex operation. It is also interesting to observe that the preferred site of the anastomosis for esophagogastroplasty has changed from cervical to intrathoracic[3]. The reason for this relevant interest in MI surgery is represented by the possible reduction of PCs and length of hospital stay (LOS) related to this approach, without negatively affecting the outcomes in terms of anastomotic leaks.

The application of laparoscopy and thoracoscopy to perform a totally MI Ivor-Lewis (TMIIL) esophagectomy follows the idea to obtain further improved results in terms of postoperative complications and QoL.

The present work reviews our initial experience with this technique and compares the short-term outcomes obtained in this group of patients with the results obtained in patients submitted to hybrid Ivor-Lewis (HIL). Data of the current literature on TMIIL are also reported and discussed.

METHODS

Since 2005, our standardized approach for patients affected by cancer of the distal esophagus and EGJ has been HIL, except in case of bulky tumors for which a relative contraindication was evidenced. From 2013 to 2016, few cases of highly selected patients were approached with TMIIL, in a stage 1 and 2a setting, according to the IDEAL recommendations [Figure 1][4-6].

From January 2017 to July 2018, in a stage 2b setting, all patients for whom the laparoscopic procedure lasted less than 3 h, completed, as intention to treat, the thoracoscopic procedure.

The research was performed in accordance with the Declaration of Helsinki and all patients gave informed consent to the procedure.

The results obtained in consecutive patients submitted to TMIIL and HIL between January 2017 and July 2018 were retrospectively analyzed. Data were collected in a prospective database.

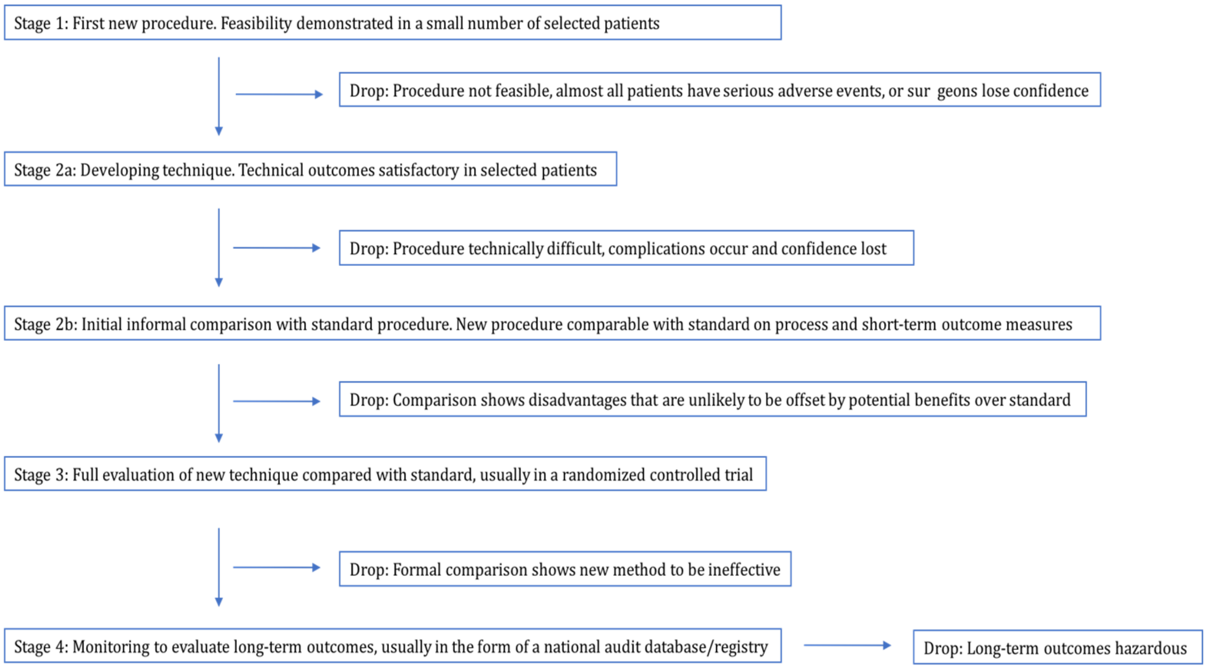


Figure 1. IDEAL recommendations framework

All procedures were performed by a single surgeon skilled in MI surgery (UFR). QoL was analyzed through the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30), which was submitted to all patients the day before surgery, and at postoperative day 7 and 90.

All patients were discussed in a multidisciplinary setting following international guidelines[7].

All the patients had a feeding jejunostomy performed either during the staging laparoscopy or during esophagectomy.

Laparoscopic gastrolysis

Dissection is performed using the hook cautery and ultrasonic device beginning with division of the gastrohepatic ligament starting distally to the crow's foot. The stomach is mobilized by dividing the left gastric vessels and short gastric vessels, and separating the right gastroepiploic arcade from the gastrocolic ligament. A standard D2-lymphadenectomy is performed. A gastric conduit is constructed by sequential firings of a linear endostapler with 45-60 mm cartridges parallel to the greater curvature. The first 45 mm cartridge is applied across the lesser curve, distally to the crow's foot, directed almost at right angle toward the greater curve; special care is required to avoid gastric tube spiralization during application of the subsequent cartridges. Interrupted 3-0 Maxon stitches are applied at the intersection of the staple lines. Feeding jejunostomy is performed in the upper left abdominal quadrant at the level of the first jejunal loop with a self-gripping barbed suture.

Thoracotomy

The right lung is excluded using a left double-lumen tube or an endobronchial blocker under fiberoptic bronchoscopic guidance, and the patient is turned to the left lateral position with a roll at the level of the tip of the scapula. A right posterolateral incision in the fifth intercostal space is performed with a section of the latissimus dorsi, sparing the serratus muscle. The lung is retracted medially. The arch of the azygos vein is divided, and the thoracic duct is selectively ligated above the diaphragm. A standard *en-bloc* esophagectomy is performed, and right paratracheal nodes are routinely removed. The esophagogastric anastomosis is performed at the apex of the right chest using a 28-mm stapler. The gastrostomy is closed with a linear stapler. A large 360° omental wrap is performed, and the pleural cavity is drained with 32 Ch drain .

Thoracoscopy

The patient is placed in the semi-prone position and the forearm flexed to improve abduction of the scapula. The chest is stabilized on the operative table using beanbag and side supports to allow rotation in a more lateral decubitus position. This is helpful to aid mediastinal exposure in patients with a protruding spine or to expedite the switch to thoracotomy if necessary. Artificial capnothorax with a pressure of 8 mmHg is induced after first 12-mm trocar is placed below the inferior angle of the scapula. Three additional trocars are inserted: two 12-mm trocars in the eighth intercostal space and the middle of the vertebral border of the scapula, and a 5-mm trocar in the superior angle of the scapula. The arch of the azygos vein is divided using Hem-o-lock clips. Incision of the mediastinal pleura is performed on both sides of the esophagus, and the dissection preferably starts between the vagal trunk and the right main bronchus. This allows *en-bloc* lymphadenectomy of the carina with nerve preservation in most circumstances. The esophagus is then mobilized up to the level of the diaphragm and the inferior pulmonary ligament is divided. The thoracic duct is identified and ligated. After an esophagotomy on the stapled side and a gastrotomy on the small gastric curvature are performed, some stitches are used to fix the mucosa to the other layers of the esophageal wall, avoiding submucosal slippage following the technique described by Irino[8]. Gastrolysis is completed. A side-to-side anastomosis is then performed with a 30-mm linear stapler. The enterotomies are closed with a self-gripping barbed suture. A large 360° omental wrap is performed and the pleural cavity is drained.

Immediately after surgery, patients recovered in the Intensive Care Unit (ICU) until the first postoperative day.

The complications were described according to the taxonomy recently proposed by the Esophagectomy Complications Consensus Group[9].

Statistical analysis

The Mann-Whitney *U* test was used to compare continuous variables not normally distributed (presented as median and range). Normality of the distribution of variables was determined using the D'Agostino-Pearson test. Chi-square or Fisher's exact test, when appropriate, were used to compare categorical variables. Two-tailed *P* values are reported universally, and the significance threshold was designated at a *P* value of 0.05. Statistical analysis was performed with statistical software for biomedical research (MedCalc Software for Windows).

RESULTS

From January 2017 to July 2018 we performed 53 esophagectomies in patients affected by esophageal or EGJ cancers. Ten patients were submitted to the McKeown procedure, 1 patient was treated with a transhiatal esophagectomy and 3 patients with squamous cancer of the cervical esophagus underwent a pharyngo-laryngo-esophagectomy. Thirty-nine patients underwent an IL procedure: 13 TMIIL, 14 HIL, and 12 OIL.

Patients submitted to TMIIL and HIL were compared according to the stage 2b IDEAL recommendation. The general characteristics of the two groups are reported in Table 1. No difference was reported between the 2 groups in terms of ASA (American Society of Anesthesiologists) Classification: 9 patients in the TMIIL group and 13 patients in the HIL group were treated with a neoadjuvant or perioperative therapy; in the TMIIL group, 6 patients received chemoradiotherapy and 3 patients received preoperative chemotherapy, while in the HIL group 10 patients received neoadjuvant chemoradiotherapy and 3 patients received preoperative chemotherapy.

Table 1. Baseline characteristics of patients undergoing TMIIL and HIL

Characteristics	TMIIL (*n* = 13)	HIL (*n* = 14)	*P* value
Age, years, median (range)	67.5 (53-82)	66 (54-77)	0.4265
Gender (M/F), *n* (%)	8/5 (61.5/38.5)	13/1 (93/7)	0.1355
ASA, median (range)	2 [1-3]	2 [1-3]	0.7623
Tumor location			
EGJ, *n* (%)	8 (61.5)	10 (71)	0.6945
Distal esophagus, *n* (%)	5 (38.5)	4 (29)	
c Stage			
< II, *n* (%)	2	1	0.5955
≥ II, *n* (%)	11	13	
Neoadjuvant treatment			
Yes, *n* (%)	9 (69)	13 (93)	0.1647
No, *n* (%)	4 (31)	1 (7)	
Chemotherapy, *n* (%)	3 (33)	3 (23)	0.6550
Chemoradiotherapy, *n* (%)	6 (66)	10 (77)	
Tumor type			
Adenocarcinoma, *n* (%)	10 (77)	9 (65)	0.6776
SCC, *n* (%)	2 (15)	4 (28)	0.6483
Other (%)	1 (8)	1 (7)	1
Comorbidity			
Hypertension, *n* (%)	7 (54)	8 (57)	1
Cardiovascular disease, *n* (%)	0	3 (21)	0.2222
Diabetes, *n* (%)	2 (15)	1 (7)	0.5955

HIL: hybrid Ivor Lewis; TMIIL: totally minimally invasive Ivor Lewis

Table 2. Intraoperative variables

Characteristics	TMIIL (*n* = 13)	HIL (*n* = 14)	*P* value
Duration of intervention median (min) (range)	360 (240-420)	330 (240-400)	0.0647
Laparoscopy converted to open surgery, *n* (%)	0	1 (7.1)	0.9699
Blood Loss (mL), median (range)	100 (50-400)	175 (50-350)	0.0831
Feeding Jejunostomy during esophagectomy, yes/no	10/3	13/1	0.5337
Duration of postoperative recovery in ICU (days), median (range)	1 (1-2)	1 (1-2)	0.9876

HIL: hybrid Ivor Lewis; TMIIL: totally minimally invasive Ivor Lewis

No differences were observed in the 2 groups for intraoperative data [Table 2], particularly for duration of intervention and blood loss.

Postoperatively, no difference was found in terms of morbidity, mortality and length of hospital stay [Table 3]. One patient in each group presented a type III anastomotic leak, (8% *vs*. 7% in TMIIL and HIL group, respectively). One patient in the HIL group (7%) presented a type I anastomotic leak. No patients were readmitted within 90 days after surgery.

The histopathological features were similar in the 2 groups, except 1 patient in the HIL group (7%) who had a neuroendocrine tumor. Complete pathological response was observed in 3 cases for each group, 21% and 23%, respectively, for TMIIL and HIL. Two patients (14%) in the HIL group presented a R1 resection for the presence of positive circumferential margins.

Results obtained from the QoL questionnaires evidenced a reduction of postoperative pain during the first 7 postoperative day for patients in the TMIIL group compared to HIL; these data were confirmed by the analysis conducted on postoperative day 90, as well for the global health status, physical functioning, and role functioning [Figure 2].

Table 3. Postoperative morbidity, mortality and pathologic examination

Characteristics	TMIIL (*n* = 13)	HIL (*n* = 14)	*P* value
Postoperative complications CD < 3, *n* (%)	3 (15)	4 (28.5)	0.6483
Postoperative complications CD ≥ 3, *n* (%)	2 (15)	2 (14)	1
Leaks, *n* (%)	1 (8%)	2 (14%)	1
Pulmonary complications	2 (15)	2 (14)	1
Overall morbidity, *n* (%)	5 (38)	6(43)	1
Mortality	0	0	n.s
Lenght of hospital stay (day), median (range)	13 (8-24)	14 (8-72)	0.5596
90-days readmission rate, *n* (%)	0	0	n.s
Pathological stage			
< II	5	3	0.4197
≥ II	8	11	
R1 resection	0	2	0.4814
Lomph nodes harvested, median (range)	23 (7-71)	27 (7-44)	0.5602

Figure 2. Quality of Life C-30 (preoperative, 7 and 90-day after surgery)

DISCUSSION

The Ivor-Lewis procedure represents the current indication for patients with cancers located in the middle, distal esophagus and EGJ; although the McKeown procedure avoids the occurrence of intrathoracic leaks, the rate of dehiscence and strictures is higher in patients with cervical anastomosis independently from the access route whether open or MI[10]. Injury to the recurrent laryngeal nerve, a complication associated with considerable morbidity, is less common if dissection in the neck is avoided[11,12]. As demonstrated by Mariette, intrathoracic anastomosis provides a lower 30-day postoperative morbidity rate compared to cervical anastomosis, and thoracotomy itself does not significantly influence postoperative morbidity[13].

In recent years particular attention has focused on improving the postoperative results of the IL procedure through application of MI approaches. Few studies, mainly retrospective, have been published in the current literature comparing HIL and OIL. Recently, a randomized prospective study by the French Eso-Gastric

Tumors Working Group, has been published: data obtained demonstrated a significant lower rate of PCs after HIL compared to OIL, particularly for major respiratory complications (18% *vs*. 30%, respectively, in the two groups); no differences in terms of long-term oncological outcomes were observed[14]. The logical evolution was to decrease invasiveness of IL, introducing thoracoscopy to obtain an even lower rate of postoperative complications without negatively affecting the rate of anastomotic leaks and mortality. A literature review of the last 7 years [Table 4] reports the results of retrospective comparisons between TMIIL and OIL. The principal limits of these studies are represented by their retrospective nature, the fact that sometimes they derived from subgroup analysis, and that the techniques to perform the intrathoracic anastomosis are different: the Orvil technique, the technique with a circular stapler but with hand sewn purse string, a side-to-side anastomosis with linear stapler, or a hand sewn anastomosis. Significant differences in terms of LOS, blood loss, and PCs in favor of TMIIL were reported. The rate of anastomotic leaks does not seem to be significantly different in the two groups, whereas operative time is generally longer for TMIIL.

The longer duration for TMIIL seems to be caused by the technical difficulty of performing the anastomosis[19]; a similar result was found in our experience, where duration of surgery was longer for TMIIL even if the difference was not significant. The new anastomotic technique implies a longer time but the results in terms of anastomotic leaks do not seem to be different: in our experience, with the use of a thoracoscopic side-to-side technique, the incidence of leaks was 7%, lower, even if not significantly, than the results of the standardized anastomotic technique used in the HIL group.

As evidenced by Van Workum[24], anastomotic leaks and operative time represent the key elements in the assessment achieving the learning curve plateau. In his multicenter retrospective analysis, the rate of anastomotic leaks at the end of the learning curve was 4.4%, starting from an incidence of 18.8%; operative time also decreased from 344 to 270 min.

The difficulties of thoracoscopic anastomosis are demonstrated by the change in technique reported in some series during the learning curve: in Mungo's small series, they moved from a circular transoral anastomosis to a linear side-to-side anastomosis and ended again with the Orvil technique[25].

In our experience, these elements were the principal issues considered as limiting factors for the application of TMIIL during stage 1 and 2a IDEAL recommendations.

Although the two groups are similar in terms of baseline characteristics, it is important to highlight that in the HIL group more patients were submitted to neaodjuvant treatment than in the TMIIL group. Considering the small size of our samples, it is difficult to evaluate how this might have influenced postoperative complications. This topic has been widely evaluated in the current literature and controversial results have been reported. In our experience, a direct correlation never emerged as reported by Woodard in the analysis of this element in a comparison of two groups of patients submitted to HIL[26].

A low rate of PCs, associated with better QoL after surgery, with possible better long-term outcomes represents the benchmark for which surgeons face the hard learning curve of TMIIL. As reported in Table 4, Tapias and Wang obtained a significant reduction of respiratory complications after TMIIL; these data positively influence the postoperative course in terms of LOS as well. The principal limit of these analyses is represented by the fact that they are obtained from comparison between TMIIL and OIL, and it is widely demonstrated that laparoscopic gastrolysis has a positive impact on this type of complication.

In our analysis, no differences were observed for respiratory complications in the two groups. Data obtained from the analysis of the QoL questionnaire evidenced lower postoperative pain for patients submitted to TMIIL and a faster recovery of health global status.

Table 4. Literature review

Author	Study	Comparison	Sample	Duration of surgery, median (min) (range)	Blood loss, median (mL) (range)	LoHS, median, day (range)	Pulmonary complications (%)	Leaks (%)	30-day mortality (%)
Bizekis *et al*.[15]	Retro	TMIIL* *vs*. HIL*	15 *vs*. 35	n.a	n.a	7 *vs*. 9° (n.a)	27 *vs*. 20	0 *vs*. 8.5	7 *vs*. 6
Noble *et al*.[16]	Prosp	TMIIL** *vs*. OIL*	53 *vs*. 53	300 (180-480) *vs*. 240° (120-420)	300 (0-1250) *vs*. 400° (0-3000)	12 (7-91) *vs*. 12 (7-101)	34 *vs*. 32	6 *vs*. 4	2 *vs*. 2
Xie *et al*.[17]	Retro	TMIIL* *vs*. OIL*	106 *vs*. 163	249 ± 41.7 *vs*. 256 ± 41.7	187 ± 37.8 *vs*. 198 ± 46.5	11.8 ± 6.7 *vs*. 13.9° ± 7.3	9.4 *vs*. 12.9	4.7 *vs*. 3.7	1.9 *vs*. 2.5
Chen *et al*.[18]	Retro	TMIIL* *vs*. OIL*	59 *vs*. 59	250 (210-320) *vs*. 200° (170-250)	190 (150-420) *vs*. 420° (250-550)	9 (7-19) *vs*. 15° (10-28)	8 *vs*. 12	4 *vs*. 5	n.a
Sihag *et al*.[19]	Retro	TMIIL[n.a] *vs*. OIL[n.a]	600 *vs*. 1291	453 (357-546) *vs*. 340° (278-415)	n.a	8 (7-14) *vs*. 10° (8-16)	29.7 *vs*. 25.4	13.8 *vs*. 10.5	2.7 *vs*. 4
Tapias *et al*.[20]	Retro	TMIIL* *vs*. OIL***	56 *vs*. 74	337 ± 48.3 *vs*. 361 ± 83.1	200 (140-200) *vs*. 250° (150-400)	7 (6-7) *vs*. 9° (8-11)	8.9 *vs*. 29.7°	0 *vs*. 1.4	0 *vs*. 2.7
Wang *et al*.[21]	Retro	TMIIL* *vs*. OIL*	334 *vs*. 285	251 ± 26.4 *vs*. 240 ± 26.4	178 ± 55 *vs*. 181 ± 64.8	12.9 ± 3.9 *vs*. 14° ± 4	9.9 *vs*. 21.4°	4.2 *vs*. 4.2	0.9 *vs*. 1.4
Straatman *et al*.[22]	Retro	TMIIL	282	333 ± 98	242 ± 228	12 (9-24)	13.1	15.2	2.1
Qi *et al*.[23]	Retro	TMIIL*/***	530	266 (213-321)	200 (150-300)	13 (11-16)	27.1	13.8	1.7

*Transthoracic circular anastomosis end to side (anvil inserted transthoracically); **Transthoracic circular anastomosis end to side [Transorally inserted anvil OrVil(™)]; ***Hand-sewn intrathoracic anastomosis, $P < 0.05$. n.a: not available

Data obtained in a recent multicenter randomized prospective analysis of QoL of patients submitted to MI esophagectomy are associated with better mid-term, 1-year QoL compared to open esophagectomy. For the authors, all differences between the groups in the specific domains result in a clinically important difference that is best understood for the pain domain due to post-thoracotomy pain. The improvement of QoL after 1 year was equal for both groups, compared to 6 weeks postoperatively. In our experience after 90 postoperative days, the QoL in the two groups was similar[27].

For what concern short-term oncological outcomes, in our experience, the two techniques resulted similar, no differences were observed for median number of lymph nodes harvested and R0 resection. In HIL group 2 patients presented a R1 resection (circumferential margin) and none in TMIIL group. The bias of this result is associated to a longer duration of laparoscopy for patients with bulky tumor of EGJ and consequently these patients were assigned to HIL group according to our methods.

The principal limit of our analysis is represented by small size of our group of patients treated with TMIIL esophagectomy, which, according to the current literature, is far from the learning curve plateau Beyond that, the power of our statistical analysis is limited by the comparison of two small groups of patients. One important element emerging from our analysis is that this anastomotic technique is safe and feasible, provided the technical details are meticulously followed.

In conclusion, TMIIL seems feasible and safe in skilled hands altought it represents a challenging procedure also for surgeons dedicated to esophagheal surgery and expert in minimally-invasive surgery. In our experience no differences were observed between the two groups, but principal limit of our analysis is represented by the small series of patients enrolled in this study and the lacking of randomization. Duration of surgery and anastomotic leaks represent the principal elements to evaluate the achieving of the plateau in the learning curve. Randomized control trials are not available and also retrospective analysis are lacking of comparison between TMIIL and HIL. Randomized controlled trials are necessary to confirm the good results evidenced in the current literature, evaluate long term oncological outcomes and create technical recommendations to approach this difficult technique avoiding a high rate of complications during the learning curve. Quality of life should also be evaluated in a randomized prospective setting as this element is considered one of principal issue in favor of a totally minimally invasive approach for IL esophagectomy.

DECLARATIONS

Authors' contributions

Conceived and designed the study: de Pascale S, Fumagalli Romario U
Implemented the study and drafted the article: de Pascale S
Made substantial contributions to the analysis of data: Ghidinelli F, Piccioli AN, Borin S
Substantially contributed to the interpretation of data, made critical revisions related to important intellectual content of the manuscript, and approved the final version of the manuscript: All authors

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Patients were not required to provide informed consent to this study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

Consent for publication

Not applicable.

REFERENCES

1. Luketich JD, Alvelo-Rivera M, Buenaventura PO, Christie NA, McCaughan JS, et al. Minimally invasive esophagectomy: outcomes in 222 patients. Ann Surg 2003;238:486-95.
2. Burdall OC, Boddy AP, Fullick J, Blazeby J, Krysztopik R, et al. A comparative study of survival after minimally invasive and open oesophagectomy. Surg Endosc 2015;29:431-7.
3. Haverkamp L, Seesing MF, Ruurda JP, Boone J, V Hillegersberg R. Worldwide trends in surgical techniques in the treatment of esophageal and gastroesophageal junction cancer. Dis Esophagus 2017;30:1-7.
4. Barkun JS, Aronson JK, Feldman LS, Maddern GJ, Strasberg SM, Balliol collaboration. Evaluation and stages of surgical innovations. Lancet 2009;374:1089-96.
5. Ergina PL, Cook JA, Blazeby JM, Boutron I, Clavien PA, et al. Challenges in evaluating surgical innovation. Lancet 2009;374:1097-104.
6. Hirst A, Philippou Y, Blazeby J, Campbell B, Campbell M, et al. No surgical innovation without evaluation: evolution and further development of the IDEAL framework and recommendations. Ann Surg 2019;269:211-20.
7. Lordick F, Mariette C, Haustermans K, Obermannová R. Oesophageal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2016;27:v50-7.
8. Irino T, Tsai JA, Ericson J, Nilsson M, Lundell L, et al. Thoracoscopic side-to-side esophagogastrostomy by use of linear stapler-a simplified technique facilitating a minimally invasive Ivor-Lewis operation. Langenbecks Arch Surg 2016;401:315-22.
9. Low DE, Alderson D, Cecconello I, Chang AC, Darling GE, et al. International consensus on standardization of data collection for complications associated with esophagectomy: Esophagectomy Complications Consensus Group (ECCG). Ann Surg 2015;262:286-94.
10. Rizk NP, Bach PB, Schrag D, Bains MS, Turnbull AD, et al. The impact of complications on outcomes after resection for esophageal and gastroesophageal junction carcinoma. J Am Coll Surg 2004;198:42-50.
11. Gockel I, Kneist W, Keilmann A, Junginger T. Recurrent laryngeal nerve paralysis (RLNP) following esophagectomy for carcinoma. Eur J Surg Oncol 2005;31:277-81.

12. van Workum F, Berkelmans GH, Klarenbeek BR, Nieuwenhuijzen GAP, Luyer MDP, et al. McKeown or Ivor Lewis totally minimally invasive esophagectomy for cancer of the esophagus and gastroesophageal junction: systematic review and meta-analysis. 2017;9:S826-33.
13. Degisors S1, Pasquer A, Renaud F, Béhal H, Hec F, et al. FREGAT working group. Are thoracotomy and/or intrathoracic anastomosis still predictors of postoperative mortality after esophageal cancer surgery? A nationwide study. Ann Surg 2017;266:854-62.
14. Mariette C, Markar SR, Dabakuyo-Yonli TS, Meunier B, Pezet D, et al. FREGAT working group. Hybrid Minimally Invasive Esophagectomy for Esophageal Cancer. N Engl J Med 2019;380:152-62.
15. Bizekis C, Kent MS, Luketich JD, Buenaventura PO, Landreneau RJ, et al. Initial experience with Minimally Invasive Ivor Lewis Esophagectomy. Ann Thorac Surg 2006;82:402-7.
16. Noble F, Kelly JJ, Bailey IS, Byrne JP, Underwood TJ. A prospective comparison of totally minimally invasive versus open Ivor Lewis esophagectomy. Dis Esophagus 2013;26:263-71.
17. Xie MR, Liu CQ, Guo MF, Mei XY, Sun XH, et al. Short-term outcomes of minimally invasive Ivor-Lewis esophagectomy for esophageal cancer. Ann Thorac Surg 2014;97:1721-7.
18. Chen X, Yang J, Peng J, Jiang H. Case-matched analysis of combined thoracoscopic-laparoscopic versus open esophagectomy for esophageal squamous cell carcinoma. Int J Clin Exp Med 2015;8:13516-23.
19. Sihag S, Kosinski AS, Gaissert HA, Wright CD, Schipper PH. Minimally invasive versus open esophagectomy for esophageal cancer: a comparison of early surgical outcomes from the society of thoracic surgeons national database. Ann Thorac Surg 2016;101:1281-9.
20. Tapias LF, Mathisen DJ, Wright CD, Wain JC, Gaissert HA, et al. Outcomes with open and minimally invasive Ivor Lewis esophagectomy after neoadjuvant therapy. Ann Thorac Surg 2016;101:1097-103.
21. Wang J, Xu M, Xie M, Mei X. Minimally Invasive Ivor-Lewis esophagectomy (MIILE): a single-center experience. Indian J Surg 2017;79:319-25.
22. Straatman J, van der Wielen N, Cuesta MA, Daams F, Roig Garcia J, et al. Minimally invasive versus open esophageal resection: three-year follow-up of the previously reported randomized controlled trial: the TIME trial. Ann Surg 2017;266:232-6.
23. Qi W, Zixiang W, Tianwei Z, Shuai F, Sai Z, et al. Long-term outcomes of 530 esophageal squamous cell carcinoma patients with minimally invasive Ivor Lewis esophagectomy. J Surg Oncol 2018;117:957-69.
24. van Workum F, Stenstra M, Berkelmans G, Slaman AE, van Berge Henegouwen MI, et al. Learning curve and associated morbidity of minimally invasive esophagectomy: a retrospective multicenter study. Ann Surg 2019;269:88-94.
25. Mungo B, Lidor AO, Stem M, Molena D. Early experience and lessons learned in a new minimally invasive esophagectomy program. Surg Endosc 2016;30:1692-1698.
26. Woodard GA, Crockard JC, Clary-Macy C, Zoon-Besselink CT, Jones K, et al. Hybrid minimally invasive Ivor Lewis esophagectomy after neoadjuvant chemoradiation yields excellent long-term survival outcomes with minimal morbidity. J Surg Oncol 2016;114:838-47.
27. Maas KW, Cuesta MA, van Berge Henegouwen MI, Roig J, Bonavina L, et al. Quality of life and late complications after minimally invasive compared to open esophagectomy: results of a randomized trial. World J Surg 2015;39:1986-93.

Jawale *et al. Mini-invasive Surg* 2019;3:19
DOI: 10.20517/2574-1225.2019.12

Mini-invasive Surgery

Letter to Editor

Open Access

Check for updates

Rigid video laparoscope: a low-cost alternative to traditional diagnostic laparoscopy and laparoscopic surgery

Sagar Jawale[1], Gnanaraj Jesudian[2], Prakash Agarwal[3]

[1]Jawale Institute of pediatric surgery, Jilha Peth, Gandhi Nagar, Jalgaon 425001, Maharashtra, India.
[2]Karunya Institute of Science and Technology, Coimbatore 641114, Tamil Nadu, India.
[3]Professor & Head of Pediatric Surgery at the Sri Ramachandra Medical College, Chennai- 600116 and Consultant Pediatric Surgeon at The Apollo hospital, Chennai 600006, Tamil Nadu, India.

Correspondence to: Sagar Jawale, Jawale Institute of pediatric surgery, Jilha Peth, Gandhi Nagar, Jalgaon 425001, Maharashtra, India. E-mail: drsagarjawale@gmail.com

How to cite this article: Jawale S, Jesudian G, Agarwal P. Rigid video laparoscope: a low- cost alternative to traditional diagnostic laparoscopy and laparoscopic surgery. *Mini-invasive Surg* 2019;3:19. http://dx.doi.org/10.20517/2574-1225.2019.12

Received: 18 Apr 2019 **First Decision**: 24 Apr 2019 **Revised**: 24 Apr 2019 **Accepted**: 15 May 2019 **Published**: 26 Jun 2019

Science Editor: Giulio Belli **Copy Editor**: Cai-Hong Wang **Production Editor**: Jing Yu

INTRODUCTION

Diagnosis of abdominal conditions is always a challenge in rural areas. The modern diagnostic facilities like CT scans and MRI are not available there. Survey of the operation registers of many rural hospitals (17 hospitals) belonging to an association of hospitals in North India revealed that Diagnostic laparotomies were a common surgical procedure in rural areas[1]. Despite the high costs and invasive nature Laparotomies were still carried out in rural areas because of the cost effectiveness and convenience. Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) have given a long list of indications for Diagnostic laparoscopy that are applicable in Urban areas too[2].

The problem in rural areas is the high costs involved in the set up for Diagnostic Laparoscopies. Traditionally it would involve almost all the equipment required for laparoscopic surgeries and most of the rural surgical facilities cannot afford such high costs especially if they are doing only diagnostic laparoscopies. We offer an alternative low- cost method for carrying out Diagnostic Laparoscopies. The second author has used this innovation for diagnostic laparoscopies in rural areas. This innovation, a unique rigid video laparoscope is the first device of its kind described in the literature of laparoscopy. A patent is filed for it at Mumbai office.

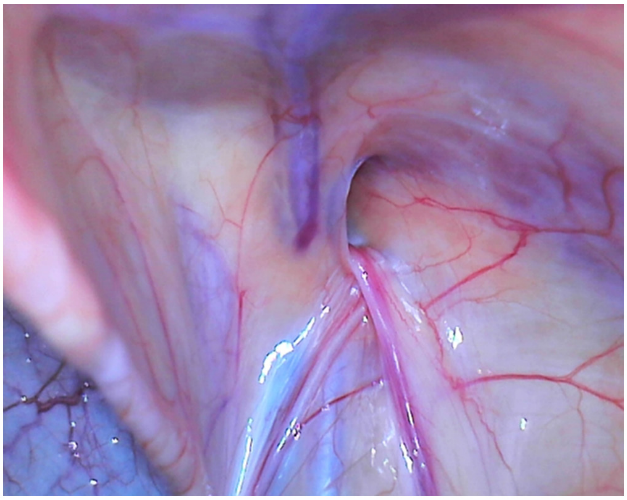


Figure 1. shows that the picture quality is excellent

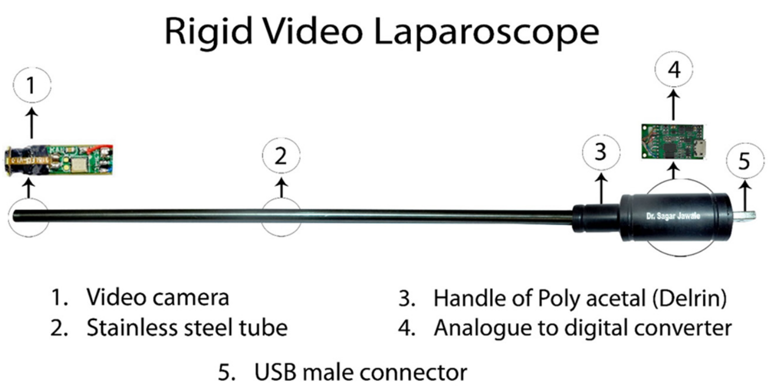


Figure 2. shows the various parts of the innovative Laparoscope

MATERIALS AND METHODS

The first author has used these laparoscopes in his hospital from last 5 years for laparoscopy in children and adults in about 356 cases and got away completely with the conventional equipment. It has been used for laparoscopic surgeries such as appendicectomy, orchidopexies [Supplementary Video 1-2], herniotomies [Supplementary Video 3], pyloromyotomy, Intussusception reduction and in diagnostic laparoscopies.

Diagnostic Laparoscopies are carried out using our innovative equipment that has the video camera and LED lights in the tip of the instrument. It is connected to the Laptop computer through a USB hub and is powered by the Laptop computer. It makes the rod lens system and the light source redundant. Since there is no image loss by the rod lenses, the image quality is phenomenal [Figure 1].

These scopes are available in 5, 8- and 10-mm sizes. The camera is fitted at the tip of a seamless joint free stainless-steel tube with 5 mm, 8 mm and 10 mm diameter [Figure 2]. The wires of the camera are connected to male USB connector which is fitted outside the holder of the scope. The holder of the scope is made up of heat resistant polymer called Delrin (Polyacetal). Polyacetal or polyformaldehyde, is an engineering thermoplastic used in precision parts requiring high stiffness, low friction, and excellent dimensional stability. The focal length is from 2 to 20 cm and the white balance, shutter, iris, colors are automatically set by the camera.

Specification of the camera used are: Sensor: 1/12 color COMS, Pixel size: 1.75 μm × 1.75 μm, Effective Pixels: 1080 (h) × 800 (v), Operation Temperature: -10 °C ~ +50 °C, S/N Ratio: 38dB

LED:6PCS 0402 LED, DC3.3 V × 50 mA, Dimensions 7 mm × 20 mm, Image Sensor: 1440 μm × 1653 μm, Fps: 30 Fps constant, Sensitivity: 960 mV (Lux × sec), Voltage: 5 volts DC, Video Output: USB, Dynamic range: 66dB, FOV: 90 degrees, DOF: 2-5 cm

DISCUSSION

The need for diagnostic laparoscopic surgeries in rural areas brought many innovations. For example the use of Gas Insufflation Less Laparoscopic Surgeries (GILLS)[2] and the use of cystoscope for laparoscopy in rural areas[1]. This would still require the Laparoscopic camera and the light source. The rigid Laparoscope is a three in one device replacing the telescope, light source and camera combining them into a single low-cost device.

The advent of Laparoscopy has widened the need for Diagnostic laparoscopies especially in gynecological practice like confirming the diagnosis of acute pelvic inflammatory disease; in the evaluation of malignancies and abdominal-pelvic trauma; and the surgical treatment of pelvic pain[2].

Since the laparoscope has a video camera in the front, the image is converted into electronic signal and there is no image loss as in the case of rod lenses of conventional optical laparoscopes. Hence the video quality is excellent [Supplementary Video 4-5]. The video quality was excellent for variety of operations such as needle assisted laparoscopic herniotomy [Supplementary Video 3], Laparoscope assisted orchidopexies [Supplementary Video 1-2], *etc*. The laparoscope is a three in one device in the sense that It is the combination of a telescope, Led light source and laparoscopic endo camera. It is equivalent to $10,000 as $4000 for optical endoscope, $4000 for endo camera and $2000 for Led light source are incorporated in it. With great hard work the first author himself commercialized it with a cost of $300 which is the cheapest laparoscope in the market today. It is being distributed in India and world over through a no profit organization called Vigyan Yog Foundation founded by the author.

CONCLUSION

The rigid video laparoscope device is safe, compact of good quality and is likely to revolutionize diagnostic and operative laparoscopy in India and other third world countries.

DECLARATIONS

Authors' contributions

Devised the manuscript and did the clinical study: Jawale S
Used the device for diagnostic laparoscopies in rural areas: Jesudian G
Helped raising the manuscript: Agarwal P

Availability of data and materials

Not applicable.

Financial support and sponsorship

The first author have done the whole research and study with his own money.

Conflicts of interest

All authors declared there are no conflicts of interest.

Ethical approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Copyright

REFERENCES
1. J. Gnanaraj. Diagnostic laparoscopies in rural areas:a different use for cystoscope tropical doctor 40: 3 July 2010 p 156. Available from: https://www.sages.org/publications/guidelines/guidelines-for-diagnostic-laparoscopy. [Last accessed on 22 May 2019]
2. Loffer FD, Pent D. Indications, contraindications and complications of diagnostic laparoscopies. Obstet Gynecol Surg 1975;30:407-27. Available from: http://mdcurrent.in/primary-care/low-cost-laparoscopic-surgeries-taking-modern-surgery-poor. [Last accessed on 22 May 2019]

Parthasarathi *et al. Mini-invasive Surg* 2019;3:20
DOI: 10.20517/2574-1225.2019.10

Mini-invasive Surgery

Original Article

Open Access

Thoraco-laparoscopic Ivor-Lewis esophagectomy: the most extensive Indian experience

Ramkrishnan Parthasarathi, GHV Raghvendra Gupta, Sandeep C. Sabnis, Palanivelu Praveen Raj, Palanisamy Senthilnathan, Subbiah Rajapandian, Chinnusamy Palanivelu

Department of Gastrointestinal and Minimal Access Surgery, GEM Hospital and Research Centre, Ramanathapuram, Coimbatore 641045, Tamil Nadu, India.

Correspondence to: Dr. Ramkrishnan Parthasarathi, Department of Gastrointestinal and Minimal Access Surgery GEM Hospital and Research Centre 45, Pankaja Mills Road, Ramanathapuram, Coimbatore 641045, Tamil Nadu, India.
E-mail: drparthu@geminstitute.in

How to cite this article: Parthasarathi R, Gupta GR, Sabnis SC, Raj PP, Senthilnathan P, Rajapandian S, Palanivelu C. Thoraco-laparoscopic Ivor-Lewis esophagectomy: the most extensive Indian experience. *Mini-invasive Surg* 2019;3:20. http://dx.doi.org/10.20517/2574-1225.2019.10

Received: 20 Mar 2019 **First Decision**: 17 Jun 2019 **Revised**: 27 Jun 2019 **Accepted**: 10 Jul 2019 **Published**: 20 Jul 2019

Science Editor: Tetsu Fukunaga **Copy Editor**: Jia-Jia Meng **Production Editor**: Jing Yu

Abstract

Aim: The overall incidence of adenocarcinoma is on the rise, mainly in the western population. Minimally invasive thoracolaparoscopic esophagectomy for adenocarcinoma of gastroesophageal junction tumors is being adopted worldwide, albeit with a slower pace. This study is to share our experience and technical modifications over two decades.

Methods: This a retrospective data from 2009-2018 at a single center, including all the 143 cases of thoracolaparoscopic Ivor Lewis esophagectomies performed. There were no exclusions. The study objectives were to evaluate postoperative recovery, complications, and pathological completeness.

Results: In 11 years, we have performed 532 cases of minimally invasive esophagectomies for both malignant and benign etiologies. Out of which 143 cases were of Ivor Lewis esophagectomy. The mean age of patients was 64.4 ± 10.86 years, and male to female ratio is 3:1. Out of these cases, 139 (97.20%) were performed for malignancy and 4 (2.79%) for benign cases, which include peptic stricture, sigmoid esophagus. The mean operative time is 457.97 ± 79.35 min. The mean blood loss was 138.08 ± 29.3mL. Out of these cases, the hand-sewn anastomosis was performed in 72 (50.34%), circular stapler anastomosis in 46 (32.16%) and, linear stapled anastomosis in 25 (17.48%). The mean lymph node retrieval rate was 22.68 ± 9.49 nodes. The average ICU stay in the postoperative period was 4.68 ± 3.95 days, and overall hospital stay was 13.48 ± 7.43 days. Among malignant cases (139), adenocarcinoma in 121

(87.05%), squamous cell carcinoma in 18 (12.94%). Among these cases T2, lesions in 56 (40.28%), T3 lesions in 77 (55.39%), T4 lesions in 6 (4.31%) The overall complication rate was 12.58% (pneumonia- 8.39%, RLN injury in 1.39%, anastomotic leak in 2.09%, chyle leak in 0.69%, anastomotic stricture in 12.58%). 3 (2.09%) cases had re-intervention in the form of combined endoscopic procedures (stenting) and re-thoracoscopic lavage in 3. Overall 30-day mortality in 1 case (0.69%).

Conclusion: Thoracolaparoscopic esophagectomy with intrathoracic Ivor Lewis anastomosis is an excellent option for selected patients, in experienced hands.

Keywords: Ivor Lewis esophagectomy, thoracolaparoscopic, carcinoma esophagus, adenocarcinoma esophagus, intrathoracic anastomosis, minimally invasive surgery

INTRODUCTION

Worldwide, an estimated 572,034 new esophageal cancer cases and 508,585 deaths are expected annually, according to data from the GLOBOCAN database[1]. Over the last decade, the incidence of squamous cell carcinoma (SCC) has declined, and the rate of adenocarcinoma of the esophagus, esophagogastric junction (EGJ) and gastric cardia is on raise[2,3].

Various minimally invasive approaches that include trans-hiatal, McKeown's, and Ivor Lewis are increasingly being used given a significant reduction in the pulmonary morbidity involved with their open counterparts. For adenocarcinoma of the distal esophagus and EGJ lesions, proximal gastrectomy with subtotal esophagectomy and intrathoracic anastomosis or total gastrectomy with lower mediastinal lymph node dissection is the surgical treatment[4]. Ivor Lewis esophagectomy (ILE) including thoracotomy and laparotomy[5] was the commonly performed surgery and now minimally invasive ILE including thoracoscopy and laparoscopy, has gained popularity[6]. The main obstacles for widespread use of minimally invasive surgery are the adequacy of esophageal resection margin and complete radical lymphadenectomy with minimal morbidity. These challenges can be addressed by improvement in techniques throughout the learning curve.

Till now very few centers are regularly performing minimally invasive ILE worldwide and to our knowledge, this is possibly most extensive series from India.

METHODS

This is a retrospective study of a prospectively maintained database of all consecutive patients who have undergone minimally invasive thoracolaparoscopic esophagectomy at a quaternary care teaching hospital from 2009 to 2018.

The primary objective of this study is to access the outcomes of the said procedure, mainly in terms of postoperative recovery, complications, and pathological completeness. There are no exclusions during this period.

The records of demographic details, investigations, perioperative data, and complications, if any were retrieved into a proforma. The pathological reports along with followup details too, were added.

All patients with suspected esophageal malignant lesion underwent routine pre-operative blood investigations, ultrasonography of the abdomen, along with esophagogastroduodenoscopy. Contrast-enhanced computerized tomography scan of the abdomen and chest were done unless there was a high

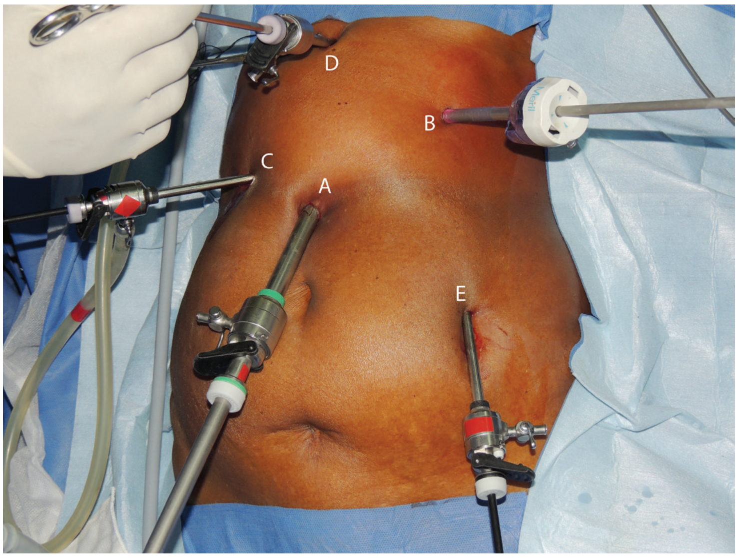


Figure 1. Port position for abdominal phase. A: Supraumbilical port for camera: 10 mm; B: Left midclavicular for right hand working port: 5 mm; C: Right midclavicular for left hand working port: 5 mm (converted to 12 mm for gastric conduit formation); D: Epigastric port for liver retraction 5 mm; E: Left anterior axillary port for gastric retraction: 5 mm (converted to 12 mm for dividing Transhiatally)

index of suspicion for metastatic disease. In all T3 and T4 patients, neoadjuvant chemotherapy was given both for adenocarcinoma and SCC. At discharge, patients were advised for follow up after seven days, three months, and 1-year post-surgery and once in a year after that. Patients received adjuvant treatment based on their final pathology reports, as well as following a preoperative treatment plan.

Data were expressed in mean/median for continuous variables, while categorical variables were shown as frequencies. SPSS Version 24 (IBM Corp. NY, US) was used to analyze the data. A P-value of less than 0.05 was considered statistically significant.

Two-stage esophagogastrectomy

Stage I: Abdominal phase

General anesthesia is induced with a single lumen endotracheal tube using double lung ventilation. The patient is positioned in the reverse Trendelenburg position for laparoscopic abdominal step. Gastric mobilization and formation of the gastric conduit are done in the first phase. Port positions: Figure 1.

Gastric mobilization: The gastrocolic omentum is divided between the stomach and transverse colon, preserving the right gastroepiploic arterial arcade and up to the first part of the duodenum. Further, proximal dissection of the stomach is done by dividing the short gastric vessels using harmonic shears. Gastric fundus is dissected carefully from the superior pole of the spleen. The attachment between the posterior wall of the stomach and pancreas is divided, and all adhesions are freed using harmonic shears.

Lymph node clearance: The gastrohepatic omentum is divided close to the liver [Figure 2]. Here, care is taken to preserve the right gastric arterial arcade. The lesser omentum is separated further and left gastric pedicle is exposed. Left gastric artery and vein dissected and clipped and divided. Lymphofatty tissues over the celiac axis, left gastric pedicle, hepatic artery and splenic artery (stations 7,8,9,11p) are dissected and skeletonized to achieve complete nodal clearance. During this dissection, the stomach is retracted anteriorly and laterally. 11 d (distal splenic) nodes are dissected out.

 Parthasarathi *et al. Mini-invasive Surg* 2019;3:20 I http://dx.doi.org/10.20517/2574-1225.2019.10

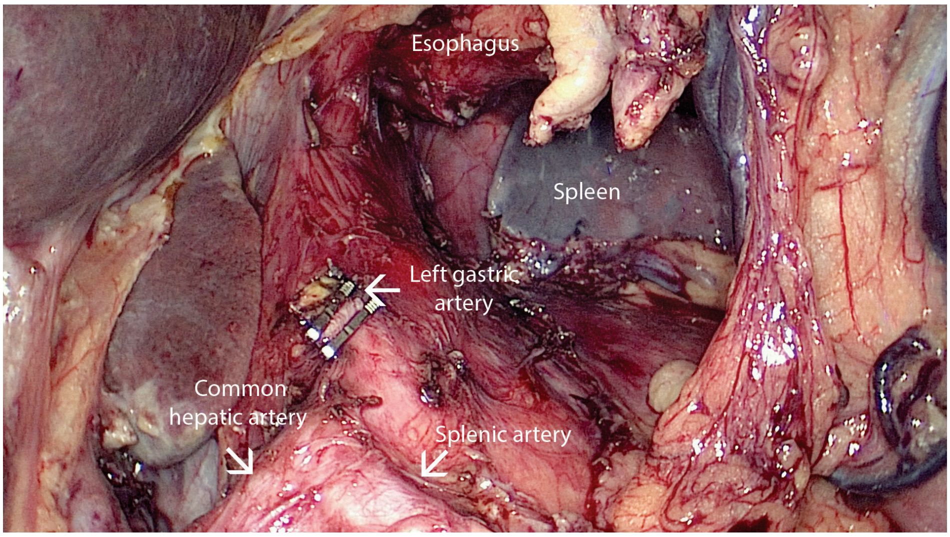


Figure 2. Laparoscopic view after D2 lymph node clearance

Abdominal Esophageal mobilization: The abdominal esophagus is separated from the right crus, and anteriorly it is freed by dividing the phrenoesophageal membrane. Right and left paracardial lymph nodes (station 1,2) dissected. The esophagus is lifted, posterior dissection is carried out, and attachment to the left crus is divided. Anterior border of the hiatus and/or left crus are divided obliquely toward the left side using harmonic shears. Sometimes, the division of the right crus may also be needed to facilitate dissection into the posterior mediastinum. Then liver retractor is advanced into the mediastinum for retraction. These two maneuvers expose the mediastinum. Dissection is carried out in the mediastinum carefully without injuring the pleura.

Trans hiatal mobilization of the thoracic esophagus: The esophagus is then retracted above and laterally [Figure 3]. Intrathoracic esophageal dissection to be started on the right side by separating right mediastinal pleura from the esophagus. The esophagus is lifted high with the left-hand instrument, and posterior attachment to preaortic fascia over the aorta is carefully dissected and divided using harmonic scalpel/vessel sealing device. Simultaneously, a complete lymph nodal dissection is performed in the posterior mediastinum with removing the lymph nodes with 5 mm harmonic shears. The esophagus is retracted to the right side and attachment of the left mediastinal pleura from mesoesophagus (Fibrofatty tissue with small blood vessels to the esophagus from the aorta) is dissected out. Lastly, anteriorly esophagus is separated from the pericardium. This dissection can be carried up to 6-7 cm above the hiatal level.

Gastric conduit creation: Gastric conduit is formed by firing a 60 mm endo GIA gold cartridge stapler (© Ethicon US, LLC) perpendicularly and 2-3 subsequent firing of blue cartridge staplers obliquely [Figure 4]. The liver retractor is passed into mediastinum above the right crus and pericardium well lifted above. After esophageal dissection, using a flexible, and curved stapler passed through left side intrathoracically, the esophagus is divided, making sure, the transection line is above the tumor [Figure 5]. A small opening formed in the right pleura and the gastric conduit is placed within in the right pleural cavity [Figure 6].

Through a Pfannenstiel incision, the specimen is removed out. In cases of smaller lesions, the stomach is not entirely divided and is pulled up in the intrathoracic phase and removed through a small thoracic incision.

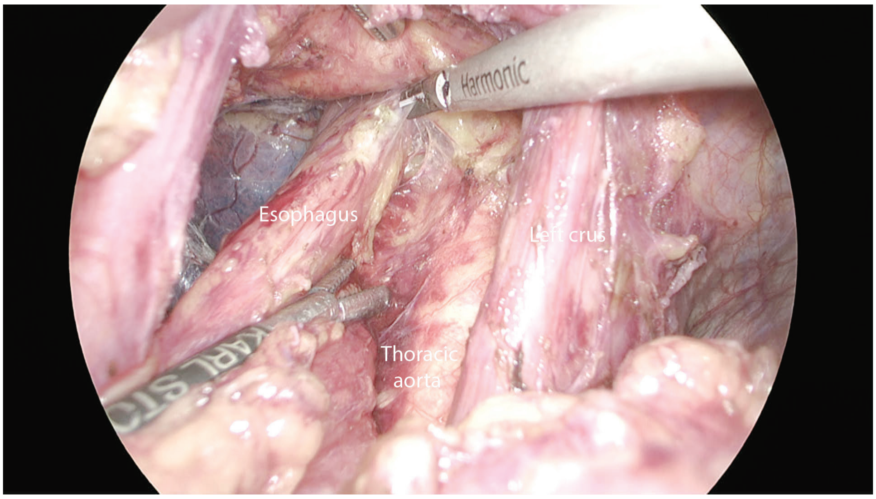


Figure 3. Laparoscopic view of trans hiatal mobilization

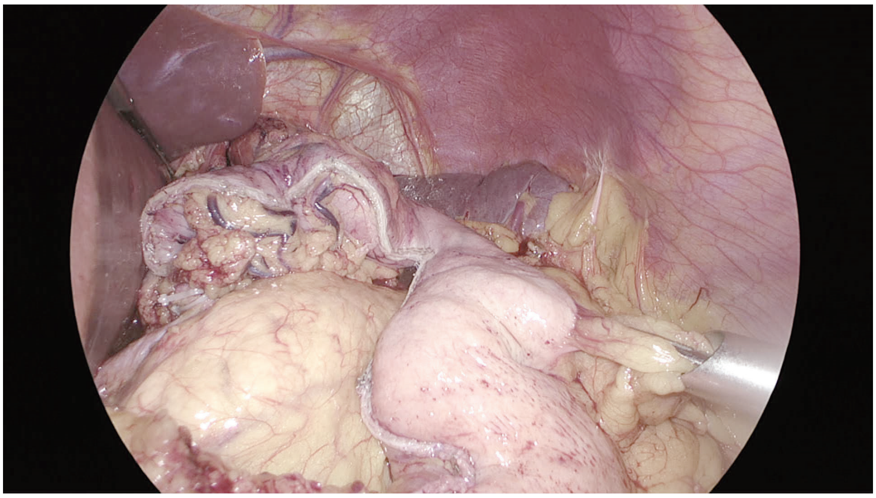


Figure 4. Gastric conduit creation

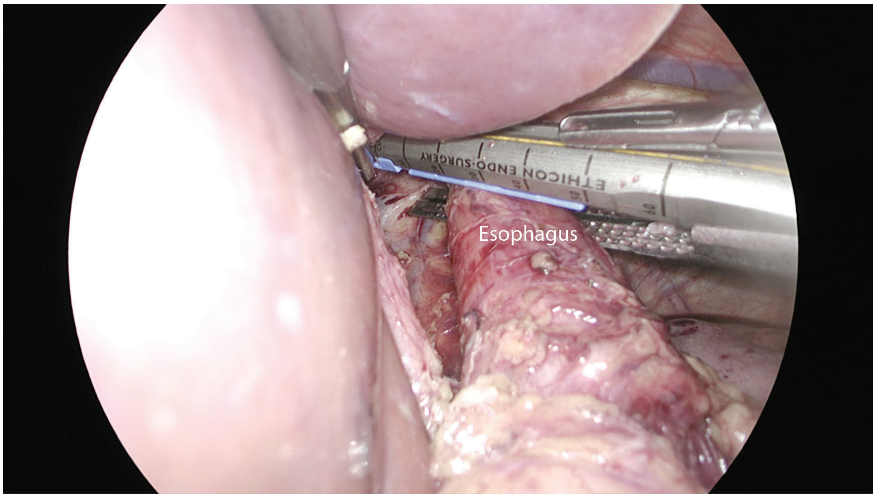


Figure 5. Transhiatal division of esophagus

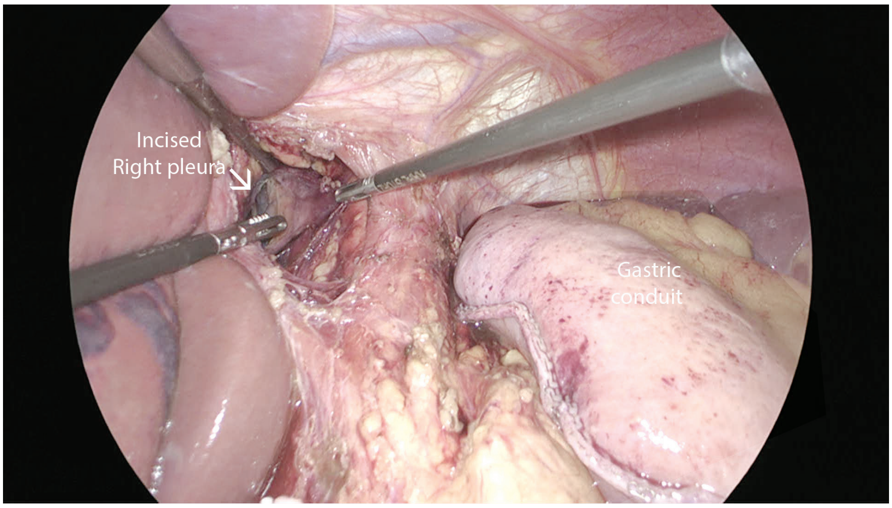


Figure 6. Placing the gastric tube in the right pleural cavity, to prevent slippage into the abdominal cavity

Figure 7. Thoracoscopic port position. A: 7th intercostal space below the inferior angle of the scapula for camera: 10 mm; B: 9th intercostal space 7cm away from the spinous process for left hand working port: 5 mm; C: 5th intercostal space 7 cm away from the spinous process for right hand working port: 5 mm

Stage II: Thoracic phase

In the second phase, thoracoscopic esophageal mobilization, resection, and the anastomosis are done in semi-prone position with the same single-lumen endotracheal tube intubation. Ports [Figure 7].

Access to the thoracic cavity can be gained by either placing a veress needle followed by port insertion or through direct port placement using optiview trocar. Before placing initial trocar scapula to be retracted medially and superiorly with the help of an assistant to provide easy access to the thoracic cavity (We prefer trocar placement under direct vision because in this part of the world most of the patients might have a tubercular infection associated with pleural adhesions).

After gaining access, CO_2 pneumo with 8 mmHg pressure to be maintained. The anesthetist is requested to keep the low tidal volume for a brief period to facilitate lung collapse. Inside the thoracic cavity, the gastric

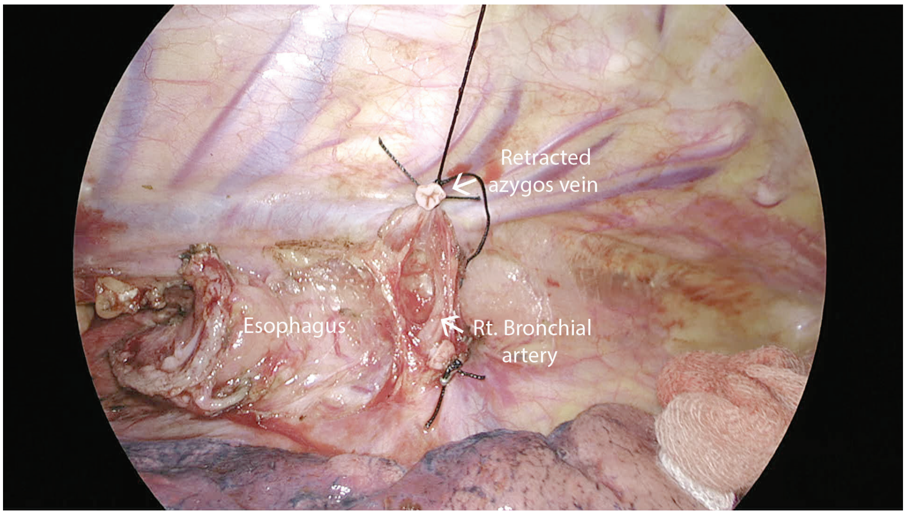


Figure 8. Exposure after retraction of the divided azygous vein

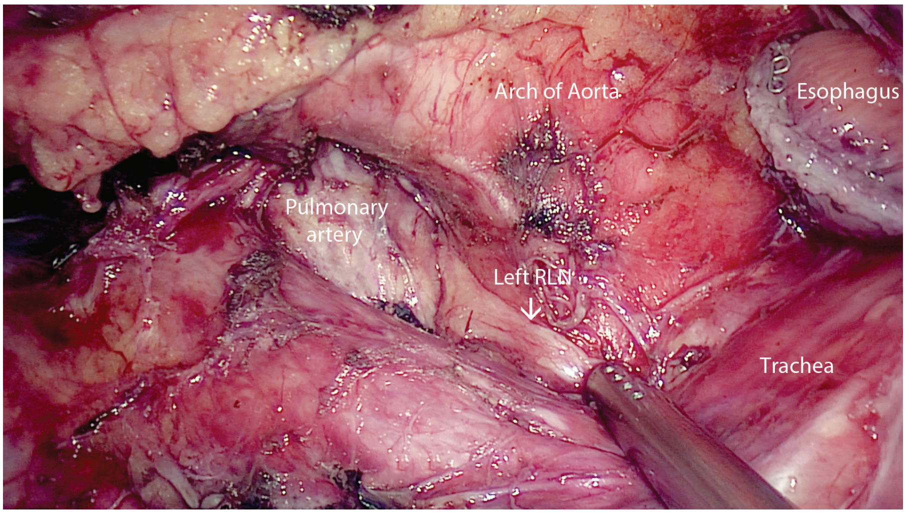


Figure 9. Subcarinal lymph node dissection

conduit to be visualized and pulled up to check for adequacy of the length of the conduit. Mediastinal pleura incised, Azygous vein is skeletonized at the level of the azygous arch, Azygous vein is doubly ligated with silk no two sutures, and one suture towards the vertebral end is left long to help in retraction of the vein during dissection of aortopulmonary window [Figure 8]. The esophagus is mobilized proximally till the subcarinal level (usually 5-6 cm above the transected end to achieve adequate proximal margin), and nodal lymph dissection is done [Figure 9]. We perform standard two-field lymphadenectomy; thoracic duct is not excised in all the cases, except in cases where the patient weight is below 35 kg.

Proximally with adequate clearance esophagus is divided using endo GIA stapler. After proximal esophageal division, four full-thickness (adventitia to the mucosa) sutures are placed anteriorly on both the sides and posteriorly to prevent esophageal mucosal retraction [Figure 10]. The gastric conduit is pulled closer, and the esophagogastric anastomosis is performed [Figure 11].

Esophagogastric anastomosis: This is accomplished in three ways: (1) End to end/side hand-sewn anastomosis; (2) End to side fully mechanical anastomosis-circular stapler; (3) Side to side fully mechanical anastomosis-linear cutter stapler. End to end/side hand-sewn anastomosis: The two ends are approximated

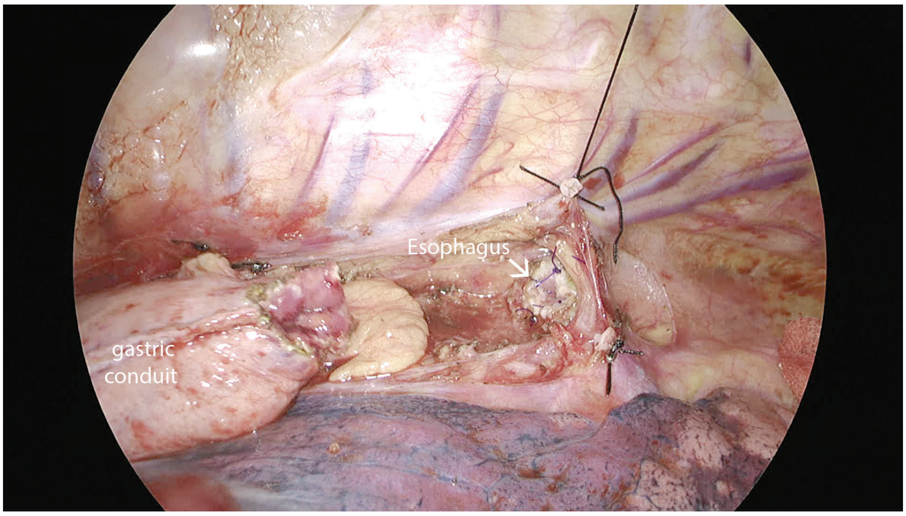


Figure 10. Proximal esophagus full-thickness sutures preventing mucosal retraction

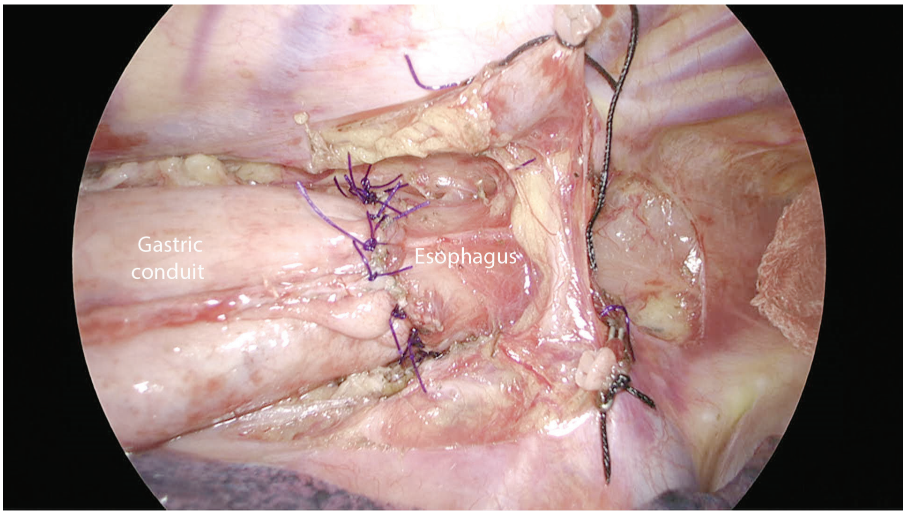


Figure 11. End to end esophagogastric anastomosis

in two layers interrupted sutures using 2-0 PDS (polydioxanone) (© Ethicon US, LLC). Side to side semi-mechanical anastomosis: Using linear staplers, intrathoracic side to side esophagogastric anastomosis done. The stapler entry wound to be closed with 2-0 PDS. End to side fully mechanical anastomosis: When gastric conduit width is more, stapling technique is preferred, and narrower tube hand-sewn anastomosis is done.

The linear stapling technique 12 mm trocar is placed in the 11/12th intercostal space for stapler insertion [Figure 12]. The trocar is placed at the angle of the rib. Using monopolar cautery, enterotomy is made on the staple line of the stomach, and similarly, entry is made at the stapled edge of the esophagus. When the esophagus is divided without a staple, then one of the jaws may be placed directly into the lumen and side to side anastomosis is done by linear anastomosis. The anterior anastomosis is done by intrathoracic hand-sewn suturing technique or a stapler in triangulation manner.

Intra-corporeal anastomosis by hand suturing technique

Ends of the gastric conduit and the esophagus are trimmed, and end to end anastomosis is done. 3-0 PDS with a small curved needle is used for suturing.

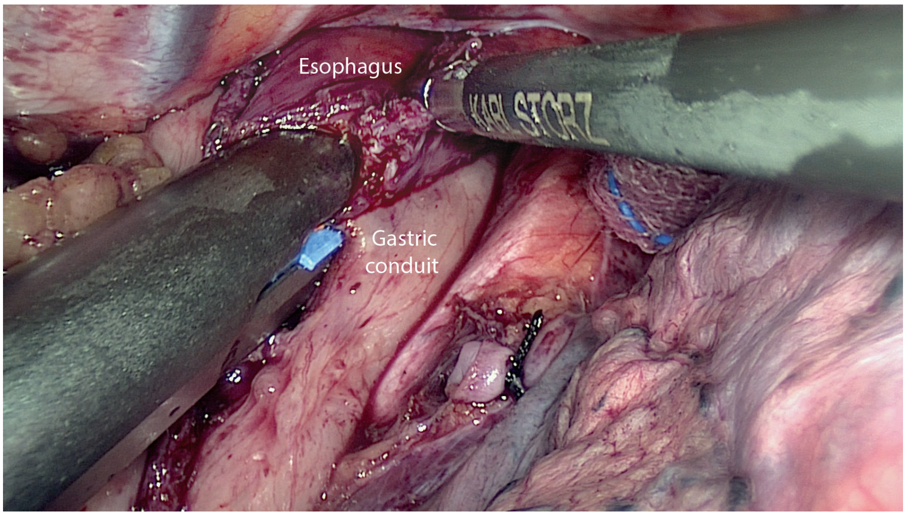


Figure 12. Esophagogastric anastomosis using linear stapler

Circular Stapling technique

Proximal Esophagus is transected using 60mm blue cartridge, 5 cm proximal to azygos arch in an oblique manner. Peroral anvil [Orvil™ (Medtronic, Covidien, MN, USA)] is passed orally, and a small opening is made at one edge of the stapled line and anvil is positioned in the divided end of the esophagus. Gastric conduit is advanced to the apex of the thoracic cavity, and an opening is made in the staple line on the lesser curvature. Then a 3-4 cm incision is formed on the right thoracic cavity at the level of 11th rib for entry of the circular stapler. 25 mm circular stapler is introduced into the thoracic cavity with the protective plastic sleeve [Figure 13]. Head of the stapler is introduced into gastric conduit and pin is pierced on to the greater curvature side and docked to the anvil and fired [Figure 14]. Stapler entry on the gastric tube is closed by intracorporeal sutures using 20 PDS [Figure 15].

In few cases of SCC of GE junction, a circular stapler is used to achieve intra thoracic anastomosis close to the thoracic inlet.

Feeding access in all our patients is by a Naso-Jejunal tube placed intraoperatively while constructing the anastomosis. Feeding jejunostomy is not routinely practiced in our patients. An-intercostal drainage is placed in the right pleural cavity.

Postoperative period

We practice the technique of early extubation in the immediate postoperative period. All the patients are shifted to ICU for observation and supportive care in the early postoperative period. Oral gastrograffin study to check the functionality of gastric conduit is performed on POD 2 following which oral liquids are initiated. CT scan with oral contrast is performed in patients with high suspicion of the leak.

RESULTS

In 11 years, we had performed 532 cases of minimally invasive esophagectomies for both malignant and benign etiologies. Out of which 143 Cases were of ILE [Table 1]. The mean age of patients was 64.4 ± 10.86 years, and male to female ratio was 3:1. Out of these cases, 139 (97.20%) were performed for malignancy and 4 (2.79%) for benign cases, which include peptic stricture, sigmoid esophagus. The mean operative time was 457.97 ± 79.35 min. The mean blood loss was 138.08 ± 29.3 mL. Out of these cases, the hand-sewn anastomosis was performed in 72 (50.34%), circular stapler anastomosis in 46 (32.16%) linear stapled

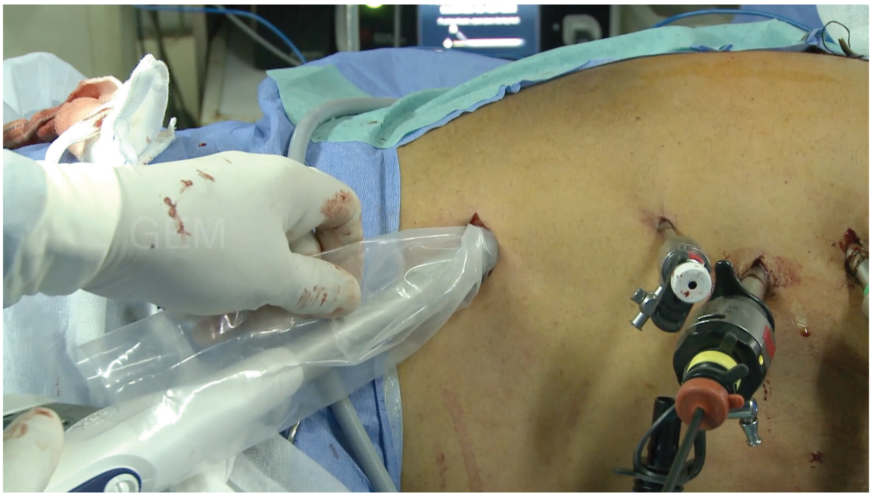


Figure 13. Transthoracic insertion of circular stapler

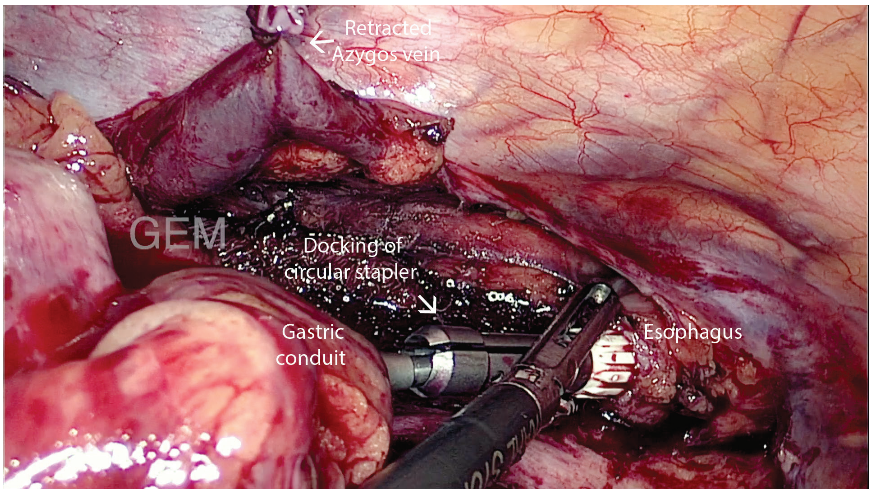


Figure 14. Docking of circular stapler

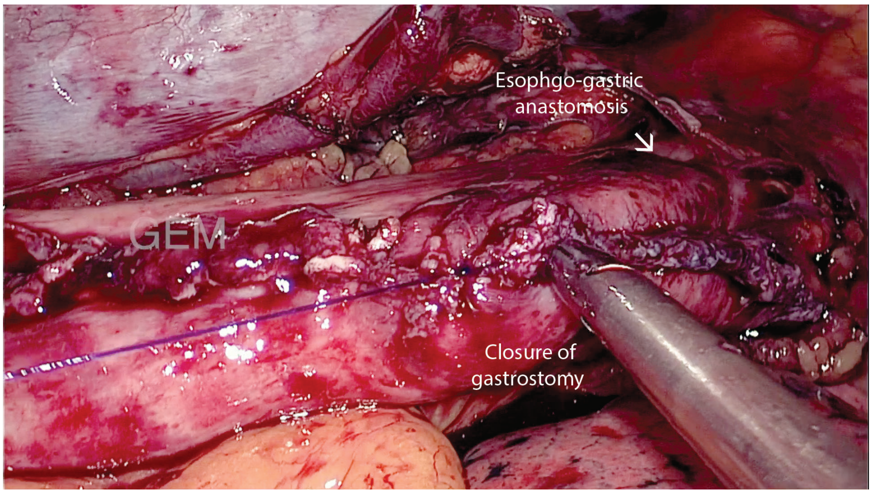


Figure 15. Closure of the gastrotomy wound after circular stapler

Table 1. Demographic, intraoperative, postoperative parameters

Sr. No.	Parameter	Value (Mean ± Standard Deviation)
(1)	Age (in years)	64.4 ± 10.86
(2)	Sex (M:F)	3:1
(3)	Etiology (a) Malignant (b) Non-malignant	Total-143 139 (97.20%) 4 (2.79%)
(4)	(a) Thoraco-laparoscopy (b) Robotic	138 (96.50%) 5 (3.49%)
(5)	Duration (in mins)	457.97 ± 79.35
(6)	Blood loss (in ml)	138.08 ± 29.3
(7)	Lymph nodes retrieved	22.68 ± 9.49
(8)	Anastomosis (a) Circular (b) Linear stapler (c) Hand sewn	 46 (32.16%) 25 (17.48%) 72 (50.34%)
(9)	ICU stay (in days)	4.68 ± 3.95
(10)	Duration of hospital stay (in days)	13.48 ± 7.43
(11)	Histology (n-139) (a) Adeno carcinoma (b) Squamous cell carcinoma	 121 (87.05%) 18 (12.94%)
(12)	T Staging (n-139) (a) T2 (b) T3 (c) T4	 56 (40.28%) 77 (55.39%) 6 (4.31%)
(13)	Complications (a) Pneumonia (b) RLN injury (c) Chyle leak (d) Anastomotic Leak (e) Anastomotic stricture	25.17% 12 (8.39%) 2 (1.39%) - 1 required tracheostomy 1 (0.69%) 3 (2.09%) 18 (12.58%)
(14)	Re-intervention (a) Endoscopic (b) Thoracoscopy	3 (2.09%) (combined endoscopic and thoracoscopic procedure done) 3 (2.09%) 3 (2.09%)
(15)	30-day mortality	1 (0.69%)

anastomosis in 25 (17.48%) of cases. The mean lymph node retrieval rate was 22.68 ± 9.49 nodes. The average ICU stay in the postoperative period was 4.68 ± 3.95 days, and overall hospital stay was 13.48 ± 7.43 days. Among malignant cases (139), adenocarcinoma in 121 (87.05%), SCC in 18 (12.94%). Among these cases T2, lesions in 56 (40.28%), T3 lesions in 77 (55.39%), T4 lesions in 6 (4.31%) The overall complication rate was 25.17% (pneumonia - 8.39%, RLN (recurrent laryngeal nerve) injury in 1.39%, anastomotic leak in 2.09%, chyle leak in 0.69%). Overall anastomotic stricture rate is 12.58%. The stricture rate was more in linear stapler technique compared to the other two. Six cases had re-intervention in the form of endoscopic procedures in 3 (2.09%) and re-thoracoscopy in 3 (2.09%). Laparoscopic feeding jejunostomy was done in 2% of patients who had re-intervention because of anastomotic leak. Overall 30-day mortality noted in 1 case (0.69%).

DISCUSSION

We have been performing minimally invasive esophagectomies since 1997[7]. Since then all esophagectomies were conducted in the prone position during the thoracic phase. For cases of GE junction tumors, we performed trans hiatal esophagectomies with excellent results[8]. But later on, to achieve better proximal clearance we have opted performing thoracolaparoscopic esophagectomies. In cases of SCC of lower esophagus close to GE junction, we have performed intrathoracic anastomosis using circular stapler close to the level of the thoracic inlet. Throughout 11 years, the rate of performing intrathoracic anastomosis improved year by year because of change in the incidence of adenocarcinoma and experience in the technique of intrathoracic anastomosis. For lesions requiring division above the level of the azygous arch, we performed the circular anastomosis. Till the level of the azygous arch, we have completed hand sewn or linear staple anastomosis. Presently Our preferred technique of anastomosis is circular stapler technique if the level of the anastomosis is above the level of azygous arch and at the level of azygous or below the azygous arch hand-sewn technique because of better ergonomics. In robotic cases because of ease of suturing, we prefer hand-sewn anastomosis in all the circumstances.

Initial reports of totally endoscopic ILE was by Watson *et al.*[9] who described, the technique of hand-assisted laparoscopy for gastric mobilization and a right thoracoscopy for esophageal dissection and anastomosis in two patients.

One of the potential advantages of the minimally invasive trans-thoracic approach is better exposure and improved lymph node dissection in the mediastinum, associated with low morbidity and mortality. The reported rate of peri-operative complications, including anastomotic leak, pneumonia, and recurrent nerve injury, was quite low[10].

Baranov *et al.*[11] in their study of 446 patients of minimally invasive ILE, 357 patients were younger than 75 years (younger group) and 89 patients were aged 75 years and older (elderly group) found that regarding severe complications there was no significant difference between the younger and the elderly group (35.9% in the younger group versus 43.8% in the elderly group, $P = 0.421$) and the 30 days mortality was 30-day mortality was 2.8% in the younger group versus 2.2% in the elderly group ($P = 0.889$). They have concluded that minimally invasive ILE can be safely performed in selected patients aged ≥ 75 years, without increasing severe complications or decreasing survival.

In a recent systemic review and meta-analysis by Deng *et al.*[12] in 2018 Comparing short-term outcomes between minimally invasive McKeown esophagectomy (MIME) and minimally Ivor Lewis esophagectomy (MILE) for esophageal or junctional cancer found that MIME was associated with more blood loss, longer operating time, and longer hospital stay than MILE. Pulmonary complications (OR = 1.96, 95%CI: 1.28-3.00) as well as total anastomotic leak (OR = 2.55, 95%CI: 1.40-4.63), stricture (OR = 2.07, 95%CI: 1.05-4.07), and vocal cord injury/palsy (OR = 5.62, 95%CI: 3.46-9.14) were significantly higher in MIME compared to MILE[12]. In TIME trial, long term results, after three years follow-up, found no differences in disease-free (37.3% *vs.* 42.9%, $P = 0.602$) and overall (41.2% *vs.* 42.9%, $P = 0.633$) 3-year survival between open esophagectomy and minimally invasive esophagectomy[13]. In their study they also found that minimally invasive esophagectomy in post neoadjuvant therapy compare to upfront surgery showed no difference in resection rates and concluded that minimally invasive surgery might be safely attempted in post neoadjuvant cases which were considered as a contraindication due to radiation fibrosis[14].

In our study, the anastomotic leak is 2.09% compared to 4.7 % shown in the meta-analysis of various studies[15]. The overall pulmonary complications in our study are 8.39% in comparison to 17.1% in minimally invasive esophagectomies, in a meta-analysis of 57 studies[16]. The lymph node retrieval rate is 22.68 ± 9.49 in comparison to 22 ± 10 in a propensity score-matched study comparing open and laparoscopic group by Rinieri *et al.*[17]. The length of ICU stay in our study is 4.68 ± 3.95 days, and length of hospital stay is 13.48 ± 7.43 days, in comparison to 3.6 days and 12 days in a similar stud of minimally invasive ILE by Zonča *et al.*[18]. The 30 day mortality rate is 0.69% in comparison to 1 % shown in a systematic review by Deng *et al.*[12].

In conclusion, thoracolaparoscopic esophagectomy with intrathoracic Ivor Lewis anastomosis is an excellent option for selected patients, in experienced hands.

DECLARATIONS

Authors' contributions

Data acquisition, conceptualization, manuscript writing, and critical revision of the manuscript: Parthasarathi R, Gupta GR, Sabnis SC, Raj PP, Senthilnathan P, Rajapandian S, Palanivelu C.
All authors contributed equally for the manuscript.

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

In-hospital GEM ethic's committee has approved this study. The ethical committee has approved a waiver of consent given the retrospective nature of the study. All efforts are made to keep the individual patient's identity anonymous.

Consent for publication

Not applicable.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, et al. Global Cancer Statistics 2018: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA-Cancer J Clin 2018;68:394-424.
2. Edgren G, Adami HO, Weiderpass E, Nyrén O. A global assessment of the oesophageal adenocarcinoma epidemic. Gut 2013;62:1406-14.
3. Bollschweiler E, Wolfgarten E, Gutschow C, Hölscher AH. Demographic variations in the rising incidence of esophageal adenocarcinoma in white males. Cancer 2001;92:549-55.
4. Hashimoto T, Kurokawa Y, Mori M, Doki Y. Surgical Treatment of Gastroesophageal Junction Cancer. J Gastric Cancer 2018;18:209-17.
5. Lewis I. The surgical treatment of carcinoma of the esophagus; with special reference to a new operation for growths of the middle third. Br J Surg 1946;34:18-31.
6. Huang L, Onaitis M. Minimally invasive and robotic Ivor Lewis esophagectomy. J Thorac Dis 2014;6:S314-21.
7. Palanivelu C, Prakash A, Senthilkumar R, Senthilnathan P, Parthasarathi R, et al. Minimally invasive esophagectomy: thoracoscopic mobilization of the esophagus and mediastinal lymphadenectomy in prone position-experience of 130 patients. J Am Coll Surg 2006;203:7-16.
8. Palanivelu C, Prakash A, Parthasarathi R, Senthilkumar R, Senthilnathan PR, et al. Laparoscopic esophagogastrectomy without thoracic or cervical access for adenocarcinoma of the gastroesophageal junction: an Indian experience from a tertiary center. Surg Endosc 2007;21:16-20.
9. Watson DI, Davies N, Jamieson GG. Totally endoscopic Ivor Lewis esophagectomy. Surg Endosc 1999;13:293-7.
10. Bizekis C, Kent MS, Luketich JD, Buenaventura PO, Landreneau RJ, et al. Initial experience with minimally invasive Ivor Lewis esophagectomy. Ann Thorac Surg 2006;82:402-6.
11. Baranov NS, van Workum F, van der Maas J, Kouwenhoven E, van Det M, et al. The Influence of Age on Complications and Overall Survival After Ivor Lewis Totally Minimally Invasive Esophagectomy. J Gastrointest Surg 2019;23:1293-300.
12. Deng J, Su Q, Ren Z, Wen J, Xue Z, et al. Comparison of short-term outcomes between minimally invasive McKeown and Ivor Lewis esophagectomy for esophageal or junctional cancer: a systematic review and meta-analysis. Onco Targets Ther 2018;11:6057-69.
13. Straatman J, van der WN, Cuesta MA, Daams F, Roig GS, et al. Minimally Invasive Versus Open Esophageal Resection: Three-year Follow-up of the Previously Reported Randomized Controlled Trial: the TIME Trial. Ann Surg 2017;266:232-6.

14. Tan L, Tang H. Oncological outcomes of the TIME trial in esophageal cancer: is it the era of minimally invasive esophagectomy? Ann Transl Med 2018;6:85.
15. van Workum F, Berkelmans GH, Klarenbeek BR, Nieuwenhuijzen GAP, Luyer MDP, et al. McKeown or Ivor Lewis totally minimally invasive esophagectomy for cancer of the esophagus and gastroesophageal junction: systematic review and meta-analysis. J Thorac Dis 2017;9:S826-33.
16. Yibulayin W, Abulizi S, Lv H, Sun W. Minimally invasive oesophagectomy versus open esophagectomy for resectable esophageal cancer: a meta-analysis. World J Surg Oncol 2016;14:304.
17. Rinieri P, Ouattara M, Brioude G, Loundou A, de Lesquen H, et al. Long-term outcome of open versus hybrid minimally invasive IvorLewis oesophagectomy: a propensity score matched study. Eur J Cardiothorac Surg 2017;51:223-9.
18. Zonča P, Peteja M, Richter V, Vávra P, Ostruszka P, et al. Complete minimally invasive Ivor-Lewis esophageal resection. Rozhl Chir 2017;96:114-9.

Hori *et al*. *Mini-invasive Surg* 2019;3:21
DOI: 10.20517/2574-1225.2019.15

Mini-invasive Surgery

Case Report

Open Access

Check for updates

Intradural lumbar disc herniation after full-endoscopic lumbar discectomy using the interlaminar approach: case report

Takeshi Hori, Kazuo Ohmori, Koichiro Ono

Center for Spinal Surgery, Nippon Koukan Hospital, 1-2-1 Koukandori, Kawasaki-ku, Kawasaki 210-0852, Japan.

Correspondence to: Takeshi Hori, Center for Spinal Surgery, Nippon Koukan Hospital, 1-2-1 Koukandori, Kawasaki-ku, Kawasaki 210-0852, Japan. E-mail: takhori1030@gmail.com

How to cite this article: Hori T, Ohmori K, Ono K. Intradural lumbar disc herniation after full-endoscopic lumbar discectomy using the interlaminar approach: case report. *Mini-invasive Surg* 2019;3:21. http://dx.doi.org/10.20517/2574-1225.2019.15

Received: 9 May 2019 **First Decision**: 9 Jul 2019 **Revised**: 10 Jul 2019 **Accepted**: 15 Jul 2019 **Published**: 20 Jul 2019

Science Editor: Giulio Belli **Copy Editor**: Jia-Jia Meng **Production Editor**: Jing Yu

Abstract

A 67-year-old man complained of the sudden onset of disabling pain in his right leg. He had already undergone full-endoscopic lumbar discectomy, interlaminar (FELD-IL) approach twice for lumbar disc herniation (LDH) at the L4/5 level. MRI showed recurrence of LDH at L4/5 level. Intradural masses were also suspected at the L4 vertebral level. Discography at the L4/5 disc showed contrast medium leakage from the disc to the subarachnoid space. Operation was performed and fragments of the herniated disc were carefully removed under a surgical microscope. The ventral dura mater could be seen adhering to the L4/5 disc. This report is the first documentation of intradural LDH after FELD-IL. Although FELD is less invasive than previous procedures, adhesion between dura mater and surrounding tissues may occur. It is most important to apply discography to confirm the presence of a hole between the intradural space and the disc.

Keywords: Intradural lumbar disc herniation, full-endoscopic lumbar discectomy, discography

INTRODUCTION

Intradural lumbar disc herniation (LDH) is rare, with a reported incidence of 0.26%-0.30% of all cases of LDH[1,2]. The first report of intradural LDH was presented by Dandy in 1942[3]. Several etiopathologies of intradural LDH have been suggested, including adhesion between the ventral dura and posterior

Figure 1. Preoperative magnetic resonance imaging, T2-weighted sagittal image

longitudinal ligament associated with congenital or chronic inflammation after previous surgery[1,4], congenital reduction in dural thickness, and congenital stenosis of the vertebral canal[5].

Full-endoscopic lumbar discectomy (FELD) is a minimally invasive technique for treating LDH. FELD has recently become widely used after being reported by Ruetten *et al.*[6] in 2008. Three approaches are used with FELD to treat LDH: transforaminal, posterolateral, and interlaminar (IL). To date, there are no reports of intradural LDH in patients following FELD-IL. Herein, we describe a case of intradural LDH after FELD-IL and discuss the specific features of diagnostic imaging, its etiopathology, and the surgical findings.

CASE REPORT

A 67-year-old man complained of the sudden onset of disabling pain in his right leg. He was admitted to our hospital. He had undergone FELD-IL twice before for LDH at the L4/5 level, 2 years and 1 year ago, respectively. There was no injury to the dura matter during the previous operations. The straight leg raising test was positive at 60° on the right side. Neurological examination demonstrated no paralysis and no sensory disturbance in his leg. There was no dysuria. Magnetic resonance imaging (MRI) showed LDH at the L4/5 level and a redundant cauda equina [Figure 1]. Intradural masses were also suspected at the L4 level. Computed tomography (CT) after myelography clearly showed an intradural mass from L4 to the sacral level [Figure 2]. It was suspected to be intradural disc herniation or a spinal tumor. Discography and CT discography showed leakage of contrast medium from the disc space to the subarachnoid space [Figures 3 and 4]. Based on these findings, we strongly suspected intradural LDH.

Laminectomy from L4 to S1 was performed, exposing a bulging dural sac at the L4/5 level. Durotomy was performed at the midline, and the herniated disc was fragmented [Figure 5]. These fragments were carefully removed under a surgical microscope until the adhesion between the herniated disc and the cauda equina was disrupted and the defect in the dura mater apparent [Figure 6]. The ventral dura was strongly adherent to the L4/5 disc.

The patient reported alleviation of his leg pain immediately after the surgery. Postoperative MRI showed complete removal of the intradural LDH.

Figure 2. Computed tomography after myelography, sagittal image. An intradural mass was observed from L4 to the sacral level

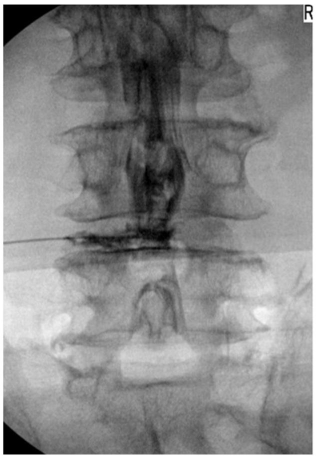


Figure 3. Discography at the L4/5 level. Contrast medium was not contained within the disc as it spread intrathecally with a myelographic appearance

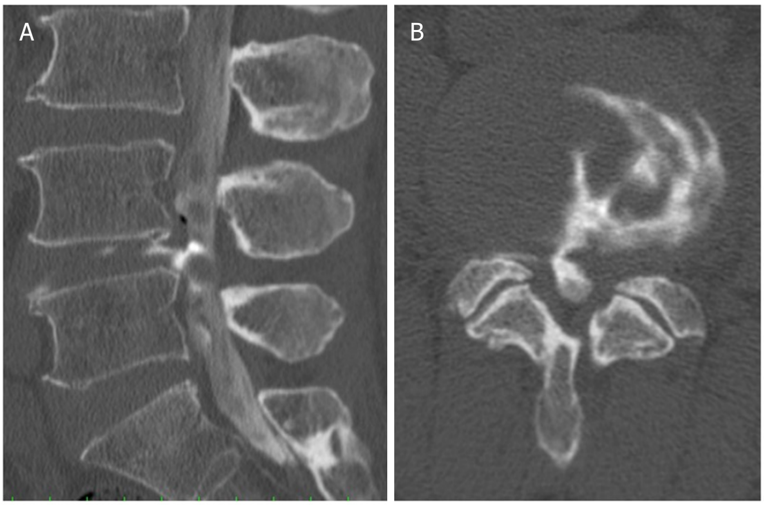


Figure 4. Computed tomography after discography. A: sagittal image; B: axial image

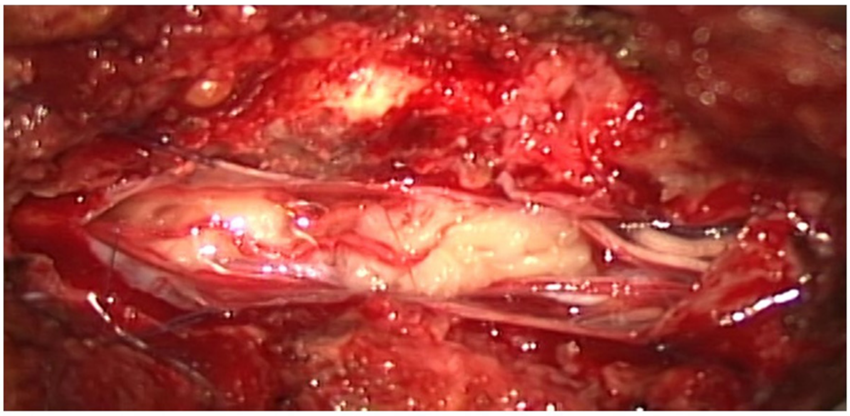


Figure 5. Intraoperative microscopic image reveals an intradural herniated mass

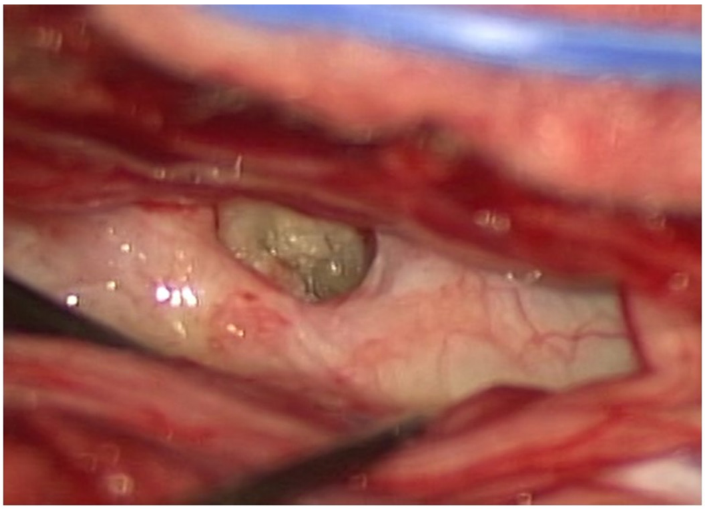


Figure 6. Intraoperative microscopic image reveals a defect in the ventral dura

DISCUSSION

First reported in 2008 by Ruetten *et al.*[6], FELD is a minimally invasive technique for treating LDH. Tamaki *et al.*[7] later reported the occurrence of intradural LDH after FELD, but the transforaminal approach was used, and a ventral dural tear was observed during the operation. Our present report is the first documentation of intradural LDH after FELD-IL.

Although FELD is less invasive than previous procedures (e.g., micro-endoscopic or open surgery), adhesion between the dura mater and surrounding tissues may occur after FELD, as in the present case. The re-operation should be performed carefully even if the previous operation procedure was FELD. Matsumoto *et al.*[8] reported that the pathophysiology of intradural LDH is typically attributed to adhesion between the annulus fibrosus, the posterior longitudinal ligament, and the dura mater after local inflammation or a prior operation. It is quite possible that intradural LDH could occur after FELD-IL even though FELD is less invasive and there was no dural tear.

Several radiological features of intradural LDH - rim enhancement of the herniated disc on gadolinium-enhanced MRI, beak-like appearance on T2-weighted images - have been reported previously. However, these radiological features are not conclusive for diagnosing intradural LDH. The most important diagnostic step is to demonstrate a hole between the intradural space and the disc space. A few reports have described discography for preoperative intradural LDH[9,10]. Benyamin *et al*.[9] reported a case of intradural LDH incidentally diagnosed during routine discography. In the present case, we performed discography to distinguish intradural LDH from other spinal pathologies, such as neurinoma and arachnoid cyst, among others.

In conclusion, preoperative diagnosis of intradural LDH is important for surgical planning. Physical examination for intradural LDH is similar to that for common LDH. Image findings, especially via discography, are important for establishing a definitive diagnosis of intradural LDH.

DECLARATIONS

Authors' contributions

Conception and design: Hori T, Ohmori K
Clinical treatment: Hori T, Ohmori K, Ono K
Manuscript writing: Hori T
Final approval of manuscript: Hori T, Ohmori K

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

All procedures used in the present literature approved by the Ethical Committee of Nippon Koukan Hospital. We obtained the patient's consent for publication of the present literature.

Consent for publication

Not applicable.

REFERENCES

1. Aydin MV, Ozel S, Sen O, Erdogan B, Yildirim T. Intradural disc mimicking: a spinal tumor lesion. Spinal Cord 2004;42:52-4.
2. Epstein NE, Syrquin MS, Epstein JA, Decker RE. Intradural disc herniations in the cervical, thoracic, and lumbar spine: report of three cases and review of the literature. J Spinal Disord 1990;3:396-403.
3. Dandy WE. Recent advances in the diagnosis and treatment of ruptured intervertebral disks. Ann Surg 1942;115:514-20.
4. Choi JY, Lee WS, Sung KH. Intradural lumbar disc herniation--is it predictable preoperatively? A report of two cases. Spine J 2007;7:111-7.
5. D'Andrea G, Trillò G, Roperto R, Celli P, Orlando ER, et al. Intradural lumbar disc herniations: the role of MRI in preoperative diagnosis and review of the literature. Neurosurg Rev 2004;27:75-80.
6. Ruetten S, Komp M, Merk H, Godolias G. Full-endoscopic cervical posterior foraminotomy for the operation of lateral disc herniations using 5.9-mm endoscopes: a prospective, randomized, controlled study. Spine 2008;33:940-8.
7. Tamaki Y, Sakai T, Miyagi R, Nakagawa T, Shimakawa T, et al. Intradural lumbar disc herniation after percutaneous endoscopic lumbar discectomy: case report. J Neurosurg Spine 2015;23:336-9.
8. Matsumoto T, Toyoda H, Terai H, Dohzono S, Hori Y, et al. Utility of Discography as a Preoperative Diagnostic Tool for Intradural

Lumbar Disc Herniation. Asian Spine J 2016;10:771-5.
9. Benyamin R, Vallejo R, Yousuf N, Tamrazi A, Kramer J. Incidental diagnosis of intradural lumbar disc herniation during discography: a case report. Pain Pract 2007;7:332-6.
10. Ducati LG, Silva MV, Brandão MM, Romero FR, Zanini MA. Intradural lumbar disc herniation: report of five cases with literature review. Eur Spine J 2013;22:S404-8.

Herbella *et al*. *Mini-invasive Surg* 2019;3:22
DOI: 10.20517/2574-1225.2019.19

Mini-invasive Surgery

Opinion

Open Access

How I teach it - a didactic approach to laparoscopic surgery at the esophagogastric junction

Fernando A. M. Herbella, Rafael C. Katayama

Department of Surgery, Federal University of Sao Paulo, Sao Paulo, SP 04037-003, Brazil.

Correspondence to: Dr. Fernando A. M. Herbella, Department of Surgery, Escola Paulista de Medicina, Federal University of Sao Paulo, Rua Diogo de Faria 1087 cj 301, Sao Paulo, SP 04037-003, Brazil. herbella.dcir@epm.br

How to cite this article: Herbella FAM, Katayama RC. How I teach it - a didactic approach to laparoscopic surgery at the esophagogastric junction. *Mini-invasive Surg* 2019;3:22. http://dx.doi.org/10.20517/2574-1225.2019.19

Received: 1 Jul 2019 **Accepted**: 12 Jul 2019 **Published**: 23 Jul 2019

Science Editor: Giulio Belli **Copy Editor**: Cai-Hong Wang **Production Editor**: Jing Yu

Abstract

We present an alternative didactic approach to the esophagogastric junction through an active liver retraction with a laparoscopic palpator. We believe this didactic approach is not necessarily carried by a well-trained team. However, it is a minor modification of the standard operation that has advantages on surgical training in academic centers.

Keywords: Laparoscopy, stomach, esophagus, esophagogastric junction

INTRODUCTION

Laparoscopic surgery of the esophagogastric junction (EGJ) is a common procedure for a great number of antireflux operations had already been performed[1]. In addition, the surgical treatment of achalasia[2], esophageal neoplasms[3] and certain modifications of bariatric operations[4] are included in the laparoscopic procedures of the EGJ as well. The classical disposition of the ports for laparoscopic surgery of the EGJ comprises 5 ports. Liver retraction is usually accomplished through the use of dedicate retractors inserted in the right flank and the retractor is frequently kept static. Alternatively, liver retraction may be obtained through a port in the epigastrium with the aid of a simple stick (palpator)[5] or a Nathanson retractor[6].

We present an alternative didactic approach to the EGJ through an active liver retraction with a laparoscopic palpator.

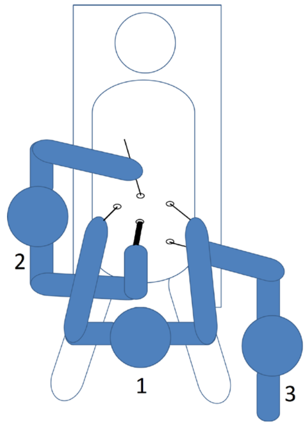


Figure 1. Ports placement for operations on the esophagogastric junction. Liver retraction is moved from the right flank of the classic approach to the epigastrium in the proposed didactic technique

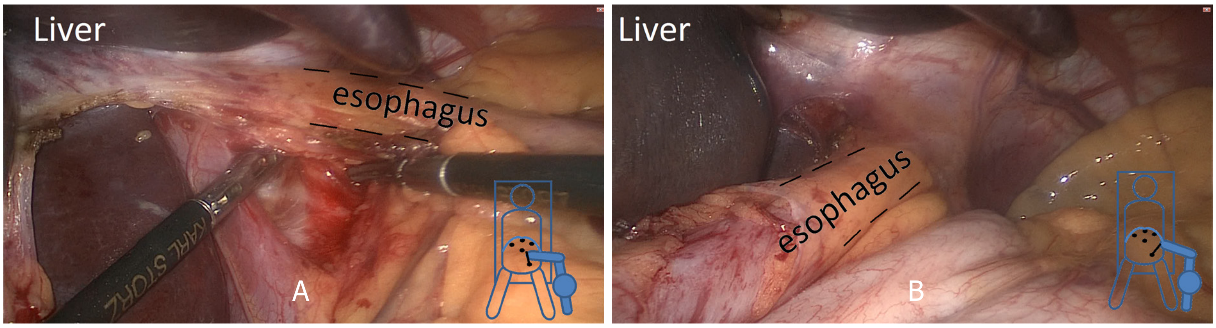


Figure 2. Esophageal exposition based on pre-taught hand positions of the second assistant. Exposure of the right side of the esophagus - Position A, and exposure of the left side of the esophagus - Position B

METHOD

Ports are placed in a similar fashion to the classic approach with the exception of the liver retraction port that is moved from the right flank to the epigastrium, closing to the xyphoid appendix [Figure 1].

The surgeon (chief resident/fellow) stands between the legs of the patient, with the first assistant to the right of the patient and the second assistant to the left of the patient. The first assistant (attending) holds the camera and a palpator (or an irrigator/aspirator although fatigue is stronger with this instrument). The assistant is sited to prevent their elbows to touch surgeon's arms.

The second assistant (2nd/3rd year resident) holds the EGJ with the aid of a Babcock or later on a Penrose drain encircling the esophagus. The assistant is instructed at the beginning of the operation to place the EGJ either in "position 1" or "position 2" as required. Position 1 exposes the right side of the esophagus pointing the tip of the Babcock at the left inguinal area of the patient. Oppositely, position 2 exposes the left side of the esophagus pointing the tip of the Babcock at the right inguinal area of the patient [Figure 2].

The palpator is active and used for liver retraction [Figure 3], exposure [Figure 4], as an extra hand to allow the surgeon to work by both hands [Figure 5] and as a pointing device to communicate instructions and show anatomic structures [Figure 6]. The palpator may be replaced by other instruments to allow suction [Figure 5] or hold a knot during tying to prevent a slip knot.

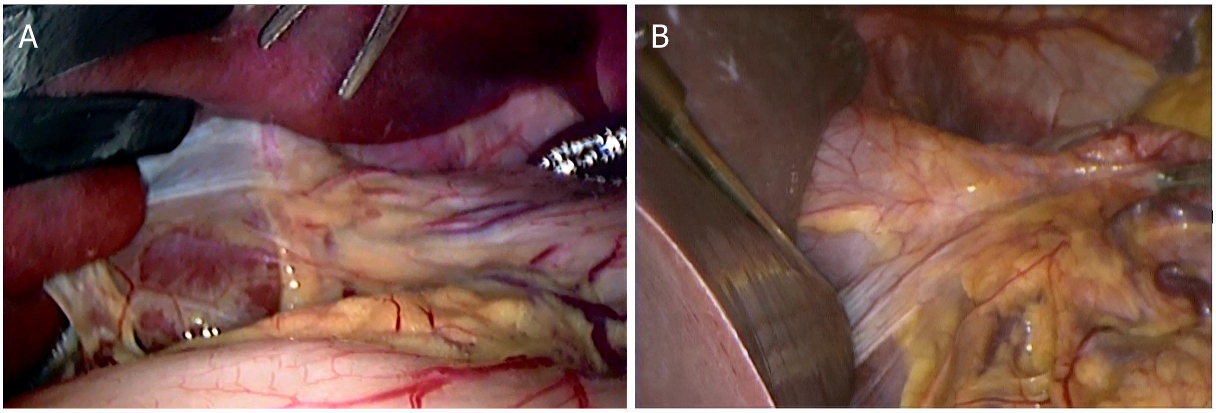


Figure 3. Exposure of the esophagogastric junction and liver retraction with the conventional approach using a liver retractor through a right flank port A and the didactic approach with a palpator through an epigastric port B

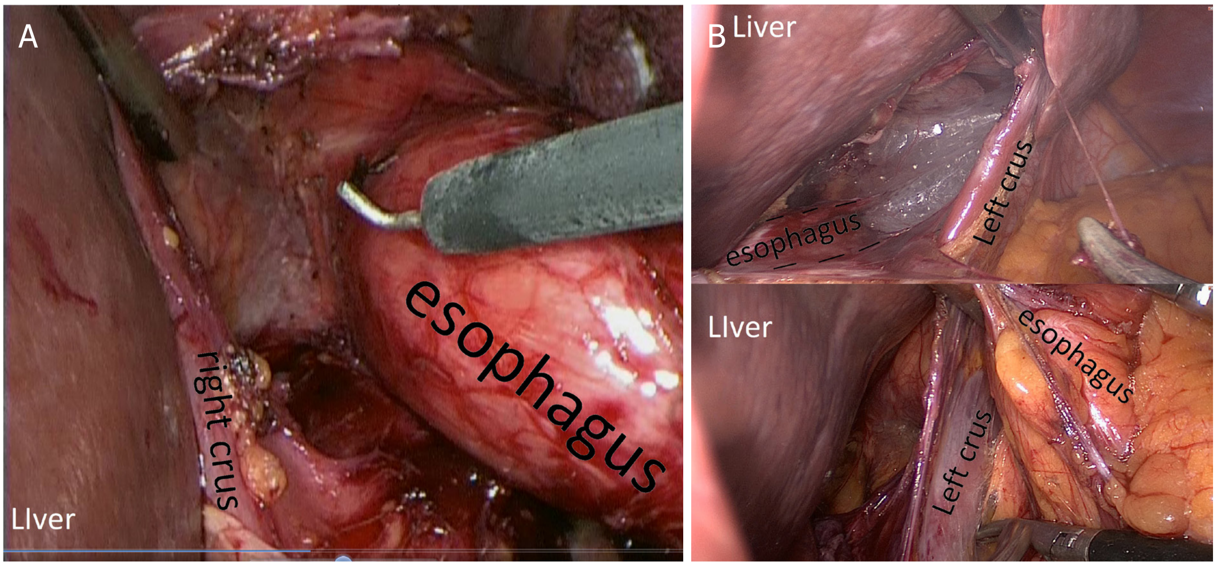


Figure 4. Dissection of the distal esophagus and esophageal hiatus with the aid of a palpator. Retraction of the right A or left crus during dissection B

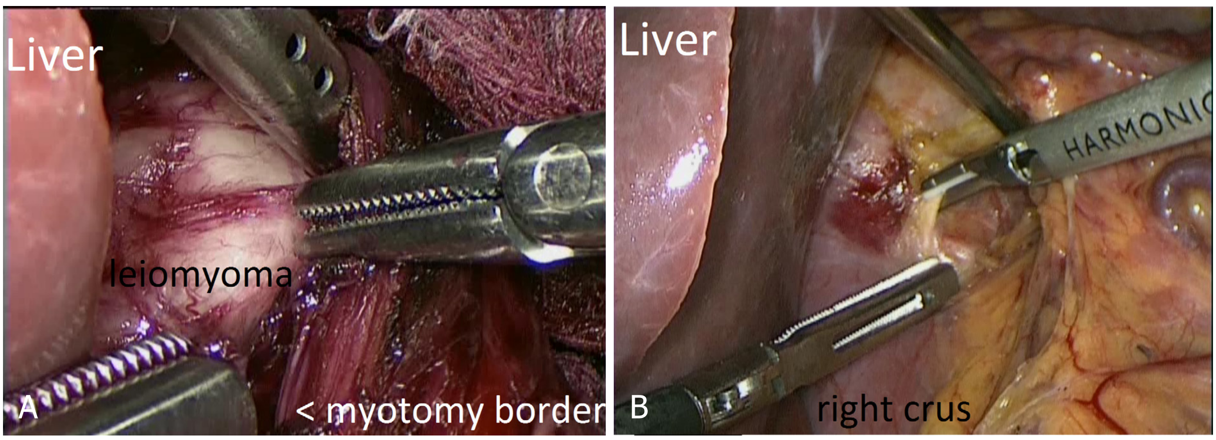


Figure 5. Palpator replaced by a suction/irrigation to help maintain a blood free surgical field and act as a third hand to allow the surgeon to work by both hands during a leiomyoma enucleation A or hiatal hernia repair B

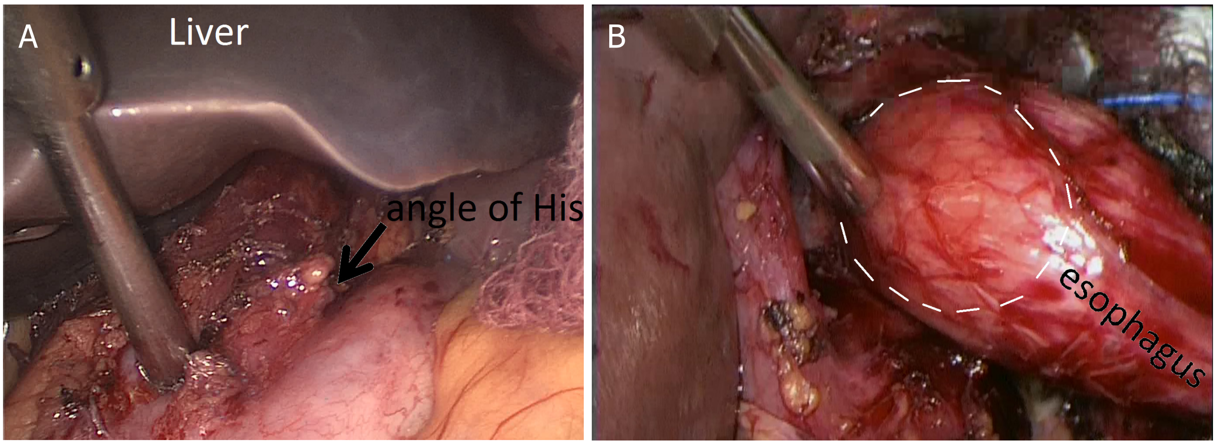


Figure 6. Palpator as a pointing device indicates the lowermost point for a cardiomyotomy A and an the identification of an esophageal leiomyoma (dotted circle) B

The hiatus and the esophagus are initially approached through the right side after opening of the gastrohepatic ligament. The palpator may be used to retract the right arm of the crus or the esophagus, allowing the learning surgeon to have both hands free for dissection. Similarly, the esophagus is dissected from the hiatus circumferentially in a clockwise direction [Figure 4].

CONCLUSION

Operations on the esophagogastric junction in our university are entirely performed by a 4th year resident under direct supervision of a senior attending that acts as the first assistant in this didactic approach. This approach was feasible for all cases of Nissen fundoplication or Heller's myotomy with exposure comparable to the classic approach [Figure 2]. In some cases of large, steatotic livers, the exposure may be cumbersome. In these cases, however, the palpator is kept immobile pushing the left lobe of the liver against the diaphragm above the esophageal hiatus. The advantages of a mobile stick are lost but the operation can be carried on similarly to the classic approach.

We believe this didactic approach is not necessarily carried by a well-trained team. However, it is a minor modification of the standard operation that has advantages on surgical training in academic centers.

DECLARATIONS

Authors' contributions

Made substantial contributions to conception and design of the study and performed data analysis and interpretation: Herbella FAM, Katayama RC

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

Both authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Copyright

REFERENCES

1. Frazzoni M, Piccoli M, Conigliaro R, Frazzoni L, Melotti G. Laparoscopic fundoplication for gastroesophageal reflux disease. World J Gastroenterol 2014;20:14272-9.
2. Herbella FA, Moura EG, Patti MG. Achalasia 2016: treatment alternatives. J Laparoendosc Adv Surg Tech A 2017;27:6-11.
3. Wiesel O, Whang B, Cohen D, Fisichella PM. Minimally invasive esophagectomy for adenocarcinomas of the gastroesophageal junction and distal esophagus: notes on technique. J Laparoendosc Adv Surg Tech A 2017;27:162-9.
4. Nadaleto BF, Herbella FA, Patti MG. Gastroesophageal reflux disease in the obese: pathophysiology and treatment. Surgery 2016;159:475-86.
5. Lopez M, Kalfa N, Forgues D, Guibal MP, Galifer RB, et al. Early laparoscopic Kasai's procedure in a low weight newborn. J Min Access Surg 2007;3:66-9.
6. Tatum RP, Pellegrini CA. How I do it: laparoscopic Heller myotomy with Toupet fundoplication for achalasia. J Gastrointest Surg 2009;13:1120-4.

Mini-invasive Surgery

Review

Open Access

Check for updates

Gastrectomy: the expanding role of minimally invasive surgery in gastric cancer

Jan Willem van den Berg, Hamish Shilton, Edward Cheong

Department of Upper GI Surgery and General Surgery, Norfolk and Norwich University Hospital, Colney lane, Norwich NR4 7UY, United Kingdom.

Correspondence to: Prof. Edward Cheong, Department of Upper GI Surgery and General Surgery, Norfolk and Norwich University Hospital, Colney lane, Norwich NR4 7UY, United Kingdom. E-mail: edward.cheong@nnuh.nhs.uk

How to cite this article: van den Berg JW, Shilton H, Cheong E. Gastrectomy: the expanding role of minimally invasive surgery in gastric cancer. *Mini-invasive Surg* 2019;3:23. http://dx.doi.org/10.20517/2574-1225.2019.07

Received: 27 Feb 2019 **First Decision**: 11 Jun 2019 **Revised**: 4 Jul 2019 **Accepted**: 19 Jul 2019 **Published**: 30 Jul 2019

Science Editor: Tetsu Fukunaga **Copy Editor**: Jia-Jia Meng **Production Editor**: Jing Yu

Abstract

Gastric cancer remains one of the most frequent cancers worldwide. Currently the only potentially curative treatment is surgery, often in combination with perioperative chemotherapy. Gastric cancer surgery is associated with significant morbidity. However, over the last few decades several potential advances have been introduced to improve the treatment for gastric cancer patients. Introduction of laparoscopic gastric cancer surgery has shown promising results and therefore gained popularity worldwide. This review describes an overview of laparoscopic gastrectomy for gastric cancer patients. In general, the introduction of laparoscopic surgery has shown improvement in the short-term outcomes of gastric cancer treatment. Laparoscopic approach for gastric cancer is feasible, safe and should be performed in experienced high volume centres. However, results from randomised trials in advanced gastric cancer are awaited to further determine the effect of a laparoscopic gastrectomy on oncological and long-term outcomes.

Keywords: Gastrectomy, laparoscopy, gastric cancer, laparoscopic gastrectomy, minimal invasive surgery

INTRODUCTION

Gastric cancer remains the fifth most frequent cancer and the third cause of cancer death worldwide[1]. Open gastrectomy (OG) has been the mainstay of curative treatment, however, an open approach is associated with significant morbidity[2]. Therefore, laparoscopic gastrectomy (LG) for gastric cancer treatment has gained popularity in the last few decades, as it potentially results in a better outcome regarding morbidity and survival. In 1994, a laparoscopic distal gastrectomy (LDG) for early gastric cancer was reported for the first time[3]. A few years later, a series of laparoscopic total gastrectomy's (LTG) with D1 and D2 lymph node dissection was published[4]. Since then, experience in laparoscopic surgery has improved with time allowing both distal gastrectomy and total gastrectomy to be performed more frequently worldwide. This report outlines the current state of LG for gastric cancer and its future outlook.

LDG FOR GASTRIC CANCER

Since the report by Kitano *et al.*[3] in 1994, LDG has been investigated intensively, predominately in the Far East. A large Korean case control study which compared both LDG and LTG with OG showed no differences in survival, morbidity and mortality[5]. Several large randomised controlled trials (RCTs) have been performed, mainly in Asia. The Chinese CLASS-01 trial compared LDG with open distal gastrectomy (ODG) for patients with early stage gastric cancer [T2-4 N0-3, M0 (stage 1 gastric cancer)[6]]. Three-year disease-free survival was 76.5% in the laparoscopic group compared with 77.8% in the open group [1-sided 97.5%CI: (-6.5% to ∞)]. In addition, three-year overall survival (OS) rate was 83.1% in patients who underwent a LDG compared with 85.2% in the ODG group (HR 1.19; 95%CI: 0.87-1.64; $P = 0.28$). About 40% of the patients in both treatment groups received adjuvant chemotherapy. The Korean KLASS-01 trial compared LDG with ODG for patients with early stage gastric cancer [T1/2, N0/1, M0 (stage 1 gastric cancer)[7]]. The 5-year OS was 94.2% in the laparoscopic group and 93.3% in the open group ($P = 0.64$). In addition, cancer-specific survival rate was 97.1% in patients who underwent a LDG compared with 97.2% in the ODG group ($P = 0.91$). Earlier, the short-term outcomes of the KLASS-01 trial were published[8]. Patients who underwent a LDG had a reduced overall complication rate (LDG *vs*. ODG; 13.0% *vs*. 19.9%; $P = 0.001$), reduced length of stay (LOS) (LDG *vs*. ODG; 7.1 ± 3.1 *vs*. 7.9 ± 4.1; $P < 0.001$), and a reduced lymph node yield (LDG *vs*. ODG; 40.5 ± 15.3 *vs*. 43.7 ± 15.7; $P < 0.001$). In addition, post-operative mortality was equal. The Japanese JCOG0912, which compares LDG with ODG, only reported their short term outcomes[9]. This study reported that a laparoscopic approach resulted in a longer operation time (LDG *vs*. ODG; median 278 min *vs*. 194 min; $P < 0.001$) and reduced blood loss (LDG *vs*. ODG; median 38 mL *vs*. 115 mL; $P < 0.001$). In addition, no differences were reported in mortality and lymph node yield. These studies show that a laparoscopic approach for early stage gastric cancer is safe and reduces the complication rate. However, we will have to wait for the long-term data to interpret the effect of a laparoscopic approach on long-term oncological outcome.

A meta-analysis has compared LDG with ODG including twenty-five studies in the analysis. They reported that a LDG was associated with longer operative times [weighted mean differences (WMD - 48.3 min; $P < 0.001$)], reduced post-operative complications (OR 0.49; $P = 0.002$), reduced blood loss (WMD - 118.9 mL; $P < 0.001$), as well as reduced LOS (WMD - 3.6 days; $P < 0.001$)[10]. However, patients in the open group had a significant higher lymph node yield (WMD 3.9; $P < 0.001$). The impact of this reduced lymph node yield on oncological and long-term outcome is unknown. The longer operating time for LDG may be because some surgeons are still on the learning curve. Overall these studies demonstrate that short-term outcomes of LDG for patients with gastric cancer are comparable to ODG.

LTG FOR GASTRIC CANCER

The laparoscopic approach for LTG has also gained in popularity worldwide since the first series was reported in 1999[4]. A meta-analysis reviewed the short-term outcomes of LTG compared with OTG in patients with gastric cancer[11]. In eight selected studies, LTG was associated with a significant reduction of intraoperative blood loss (WMD - 227.6 mL; 95%CI: 144.3-310.9; $P < 0.001$), reduced LOS (WMD - 4.0 days; 95%CI: 1.4-6.5; $P < 0.001$) and reduced postoperative complications (RR 0.51; 95%CI: 0.33-0.77). However, a prolonged operation time was seen in patients who underwent a LTG (WMD - 55.5 min; 95%CI: 24.8-86.2;

P < 0.001). In addition, there was no difference in the in-hospital mortality between both groups. A further meta-analysis for LTG was performed which reviewed 10 retrospective cohort studies and 2 case-controlled studies[12]. A laparoscopic approach for gastric cancer resulted in reduced postoperative complications (OR 0.66; *P* = 0.02), reduced blood loss (WMD - 160.70 mL; *P* < 0.00001), as well as reduced LOS (WMD - 2.43 days; *P* = 0.0002). In addition, there was no significant difference in mortality (OR 0.60, *P* = 0.52), lymph node yield (WMD - 2.30; *P* = 0.06), radicality or negative resection margin status. However, again it was observed that a minimally invasive approach resulted in a significantly prolonged operation time (WMD - 48.06 min; *P* < 0.00001).

A case control study which compared laparoscopic with OG (for both distal and total gastrectomy) showed similar results in line with the meta-analysis. A laparoscopic approach resulted in reduced blood loss, reduced LOS, reduced minor complications and a prolonged length of operation time[13]. However, interestingly this study also demonstrated that a laparoscopic approach for gastric cancer resulted in a significant increased likelihood of receiving and completing the course of adjuvant therapy. In the well-known MAGIC trial only 49.5% of the patients who successfully completed neo-adjuvant chemotherapy and surgery also completed 3 cycles of adjuvant chemotherapy[14]. As adjuvant treatment is critically important for patients with (advanced) gastric cancer this may demonstrate an important benefit of a laparoscopic approach. A propensity scored matched analysis compared LG to OG during the introduction of LG in the Netherlands[15]. Analyses in 884 patients showed less wound complications (2% *vs*. 5%, *P* = 0.006) and less chyle leakage (1% *vs*. 4%, *P* = 0.004) in patients who underwent LG. However, there was no difference in overall postoperative morbidity or anastomotic leakage.

Overall these studies show that LTG is feasible and safe. Further research in the form of RCTs are warranted to confirm short term morbidity and quality of resection, but in particular provide the best data to evaluate the long-term oncological outcomes. So far, most of the studies are conducted in the Far East. A RCT which compares LTG gastrectomy with OTG is currently ongoing[16]. The primary endpoint of this study is to evaluate the effect of surgical approach on morbidity and mortality in patients with T1/2, N0/1, M0 (stage 1) gastric cancer. More recently, a Korean RCT comparing open with LTG for advanced gastric cancer has started (KLASS-06). However, results from the Far East cannot be easily translated to the Western population. This is mainly due to the different population and body mass index, a less advanced stage of gastric cancer in Asia, and a much lower utilization of (neo)-adjuvant chemotherapy. In Europe two RCTs are ongoing, the STOMACH trial and the LOGICA trial[17,18]. Both multicentre randomised trials study the effect of LG with OG in patients with more advanced gastric cancer (T1-3, N0-1, M0) in the Western population. Patients included in these studies predominantly received neoadjuvant chemotherapy. Primary endpoints in these trials are the quality of the oncologic resection and postoperative complications. Recently, preliminary results of these two trials were presented at the International Gastric Cancer Congress 2019. Laparoscopic and OG resulted in comparable oncological outcomes, and comparable morbidity and mortality. Overall, final results of these studies will provide more information on which surgical technique is optimal for treatment of resectable gastric cancer.

COMPLICATIONS FOLLOWING LG

Gastric cancer surgery is associated with high morbidity. One of the benefits of a laparoscopic approach is reducing morbidity. A propensity matched analysis assessed complications in 4124 patients who underwent a LG or OG, of whom 627 patients developed complications[19]. No significant differences were found in overall complications (14.2% *vs*. 16.5 %; *P* = 0.093). However, hospital mortality was reduced in the LG group (0.3% *vs*. 1.2%; *P* = 0.004) as was failure to rescue rates (2.1% *vs*. 7.6%; *P* = 0.008). Multivariate analysis showed that older age, tumour location, TNM stage, extent of gastric resection, operative time and operative blood loss were adverse risk factors for complications. They concluded that whilst overall complications were similar, patients were more likely to die when they experienced complications following OG.

A systematic review of 16 non-RCTs of anastomotic complications following LTG *vs*. OTG did not find any statistical difference in the incidence of anastomotic leakage, 3.0% *vs*. 2.1% respectively (OR 1.42, 95%CI: 0.86-2.33; $P = 0.17$)[20]. The incidence of anastomotic stenosis was also not significantly different between groups, 3.2% *vs*. 2.7% following LTG and OTG respectively (OR 1.55, 95%CI: 0.94-2.54; $P = 0.08$). When the LTG was classified into six categories for the various anastomotic techniques, review of the case studies demonstrated a similar anastomotic leak rate (1.1%-3.2%), however the incidence of stenosis was relatively high when the OrVil™ device was used (8.8%) compared with other procedures (1.0%-3.6%).

LONG TERM ONCOLOGICAL OUTCOMES AND MORBIDITY

So far, there are no publications of randomised control trials comparing LG with OG which report long term survival data. However, long term survival has been assessed in a meta-analysis looking at 5-year results, for OS, recurrence or gastric cancer related death[21]. In this analysis, 23 studies with a total of 7336 patients who underwent a distal or total gastrectomy were included. Excluding the studies that didn't have well balanced groups, they reported no differences between LG and OG as 5-year OS (OR 1.07, 95%CI: 0.90-1.28; $P = 0.45$), recurrence (OR 0.83, 95%CI: 0.68-1.02; $P = 0.08$), and gastric cancer-related death (OR 0.86, 95%CI: 0.65-1.13; $P = 0.28$) rates were similar. They conclude that long term results of LG are comparable to open surgery for both early and advanced gastric cancer.

Large propensity matched cohort studies have been performed to assess the long-term outcomes between OG and LG for advanced gastric cancer to achieve an immediate assessment whilst we await the results of RCTs. Li *et al*.[22] matched 459 and 856 patients undergoing laparoscopic or OG (both distal and total) respectively for advanced gastric cancer with D2 lymph node resection. No significant difference was identified in the 5-year OS (52.0% and 53.4%; $P = 0.805$) and disease-free survival (46.8% *vs*. 47.3%; $P = 0.963$) between the laparoscopic and open groups. Stratified assessment also did not identify any differences according to tumour stage. The operation method was not an independent prognostic factor for OS or disease-free survival. In addition, the recurrence pattern was similar between the laparoscopic and OG groups.

Another propensity matched cohort study, the LOC-A study, matched 610 cases with advanced gastric cancer (stage 2/3) who underwent a laparoscopic or open distal, proximal or total gastrectomy[23]. No significant differences in 5-year survival or recurrence was found. Five-year survival for OG was 53.0% compared to 54.2% following LG. In addition, the recurrence rate was 30.8% and 29.8% respectively. High risk patients have also been assessed in a further propensity matched cohort study comparing LG with OG[24]. The patients underwent a distal or total gastrectomy. High risk patients were deemed to have at least one of: age > 80 years, BMI > 30 kg/m^2, ASA grade ≥ 3, or clinical T stage 4. After matching, each group had 341 patients with no difference in clinico-pathological data between the open and laparoscopic groups. Operating time (181.70 min *vs*. 266.71 min; $P < 0.001$) and blood loss (68.11 mL *vs*. 225.54 mL; $P < 0.001$) were significantly lower in the LG group, whilst postoperative complications occurred in 11.4% and 18.5%, in the LG and OG group respectively ($P = 0.010$). Therefore, laparoscopic surgery was a significant protective factor against post-operative complications ($P = 0.019$). In addition, the number of risk factors present was an independent risk factor for post-operative complications ($P = 0.021$). Again, the 5-year OS rate was similar between the LG and OG groups (55.0% *vs*. 52.0%; $P = 0.086$).

ENHANCED RECOVERY AFTER SURGERY

Enhanced recovery after surgery (ERAS) program has been described for the first time in the nineties[25]. Since then, the success of programs has been described in various fields of surgery, including both open and laparoscopic techniques in the specialty of Gastro-Oesophageal surgery[26,27]. A recent meta-analysis described the results of ERAS in LG patients[28]. In this analysis of six studies, with predominantly patients who underwent a LDG, ERAS resulted in shorter LOS (WMD - 2.65; $P < 0.01$) and less hospitalisation expenditure (WMD - 523.43; $P < 0.01$). However, no significant difference was found regarding complication rate. This meta-analysis shows that ERAS can be applied to laparoscopic gastric surgery. However, large sample RCT's should be conducted to fully show the effect of an ERAS program in LG patients.

LEARNING CURVE

A LTG remains a challenging surgical procedure with substantial technical difficulties, such as the extended lymph node dissection and the anastomoses of the oesophagus to the jejunum. Limited studies have addressed the learning curve for LTG. A Korean study described that the learning curve for LTG is approximately 100 cases[29]. Earlier, another Korean study described using the cumulative sum technique showed that postoperative morbidity reached a plateau after around 45 cases[30]. In addition, for LDG a learning curve of 20 to 40 cases has been reported[31]. Overall, these studies show that a lengthy learning curve will be required to achieve acceptable morbidity. In addition, the learning curve for LTG in the Western countries may differ as in general this includes patients with more advanced gastric cancer as well as higher BMI.

CENTRALISATION

Worldwide centralisation for the care for gastric cancer patients is increasing. In the Netherlands it has been imposed since 2012. A recent analysis on the outcomes from this process has shown an increase in the utilisation of laparoscopic surgery for gastric cancer from 6% to 40% ($P < 0.01$)[32]. Whilst the volume of laparoscopic surgery has increased, adequate lymphadenectomy has improved from 21% to 93% ($P < 0.01$). Other benefits included decreased median LOS (8 days *vs.* 10 days; $P < 0.01$), and greater utilisation of perioperative chemotherapy (25% *vs.* 42%; $P < 0.01$). They reported no significant change in 30-day mortality (4.2% *vs.* 1.9%; $P = 0.17$), 1 year overall (78% *vs.* 80%; $P = 0.17$) and disease-free survival (73% *vs.* 74%; $P = 0.66$). This demonstrates that in western countries, centralisation of gastric cancer results in better rates of laparoscopic resection, improved short term outcomes without impacting on postoperative mortality and intermediate-term survival.

TECHNICAL ASPECTS OF LG

Anastomoses technique

LTG is technically difficult. The main concerns are the anastomoses technique and oncological safety. Currently there is no standardised method for the esophago-jejunostomy, and many different techniques have been described. A retrospective study in 687 patients who underwent a LTG compared oesophago-jejunostomy using a linear stapler with a circular stapler[33]. Complication rates were similar between the two groups, however the linear stapler resulted in a shorter operation time (149 min *vs.* 170 min, $P < 0.001$) as well as shorter length of hospital stay. Therefore, concluded was that a linear stapler technique for an oesophago-jejunostomy is a feasible procedure. A retrospective study compared a circular stapler (OrVil™) esophago-jejunostomy with an overlap esophago-jejunostomy using a linear stapler[34]. The rate of anastomotic anastomotic leakage was lower in the linear stapler group compared with the OrVil™ group (0.7% *vs.* 4.1%) although this was not significant. In addition, the rate of anastomotic stenosis was significantly lower in the linear stapler group compared with the OrVil™ group (0.0% *vs.* 4.1%, $P = 0.017$). However, there are no RCT's comparing the optimal anastomoses technique in patients undergoing LTG.

Extent of lymph node dissection

Numerous studies have reported the impact of lymph node dissection on survival in gastric cancer surgery. Fifteen year follow up of a Dutch trial comparing a limited lymph node dissection (D1) with an extended lymph node dissection (D2) reported that D2 lymphadenectomy is associated with lower locoregional recurrence (D1; 22% *vs*. D2; 12%) and significantly reduced gastric-cancer related deaths (D1; 48% *vs*. D2; 37%)[35]. A systematic review of RCTs comparing different types of lymph node dissection in patients with gastric cancer was reported[36]. In this review no significant difference in OS was seen after D1 lymphadenectomy compared with D2 lymphadenectomy (n = 5; HR 0.91, 95%CI: 0.71 to 1.17). In contrast, D2 lymphadenectomy was related to a significantly improved disease specific survival compared to D1 lymphadenectomy (HR 0.81, 95%CI: 0.71-0.92). However, the D2 lymphadenectomy was associated with a higher postoperative mortality rate (RR 2.02, 95%CI: 1.34-3.04). The high post-operative morbidity and mortality following D2 dissection in this study was attributed to performing a splenectomy. Therefore, a spleen-preserving D2 lymphadenectomy is the recommend surgical approach for resectable advanced gastric cancer.

In a meta-analysis comparing open with LG, 11 of 12 studies described lymph node resection, with no significant differences between OTG and LTG groups[12]. Eight of the studies individually favoured open resection for lymph node resection. Only three studies reported resection margin status, with no difference in proximal, distal or circumferential margin R0 resection status. Overall, lymph node yield was equal after both methods of gastric surgery. The recently published long-term results of the CLASS-01 trial showed a mean retrieval of lymph nodes of 36 in the laparoscopic group compared with 37 in the open group[6]. Overall, these numbers are higher compared with the number of lymph nodes retrieved in the West. Therefore, the results of ongoing RCTs in Europe are needed to establish the optimal surgical approach in patients with gastric cancer in Western countries.

Omentectomy

A Dutch prospective trial studied the presence of metastases in the greater omentum in patients undergoing a (sub) total gastrectomy with omentectomy and D2 lymphadenectomy for gastric cancer[37]. Five percent of the patients had metastases in the greater omentum, however all these patients also had a positive proximal or distal resection margin (R1 resection). In addition, another Dutch prospective trial demonstrated that omental lymph node metastases or tumour deposits are present in 10% of the patients[38]. Worldwide there is no consensus on whether to perform an omentectomy or not for gastric cancer surgery. RCTs are warranted to investigate the effect of omentectomy on long-term survival. Traditionally, an omentectomy has been considered the standard approach to gastrectomy for gastric cancer patients. Due to possible presence of omental lymph node metastases and difficulty in predicting presence of these nodes, omentectomy should be performed as standard, unless proven otherwise by randomised trials.

Bursectomy

In eastern Asia, a bursectomy has been performed to remove the peritoneum covering the pancreas and the anterior plane of the transverse mesocolon. Two Japanese RCTs compared bursectomy with omentectomy for patients with resectable gastric cancer. First, Hirao *et al*.[39] reported in patients with cT2-3 gastric adenocarcinoma and D2 gastrectomy a 5-year survival of 77.5% in patients who underwent a bursectomy compared with 71.3% in patients without bursectomy (P = 0.16). However, multivariate analysis that bursectomy was an independent prognostic factor of good OS (P = 0.033). More recently, Kurokawa *et al*.[40] reported no survival advantage for bursectomy combined with omentectomy over omentectomy alone. Five-year OS was 76.7% in the non-bursectomy group and 76.9% in the bursectomy group (HR 1.05, 95%CI: 0.81-1.37; P = 0.65). In addition, a recent meta-analysis reported that a bursectomy for advanced gastric cancer has no positive influence on the number of harvested lymph nodes (WMD 5.86; P = 0.157) or on the OS (HR 0.95; P = 0.647)[41]. A study describing patients who underwent a LTG with complete bursectomy showed that this technique is feasible and safe in experienced hands[42].

Jejunal pouch

The most common reconstruction technique after a total gastrectomy is the oesophago-jejunostomy Roux-en-Y reconstruction. However, this technique is associated with complaints like reflux, weight loss, and dumping syndrome[43]. One of the techniques performed to potentially improve long-term outcome is the formation of a jejunal pouch[44]. A recent meta-analysis which includes 25 studies comparing reconstruction with or without a pouch, mainly in patients who underwent open surgery, showed a reduction of the risk of dumping syndrome[45], reduced heartburn and oesophagitis, as well as a significantly higher body mass index (22.2 kg/m^2 *vs*. 20.9 kg/m^2; WMD 1.28; 95%CI: 0.61-1.94). However, minimal reports of jejunal pouch reconstruction in a laparoscopic approach have been published so far[46].

NOVEL TECHNIQUES

Robotic gastrectomy

Robotic surgery for gastric cancer remains experimental and controversial, in part due to the lack of RCTs. However, several Western and Asian centres have reported their series of robotic surgery in gastric cancer patients. A meta-analysis comparing LG to robotic gastrectomy included three non-randomised controlled studies[47]. Robotic gastrectomy was associated with a longer operation time but reduced intra-operative blood loss. No differences were found in lymph node yield, morbidity, mortality, and LOS. The authors therefore concluded that a robotic approach is safe and feasible, however, that further research is warranted to investigate the effect on long-term oncological outcomes. More recently, a meta-analysis which included 19 studies comparing LG with robotic gastrectomy again showed that robotic gastrectomy was associated with a prolonged operation time (WMD - 49.05 min; $P < 0.01$)[48]. In addition, reduced intraoperative blood loss (WMD - 24.38 mL; $P < 0.01$) as well as higher costs were observed (WMD - 3944.8 USD; $P < 0.01$). Again, there were no differences in morbidity, mortality, LOS, and lymph node yield. In general, robotic gastrectomy is as safe as LG. However, as the robotic approach is associated with longer operation times and higher costs, without any significant advantages over LG, the laparoscopic approach for gastric cancer is generally preferred.

CONCLUSION

Minimally invasive gastrectomy is feasible and safe in eastern and western countries. It has benefits for both early and advanced gastric cancer, as well as total and subtotal gastrectomy. The increasing worldwide trend for centralisation of gastric cancer treatment facilitates the use of a laparoscopic approach. These both aspects will increase treatment with neo-adjuvant and adjuvant chemotherapy, whilst LG also improves tolerance of adjuvant chemotherapy. Short term benefits include less blood loss, decreased LOS and lower postoperative morbidity and mortality. Quality of surgery markers such as lymph node yield and resection margin status appear to be comparable to open surgery. Long term survival data available currently indicate overall and disease-free survival is not inferior to open surgery, however the results from ongoing RCTs are awaited.

DECLARATIONS

Authors' contributions

All authors had equal contribution in the writing process of this article.

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Copyright

REFERENCES

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015;136:E359-86.
2. Memon MA, Subramanya MS, Khan S, Hossain MB, Osland E,et al. Meta-analysis of D1 versus D2 gastrectomy for gastric adenocarcinoma. Ann Surg 2011;253:900-11.
3. Kitano S, Iso Y, Moriyama M, Sugimachi K. Laparoscopy-assisted Billroth I gastrectomy. Surg Laparosc Endosc 1994;4:146-8.
4. Azagra JS, Goergen M, De Simone P, Ibanez-Aguirre J. Minimally invasive surgery for gastric cancer. Surg Endosc 1999;13:351-7.
5. Kim HH, Han SU, Kim MC, Hyung WJ, Kim W, et al. Long-term results of laparoscopic gastrectomy for gastric cancer: a large-scale case-control and case-matched Korean multicenter study. J Clin Oncol 2014;32:627-33.
6. Yu J, Huang C, Sun Y, Su X, Cao H, et al. Effect of Laparoscopic vs Open Distal Gastrectomy on 3-Year Disease-Free Survival in Patients With Locally Advanced Gastric Cancer: The CLASS-01 Randomized Clinical Trial. Jama 2019;321:1983-92.
7. Kim HH, Han SU, Kim MC, Kim W, Lee HJ, et al. Effect of Laparoscopic Distal Gastrectomy vs Open Distal Gastrectomy on Long-term Survival Among Patients With Stage 1 Gastric Cancer: The KLASS-01 Randomized Clinical Trial. JAMA Oncol 2019;5:505-513.
8. Kim W, Kim HH, Han SU, Kim MC, Hyung WJ, et al. Decreased Morbidity of Laparoscopic Distal Gastrectomy Compared With Open Distal Gastrectomy for Stage I Gastric Cancer: Short-term Outcomes From a Multicenter Randomized Controlled Trial (KLASS-01). Ann Surg 2016;263:28-35.
9. Katai H, Mizusawa J, Katayama H, Takagi M, Yoshikawa T, et al. Short-term surgical outcomes from a phase III study of laparoscopy-assisted versus open distal gastrectomy with nodal dissection for clinical stage IA/IB gastric cancer: Japan Clinical Oncology Group Study JCOG0912. Gastric Cancer 2017;20:699-708.
10. Vinuela EF, Gonen M, Brennan MF, Coit DG, Strong VE. Laparoscopic versus open distal gastrectomy for gastric cancer: a meta-analysis of randomized controlled trials and high-quality nonrandomized studies. Ann Surg 2012;255:446-56.
11. Haverkamp L, Weijs TJ, van der Sluis PC, van der Tweel I, Ruurda JP, et al. Laparoscopic total gastrectomy versus open total gastrectomy for cancer: a systematic review and meta-analysis. Surg Endosc 2013;27:1509-20.
12. Straatman J, van der Wielen N, Cuesta MA, de Lange-de Klerk ES, Jansma EP, et al. Minimally Invasive Versus Open Total Gastrectomy for Gastric Cancer: A Systematic Review and Meta-analysis of Short-Term Outcomes and Completeness of Resection : Surgical Techniques in Gastric Cancer. World J Surg 2016;40:148-57.
13. Kelly KJ, Selby L, Chou JF, Dukleska K, Capanu M, et al. Laparoscopic Versus Open Gastrectomy for Gastric Adenocarcinoma in the West: A Case-Control Study. Ann Surg Oncol 2015;22:3590-6.
14. Cunningham D, Allum WH, Stenning SP, Thompson JN, Van de Velde CJ, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med 2006;355:11-20.
15. Brenkman HJF, Gisbertz SS, Slaman AE, Goense L, Ruurda JP, et al. Postoperative Outcomes of Minimally Invasive Gastrectomy Versus Open Gastrectomy During the Early Introduction of Minimally Invasive Gastrectomy in the Netherlands: A Population-based Cohort Study. Ann Surg 2017;266:831-8.
16. He H, Li H, Su X, Li Z, Yu P, et al. Study on safety of laparoscopic total gastrectomy for clinical stage I gastric cancer: the protocol of the CLASS02-01 multicenter randomized controlled clinical trial. BMC Cancer 2018;18:944.
17. Haverkamp L, Brenkman HJ, Seesing MF, Gisbertz SS, van Berge Henegouwen MI, et al. Laparoscopic versus open gastrectomy for gastric cancer, a multicenter prospectively randomized controlled trial (LOGICA-trial). BMC Cancer 2015;15:556.
18. Straatman J, van der Wielen N, Cuesta MA, Gisbertz SS, Hartemink KJ, et al. Surgical techniques, open versus minimally invasive gastrectomy after chemotherapy (STOMACH trial): study protocol for a randomized controlled trial. Trials 2015;16:123.
19. Tu RH, Lin JX, Zheng CH, Li P, Xie JW, et al. Complications and failure to rescue following laparoscopic or open gastrectomy for gastric cancer: a propensity-matched analysis. Surg Endosc 2017;31:2325-37.
20. Inokuchi M, Otsuki S, Fujimori Y, Sato Y, Nakagawa M, et al. Systematic review of anastomotic complications of esophagojejunostomy after laparoscopic total gastrectomy. World J Gastroenterol 2015;21:9656-65.
21. Chen XZ, Wen L, Rui YY, Liu CX, Zhao QC, et al. Long-term survival outcomes of laparoscopic versus open gastrectomy for gastric

cancer: a systematic review and meta-analysis. Medicine (Baltimore) 2015;94:e454.
22. Li Z, Li B, Bai B, Yu P, Lian B, et al. Long-term outcomes of laparoscopic versus open D2 gastrectomy for advanced gastric cancer. Surg Oncol 2018;27:441-8.
23. Kinoshita T, Uyama I, Terashima M, Noshiro H, Nagai E, et al. Long-term Outcomes of Laparoscopic Versus Open Surgery for Clinical Stage II/III Gastric Cancer: A Multicenter Cohort Study in Japan (LOC-A Study). Ann Surg 2019;269:887-94.
24. Xu BB, Lu J, Zheng ZF, Huang CM, Zheng CH, et al. Comparison of short-term and long-term efficacy of laparoscopic and open gastrectomy in high-risk patients with gastric cancer: a propensity score-matching analysis. Surg Endosc 2019;33:58-70.
25. Bardram L, Funch-Jensen P, Jensen P, Crawford ME, Kehlet H. Recovery after laparoscopic colonic surgery with epidural analgesia, and early oral nutrition and mobilisation. Lancet 1995;345:763-4.
26. Preston SR, Markar SR, Baker CR, Soon Y, Singh S, et al. Impact of a multidisciplinary standardized clinical pathway on perioperative outcomes in patients with oesophageal cancer. Br J Surg 2013;100:105-12.
27. Kang SH, Lee Y, Min SH, Park YS, Ahn SH, et al. Multimodal Enhanced Recovery After Surgery (ERAS) Program is the Optimal Perioperative Care in Patients Undergoing Totally Laparoscopic Distal Gastrectomy for Gastric Cancer: A Prospective, Randomized, Clinical Trial. Ann Surg Oncol 2018;25:3231-8.
28. Li MZ, Wu WH, Li L, Zhou XF, Zhu HL, et al. Is ERAS effective and safe in laparoscopic gastrectomy for gastric carcinoma? A meta-analysis. World J Surg Oncol 2018;16:17.
29. Jung DH, Son SY, Park YS, Shin DJ, Ahn HS, et al. The learning curve associated with laparoscopic total gastrectomy. Gastric Cancer 2016;19:264-72.
30. Jeong O, Ryu SY, Choi WY, Piao Z, Park YK. Risk factors and learning curve associated with postoperative morbidity of laparoscopic total gastrectomy for gastric carcinoma. Ann Surg Oncol 2014;21:2994-3001.
31. Kim HG, Park JH, Jeong SH, Lee YJ, Ha WS, et al. Totally laparoscopic distal gastrectomy after learning curve completion: comparison with laparoscopy-assisted distal gastrectomy. J Gastric Cancer 2013;13:26-33.
32. Nelen SD, Heuthorst L, Verhoeven RHA, Polat F, Kruyt PM, et al. Impact of Centralizing Gastric Cancer Surgery on Treatment, Morbidity, and Mortality.J Gastrointest Surg 2017;21:2000-8.
33. Gong CS, Kim BS, Kim HS. Comparison of totally laparoscopic total gastrectomy using an endoscopic linear stapler with laparoscopic-assisted total gastrectomy using a circular stapler in patients with gastric cancer: A single-center experience. World J Gastroenterol 2017;23:8553-61.
34. Kawamura H, Ohno Y, Ichikawa N, Yoshida T, Homma S, et al. Anastomotic complications after laparoscopic total gastrectomy with esophagojejunostomy constructed by circular stapler (OrVil()) versus linear stapler (overlap method). Surg Endosc 2017;31:5175-82.
35. Songun I, Putter H, Kranenbarg EM, Sasako M, van de Velde CJ. Surgical treatment of gastric cancer: 15-year follow-up results of the randomised nationwide Dutch D1D2 trial. Lancet Oncol 2010;11:439-49.
36. Mocellin S, McCulloch P, Kazi H, Gama-Rodrigues JJ, Yuan Y, et al. Extent of lymph node dissection for adenocarcinoma of the stomach. Cochrane Database Syst Rev 2015:CD001964.
37. Jongerius EJ, Boerma D, Seldenrijk KA, Meijer SL, Scheepers JJ, et al. Role of omentectomy as part of radical surgery for gastric cancer. Br J Surg 2016;103:1497-503.
38. Haverkamp L, Brenkman HJ, Ruurda JP, Ten Kate FJ, van Hillegersberg R. The Oncological Value of Omentectomy in Gastrectomy for Cancer. J Gastrointest Surg 2016;20:885-90.
39. Hirao M, Kurokawa Y, Fujita J, Imamura H, Fujiwara Y, et al. Long-term outcomes after prophylactic bursectomy in patients with resectable gastric cancer: Final analysis of a multicenter randomized controlled trial. Surgery 2015;157:1099-105.
40. Kurokawa Y, Doki Y, Mizusawa J, Terashima M, Katai H, et al. Bursectomy versus omentectomy alone for resectable gastric cancer (JCOG1001): a phase 3, open-label, randomised controlled trial. Lancet Gastroenterol Hepatol 2018;3:460-8.
41. Nie RC, Yuan SQ, Chen S, Yan SM, Chen YM, et al. Bursectomy for advanced gastric cancer: an update meta-analysis. World J Surg Oncol 2018;16:66.
42. Zou L, Xiong W, Mo D, Chen G, He Y, et al. Totally laparoscopic complete bursectomy and D2 lymphadenectomy in radical total gastrectomy: an outside bursa omentalis approach. Surg Endosc 2016;30:4152.
43. Liedman B. Symptoms after total gastrectomy on food intake, body composition, bone metabolism, and quality of life in gastric cancer patients--is reconstruction with a reservoir worthwhile? Nutrition 1999;15:677-82.
44. Lehnert T, Buhl K. Techniques of reconstruction after total gastrectomy for cancer. Br J Surg 2004;91:528-39.
45. Syn NL, Wee I, Shabbir A, Kim G, So JB. Pouch Versus No Pouch Following Total gastrectomy: Meta-analysis of Randomized and Non-randomized Studies. Ann Surg 2019;269:1041-53.
46. Brenkman HJ, Correa-Cote J, Ruurda JP, van Hillegersberg R. A Step-Wise Approach to Total Laparoscopic Gastrectomy with Jejunal Pouch Reconstruction: How and Why We Do It. J Gastrointest Surg 2016;20:1908-15.
47. Xiong B, Ma L, Zhang C. Robotic versus laparoscopic gastrectomy for gastric cancer: a meta-analysis of short outcomes. Surg Oncol 2012;21:274-80.
48. Chen K, Pan Y, Zhang B, Maher H, Wang XF, et al. Robotic versus laparoscopic Gastrectomy for gastric cancer: a systematic review and updated meta-analysis. BMC Surg 2017;17:93.

Mini-invasive Surgery

Perspective

Open Access

Minimally invasive surgery for non-achalasia primary esophageal motility disorders is currently underused

Fernando A. M. Herbella[1], Francisco Schlottmann[2]

[1]Department of Surgery, Federal University of Sao Paulo, Sao Paulo, SP 04037-003, Brazil.
[2]Department of Surgery, Hospital Alemán of Buenos Aires, Buenos Aires C1118 AAT, Argentina.

Correspondence to: Dr. Fernando A. M. Herbella, Department of Surgery, Escola Paulista de Medicina, Federal University of Sao Paulo, Rua Diogo de Faria 1087 cj 301, Sao Paulo, SP 04037-003, Brazil. E-mail: herbella.dcir@epm.br

How to cite this article: Herbella FAM, Schlottmann F. Minimally invasive surgery for non-achalasia primary esophageal motility disorders is currently underused. *Mini-invasive Surg* 2019;3:24. http://dx.doi.org/10.20517/2574-1225.2019.20

Received: 2 Jul 2019 **Accepted:** 16 Jul 2019 **Published:** 12 Aug 2019

Science Editor: Giulio Belli **Copy Editor:** Cai-Hong Wang **Production Editor:** Tian Zhang

Abstract
Surgical treatment for non-achalasia primary esophageal motility disorders is reserved for few situations. Proper selection of patients brings good outcomes with low morbidity, which makes surgical therapy an adequate therapeutic option. High resolution manometry reclassifies esophageal motility disorders. Interestingly, literature is scarce on surgical therapy for this new classification with per oral endoscopic myotomy as the leading treatment.

Keywords: Esophageal manometry, motility disorders, distal esophageal spasm, jackhammer esophagus

High resolution manometry reclassifies esophageal motility disorders based on the Chicago 3.0 classification[1]. Even though there is a certain correspondence between previous and current classifications[2], a distinct nomenclature arrived based on newly developed - and putatively more objective and accurate - parameters. Thus, primary esophageal motility disorders (PEMD) are probably better diagnosed and evaluated.

Achalasia is surely the most understood PEMD. Other PEMD are not as well comprehended nor have defined therapy options. These other diseases defined by specific manometric pictures may occur as PEMD or secondary to gastroesophageal reflux disease (GERD)[3]. If GERD is present, the motility abnormality is considered secondary, and treatment is directed toward reflux. In the absence of GERD, therapy is aimed at the modulation of the esophageal dysmotility with pharmacological agents or at the permeabilization of the gastroesophageal junction with endoscopic or surgical procedures[4].

Surgical treatment for non-achalasia PEMD was reserved for few situations during the conventional manometry era. Cardiomyotomy (Heller's operation) and fundoplication are used for patients with hypertensive lower esophageal sphincter, diffuse esophageal spasm or nutcracker esophagus and obstructive symptoms[5,6]. Proper selection of patients is linked to good outcomes with low morbidity, which makes surgical therapy an adequate therapeutic option. Interestingly, literature is scarce on surgical therapy for this new classification with per oral endoscopic myotomy (POEM) as the leading treatment.

Ineffective esophageal motility is not treated by surgery. Hypertensive lower esophageal sphincter is no longer a PEMD according to Chicago 3.0.

There are no studies on Heller's myotomy for distal esophageal spasm (previously diffuse spasm) based on the new classification. Some case reports of POEM for distal spasm have been reported[7-9] with multicenter studies encompassing a larger number of patients but always inferior to 20 in total[10]. Experience with the method is too short to draw conclusions. The same is true for jackhammer esophagus: no studies on Heller's myotomy and few case reports for POEM[9,11]. A recent systematic review compiling these small series[12] showed a clinical success of 90%.

Esophagogastric junction outflow obstruction is an altered motility pattern contemplated by Chicago 3.0 classification. Most cases are associated to mechanical obstruction especially after operations in the area. Few cases are considered PEMD[13]. Interestingly, some cases treated by Heller's myotomy[13-15] showed good outcomes while POEM did not show good results[16].

In conclusion, Heller's myotomy and fundoplication are currently underused for the treatment of non-achalasia PEMD. POEM is the preferred treatment, but long-term results with larger series are still elusive.

DECLARATIONS

Authors' contributions
Made substantial contributions to conception and design of the study and performed data analysis and interpretation: Herbella FAM, Schlottmann F

Availability of data and materials
Not applicable.

Financial support and sponsorship
None.

Conflicts of interest
All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

REFERENCES

1. Kahrilas PJ, Bredenoord AJ, Fox M, Gyawali CP, Roman S, et al. The Chicago Classification of esophageal motility disorders, v3.0. Neurogastroenterol Motil 2015;27:160-74.
2. Schlottmann F, Herbella FA, Patti MG. Understanding the Chicago classification: from tracings to patients. J Neurogastroenterol Motil 2017;23:487-94.
3. Herbella FA, Raz DJ, Nipomnick I, Patti MG. Primary versus secondary esophageal motility disorders: diagnosis and implications for treatment. J Laparoendosc Adv Surg Tech A 2009;19:195-8.
4. Patti MG, Herbella FA. Achalasia and other esophageal motility disorders. J Gastrointest Surg 2011;15:703-7.
5. Herbella FA, Tineli AC, Wilson JL Jr, Del Grande JC. Surgical treatment of primary esophageal motility disorders. J Gastrointest Surg 2008;12:604-8.
6. Schlottmann F, Shaheen NJ, Madanick RD, Patti MG. The role of Heller myotomy and POEM for nonachalasia motility disorders. Dis Esophagus 2017;30:1-5.
7. Albers D, Frieling T, Dakkak D, Kuhlbusch-Zicklam R, Töx U, et al. Peroral endoscopic myotomy (POEM) is effective in treatment of noncardiac chest pain caused by hypercontractile esophageal motility disorders: results of the POEM-HYPE-Study. Z Gastroenterol 2018;56:1337-42.
8. Orlandini B, Barret M, Guillaumot MA, Léandri C, Leblanc S, et al. Per-oral endoscopic myotomy for esophageal diverticula with or without esophageal motility disorders. Clin Res Hepatol Gastroenterol. 2019; doi: 10.1016/j.clinre.2019.03.013.
9. Sugihara Y, Harada K, Kato R, Yamauchi K, Takashima S, et al. Ten initial cases of peroral endoscopic myotomy for treatment of esophageal motility disorders at Okayama University Hospital. Acta Med Okayama 2018;72:99-104.
10. Khashab MA, Familiari P, Draganov PV, Aridi HD, Cho JY, et al. Peroral endoscopic myotomy is effective and safe in non-achalasia esophageal motility disorders: an international multicenter study. Endosc Int Open 2018;6:E1031-6.
11. Kandulski A, Fuchs KH, Weigt J, Malfertheiner P. Jackhammer esophagus: high-resolution manometry and therapeutic approach using peroral endoscopic myotomy (POEM). Dis Esophagus 2016;29:695-6.
12. Chandan S, Mohan BP, Chandan OC, Jha LK, Mashiana HS, et al. Clinical efficacy of per-oral endoscopic myotomy (POEM) for spastic esophageal disorders: a systematic review and meta-analysis. Surg Endosc 2019; doi: 10.1007/s00464-019-06819-6.
13. Lynch KL, Yang YX, Metz DC, Falk GW. Clinical presentation and disease course of patients with esophagogastric junction outflow obstruction. Dis Esophagus 2017;30:1-6.
14. Lin KH, Lee SC, Huang TW, Huang HK. Esophagogastric junction outflow obstruction-related functional chest pain treated using robotic-assisted thoracoscopic esophageal myotomy. J Thorac Dis 2017;9:E432-6.
15. Pereira PF, Rosa AR, Mesquita LA, Anzolch MJ, Branchi RN, et al. Esophagogastric junction outflow obstruction successfully treated with laparoscopic Heller myotomy and Dor fundoplication: first case report in the literature. World J Gastrointest Surg 2019;11:112-6.
16. Teitelbaum EN, Dunst CM, Reavis KM, Sharata AM, Ward MA, et al. Clinical outcomes five years after POEM for treatment of primary esophageal motility disorders. Surg Endosc 2018;32:421-7.

Cicero *et al*. *Mini-invasive Surg* 2019;3:25
DOI: 10.20517/2574-1225.2018.012

Mini-invasive Surgery

Review

Open Access

Check for updates

Imaging

Calogero Cicero[1], Andrea Casarin[1], Francesca Currò[2], Irene Campo[2], Maida Bada[3], Tommaso Silvestri[3]

[1]UC Radiologia, ASL7 Pedemontana, San Bassiano Hospital, 36061 Bassano del Grappa (VI), Italy.
[2]UC Radiologia, Azienda Sanitaria Universitaria Integrata, Trieste 34149, Italy.
[3]UC Urologia, ASL7 Pedemontana, 36061 Bassano del Grappa (VI), Italy.

Correspondence to: Dr. Calogero Cicero, UC Radiologia, ASL7 Pedemontana, San Bassiano Hospital, 36061 Bassano del Grappa (VI), Italy. E-mail: calogero.cicero@aulss7.veneto.it

How to cite this article: Cicero C, Casarin A, Currò F, Campo I, Bada M, Silvestri T. Imaging. *Mini-invasive Surg* 2019;3:25. http://dx.doi.org/10.20517/2574-1225.2018.012

Received: 27 Dec 2018 **First Decision**: 10 Apr 2019 **Revised**: 3 Aug 2019 **Accepted**: 19 Aug 2019 **Published**: 28 Aug 2019

Science Editor: Richard Lawrence John Naspro **Copy Editor**: Jia-Jia Meng **Production Editor**: Jing Yu

Abstract

The incidence of renal cell carcinoma is rising and its represents the 2%, 3% of all cancers. The increased use of ultrasonography, contrast enhanced ultrasonography, computed tomography and magnetic resonance imaging have resulted in incidentally detected small renal masses (SRMs). SRMs represent a heterogeneous group of tumors that included metastatic lesions, benign, malignant, and cystic lesions. With the increase number of renal incidentalomas, we have seen an increase in therapeutic choices (surgery, ablation therapies and active surveillance). The role of imaging has progressively grown over the decades and became currently a cornerstone that is needed to perform diagnosis, treatment and follow-up of SRMs after ablation treatment. Hence, in this review, we critically assess recent literature on the role of imaging in the context of ablation management of SRMs with a focus on the diagnosis and follow-up protocol.

Keywords: Ultrasonography, contrast-enhanced ultrasound, contrast enhanced ultrasonography, small renal masses

INTRODUCTION

During the last decades, there has been an increase in the incidence of small renal masses (SRMs). This is likely because of increased use of axial and abdominal imaging and longer life expectancy[1].

SRMs are defined as renal masses with a maximum diameter of less than 4 cm and represent an extremely heterogeneous category of lesions including benign, malignant, solid or cystic ones. Though SRMs in 80%

of cases are malignant tumors, they show a good natural history according to DISSRM Registry. Indeed, SRMs growth rate and variability decrease with time during active surveillance: in patients of advanced age or with serious comorbid conditions, SMRs can be managed conservatively with little change in overall survival or cancer-specific survival rate[2]. The treatment paradigm historically centered around surgery, from open one to minimally invasive surgery, such as enucleation or enucleoresection, in order to preserve as much as possible healthy renal parenchyma, reducing the risk of chronic kidney disease (CKD)[3]. However, thanks to more modern technologies, the concept of active surveillance has grown rapidly and nowadays in selected patients, we could offer a standardized protocol of surveillance or a focal management strategy. In addition, renal tumor ablation (focal management) has been developed rapidly during the last 2 decades and currently could be a real alternative option in the opportunely selected candidate to obtain local tumor control, functional preservation, fewer complications and a shorter recovery in comparison to surgery[2,3].

The imaging in the context of ablation therapy for SRMs is a cornerstone that is needed in all the pathway schedules: from diagnosis to treatment and eventually for surveillance and follow-up protocols. Hence, in this review, we critically assess recent literature on the role of imaging in the context of minimally invasive management of SRMs, focusing in particular on diagnosis and follow-up after ablative treatment.

IMAGING MODALITIES - DIAGNOSIS

The improvement and wide spreading of ever more efficient imaging techniques have leaded in the last years to a sensible increase in the diagnosis of incidental renal masses (IRM). Different imaging modalities are used: (1) ultrasonography (US); (2) contrast enhancement ultrasonography (CEUS); (3) computed tomography (CT); and (4) magnetic resonance imaging (MRI).

US

In every day clinical practice, US is the first imaging technique that allows the discovery of IRM. Generally, after having been discovered, IRM are better categorized and staged by using CT scan or abdominal MRI. The choice is extremely related to the comorbidity of the patients and the presence of a CKD and the experience of the radiologist.

According to Oh *et al.*[4], US has the sensitivity (SE), specificity (SP), positive predictive value (PPV), negative predictive value (NPV) and accuracy for renal cell carcinoma (RCC) diagnostic efficacy of 60.5%, 72.7%, 34.8%, 63.6% respectively.

The advange of US included that the target of examination (SMRs) is clearly visible. All the conditions that limit the US examination, such as obesity or meteorism, represent limits also for CEUS.

CEUS

Otherwise, CEUS has a good potential in the categorization of focal SRMs and has had an increasing use and widespread adoption worldwide due to its advantages in the evaluation of enhancement pattern of the renal lesion without the risk of nephrotoxicity and the lack of ionizing radiation. The contrast agent is made of microbubbles and has no toxic effects on renal parenchyma. As concerning CEUS, PPV, SE, SP, NPV are 86.8%, 63.6%, 89.2%, 58.3% and 81.6% respectively, for RCC diagnostic efficacy[4]. CEUS advantages include safety, patient tolerance, real-time imaging capability, and costs[5].

Hence, CEUS could be a useful instrument in the pre-operatively settings for characterization and diagnosis of SRMs but also in the follow-up, due for its strength in the detection of acute complication and early intralesional enhancement[6].

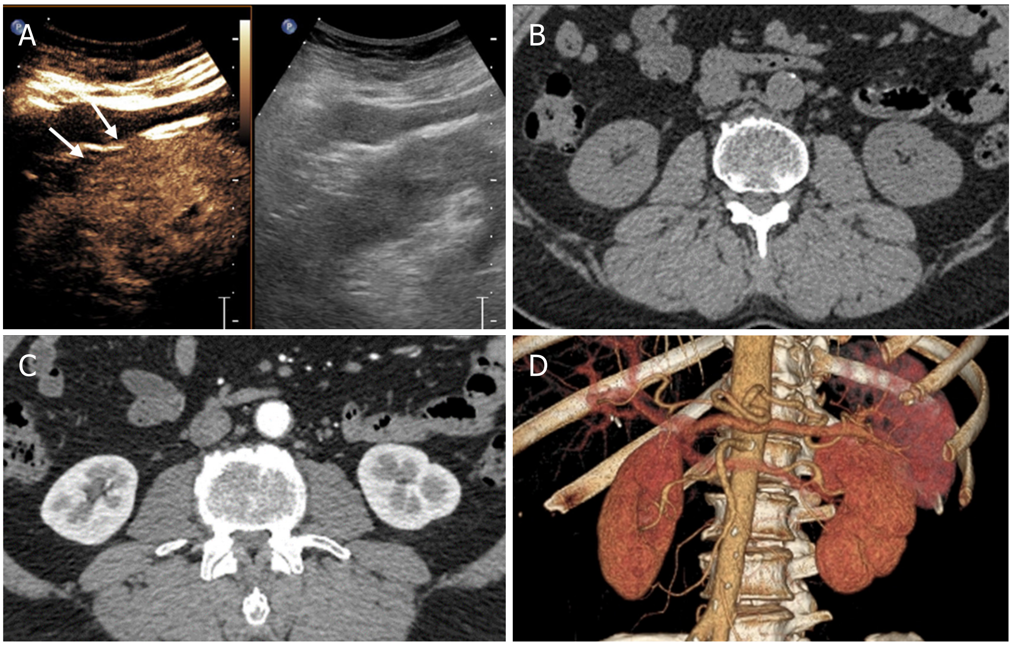


Figure 1. Pseudotumor. A: Grey-scale sonography shows isoechoic cortical mass (or dromedary hump?) in the midportion of the kidney (arrows); on contrast-enhanced sonograms the lesion shows enhancement equal (or similar) to the kidney in all vascular phases. Computed tomography with contrast injection before (B), after (C) and 3D reconstruction (D) doesn't show focal renal lesions

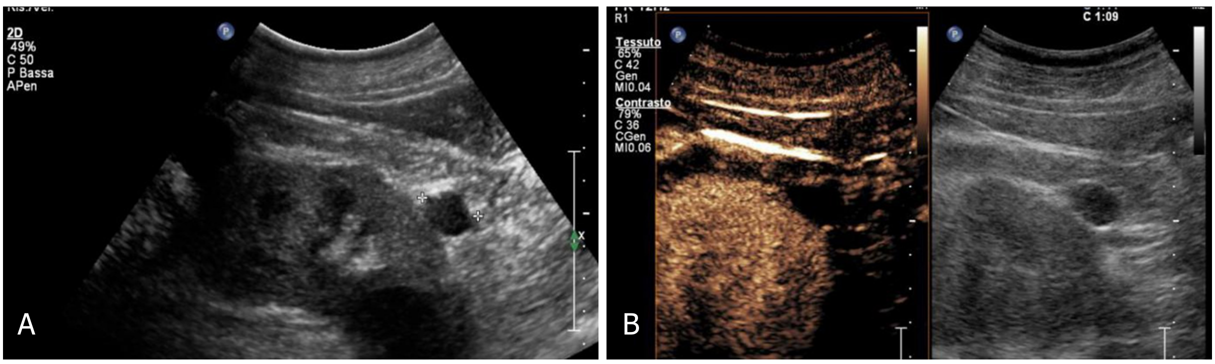


Figure 2. Bosniak 2 cyst. A: Grey scale and contrast enhanced sonograms shows small exophitic hypoechoic mass with smooth margin in lower pole; B: Completely avascular after microbubble injection

Another use of CEUS is to distinguish kidney tumors and/or other conditions in which the convective B mode and US Doppler have not helpful the radiologist to a definitive diagnosis: for example, the pseudotumors have the same degree of enhancement as the remaining healthy renal parenchyma[7,8].

Particularly CEUS seems to be useful in some mimicking anatomical variations: pseudotumors, for example, have the same enhancing characteristics of the surrounding parenchyma [Figure 1] in all phases[9,10]. Conversely, in the majority of cases, the enhancement in kidney tumors is different from the nearly parenchyma: at least one vascular phase has a variation in the degree or distribution of enhancement. CEUS is also appropriate in the analysis and characterization of complex kidney cysts and particularly in the differentiation of Bosniak classification of renal cysts [Figures 2-5].

Compared with CT, CEUS seems to have the higher preciseness of CT for the characterization of renal cystic lesions according to lesional enhancement (LE). Infact, in some cases, CT and/or RMI can't

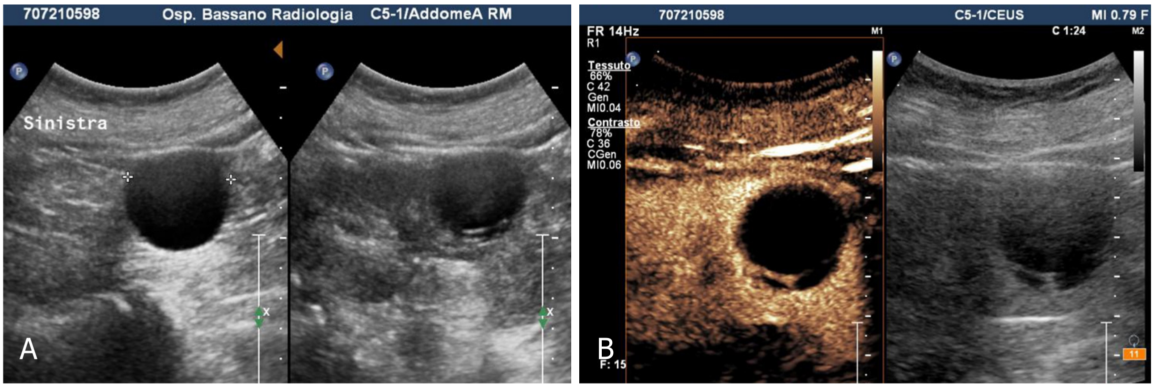


Figure 3. Bosniak 2F cyst. A: Grey scale sonography shows in the mid portion of the left kidney cystic lesion with thin hyperechoic septum; B: Contrast enhanced sonography reveal homogeneous enhancement of the septum without parietal nodule

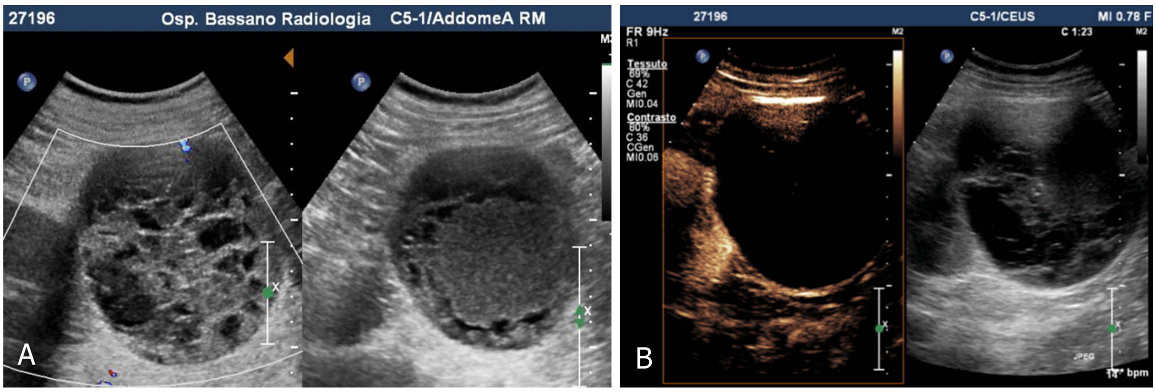


Figure 4. Bosniak 3 cyst. A: Greyscale sonography shows voluminous mass with mixed echo structure (anechoic and hyperechoic components); B: Contrast enhanced sonography reveals cystic lesion characterized by irregular, thickened and vascularized walls

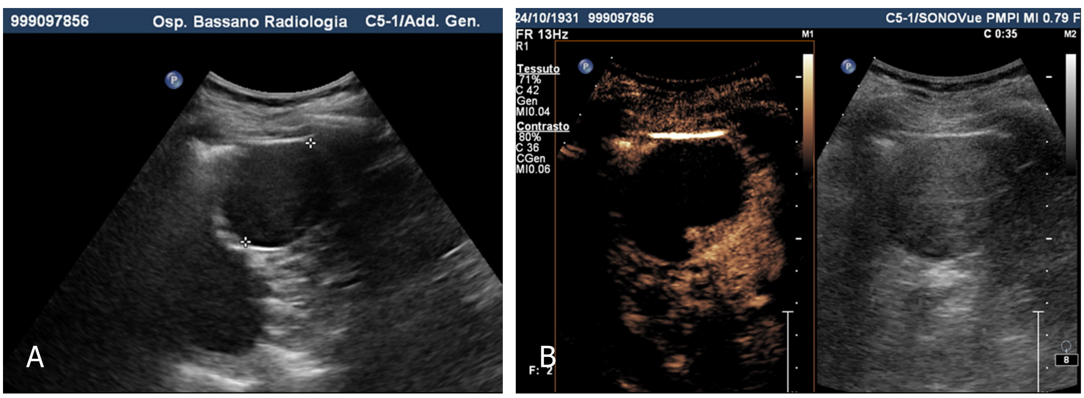


Figure 5. Bosniak 4 cyst. A: Grey scale shows hypoechoic round lesion with smooth margin; B: Contrast- enhanced sonography reveals a cystic lesion with mural nodules characterized by strong enhancement

recognize LE with inconclusive findings[11-13]. CEUS has a greater SP in characterizing renal cystic lesions, in particular the presence and thickness of a septum and/or the presence of a solid intracystic components[14-16].

Anyway, it is well-known the role of CT in the malignant cystic lesion for staging: now the CEUS is useful in the follow up of complex cystic lesions that are not suitable for surgery and in the future it could replace the CT[15].

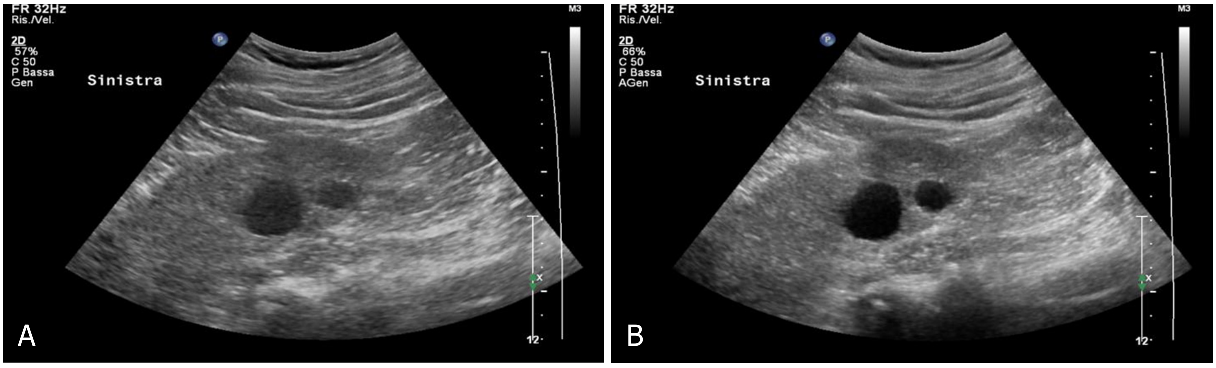


Figure 6. Simple cyst. A: Greyscale sonograms of the left kidney shows hypoechoic round lesion with smooth margins without perceptible wall; B: Tissue harmonic imaging may be useful to show better the posterior acoustic

CEUS plays an important role during the follow up: it avoids unnecessary studies with CT. The advantages of CEUS are considerable: a conventional US B-mode diagnosis in most cases a simple cyst [Figure 6], but CEUS detects neoangiogenesis (blood flow in hypovascularized lesions) with greater accuracy[16]. It allows a clearer distinction between solid and complex cystic lesions, above all it helps to characterize non-diagnostic lesions with other imaging (CT, US, B-mode)[17]. In agreement with Bertolotto *et al.*[18], CEUS allows a better identification of the lesions, expecially in the case of small or multifocal lesions, with the help of the image fusion system.

CT

CT exposes the subject to a relatively high dose of radiation, and the iodinated contrast agents have a potential risk of nephrotoxicity in patients with renal impairment. Furthermore, on CT examination, enhancement is defined when an increase in attenuation > 15 Hounsfield Units is observed between the unenhanced and enhanced phases[19].

CT is the gold standard in the worldwide for staging renal tumors and SRMs. However, in clinical practice, most CT scan studies are not performed with a specific renal protocol: most of time protocol are inadequate to characterize the lesions. Hence, indeterminate renal lesions are frequently identified [Figure 7]. In addition, during follow-up US assessment should be comprehensive, including CEUS, to obviate an unnecessary CT study[16].

MRI

MRI is considered the most accurate diagnostic tool, with SE and SP in characterizing SMRs ranging from 88% to 100% and from 83% to 93%, respectively[6]. However, it is also the most expensive imaging technique[6] and cannot be used in patients with a pacemaker, uncooperative patients, and patients with severe renal failure. There are occasionally issues related to patient tolerance and safety, in particular the risk of nephrogenic systemic fibrosis in patients with estimated glomerular filtration rates under 30 mL/min, when exposed to MRI contrast agents[7-9]. Moreover, the MRI characterization of SMRs may be difficult, as image subtraction cannot be effectively performed.

MRI indication is used both to evaluate renal masses of nature to be and determined to stage RCC, considering that MRI is more specific than CT scan for benign lesions [Figure 8][19,20].

Moreover, MRI helps to classify renal tumors according to specific characteristics (solid *vs.* cystic), expecially in cases of doubtful CT[18]. The most recent MRI schemes to study SMRs, use different

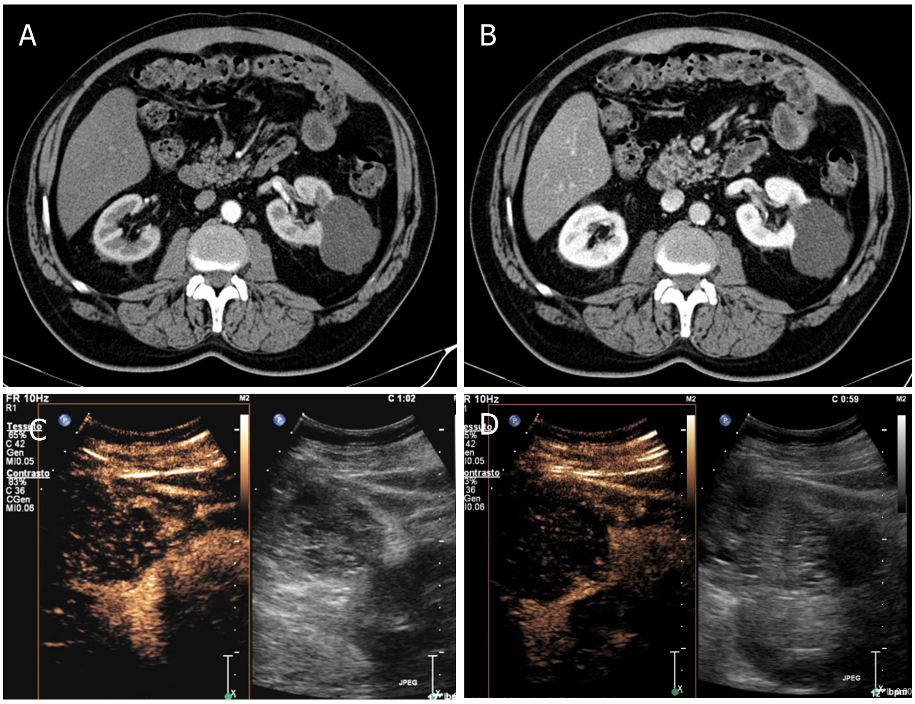


Figure 7. Indeterminate renal lesions at CT study. Contrast CT shows in the left kidney voluminous, partially exophitic, hypodense lesion with irregular margins and without enhancement in phases arterial (A) and venous phase (B). Greyscale and contrast-enhanced sonography (C-D) shows a lesion with mixed echo structure and after microbubble injection shows multiple vascularized septa (Bosniak 4)

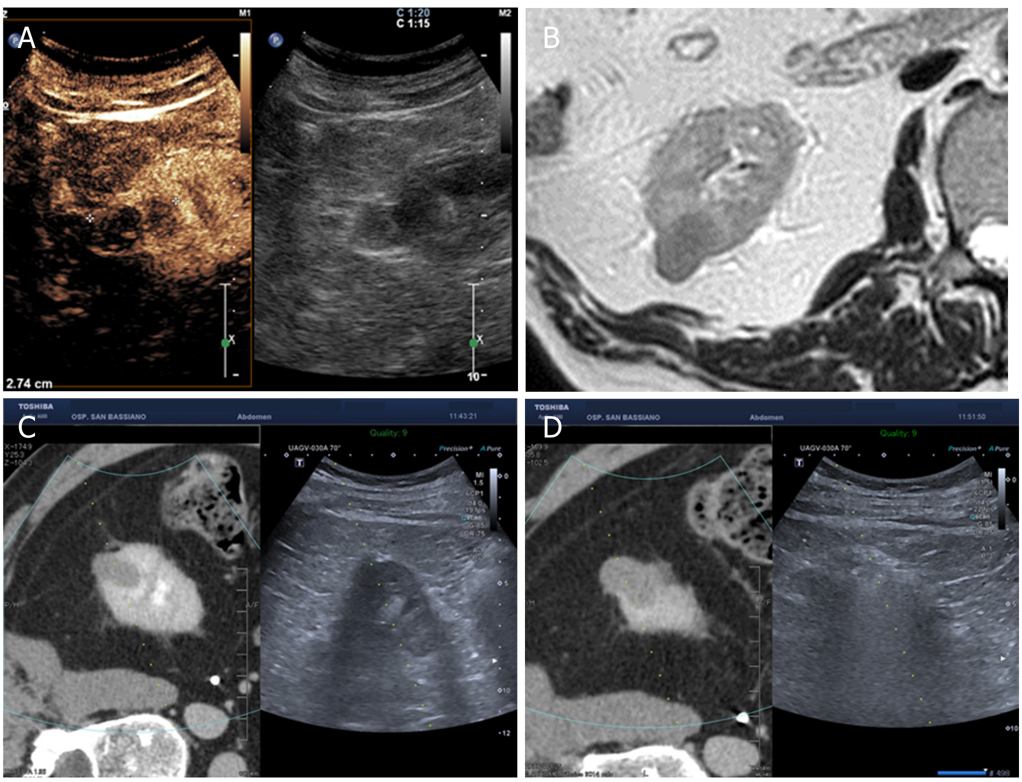


Figure 8. Fusion-guided microwave ablation. 75 years old patient with exophitic in the right kidney, identified by sonography and contrast-enhanced ultrasound (A) and confirmed by MR (B), it was a RCC (biopsy proven) treated with microwaves through guided fusion technique (C-D). RCC: renal cell carcinoma

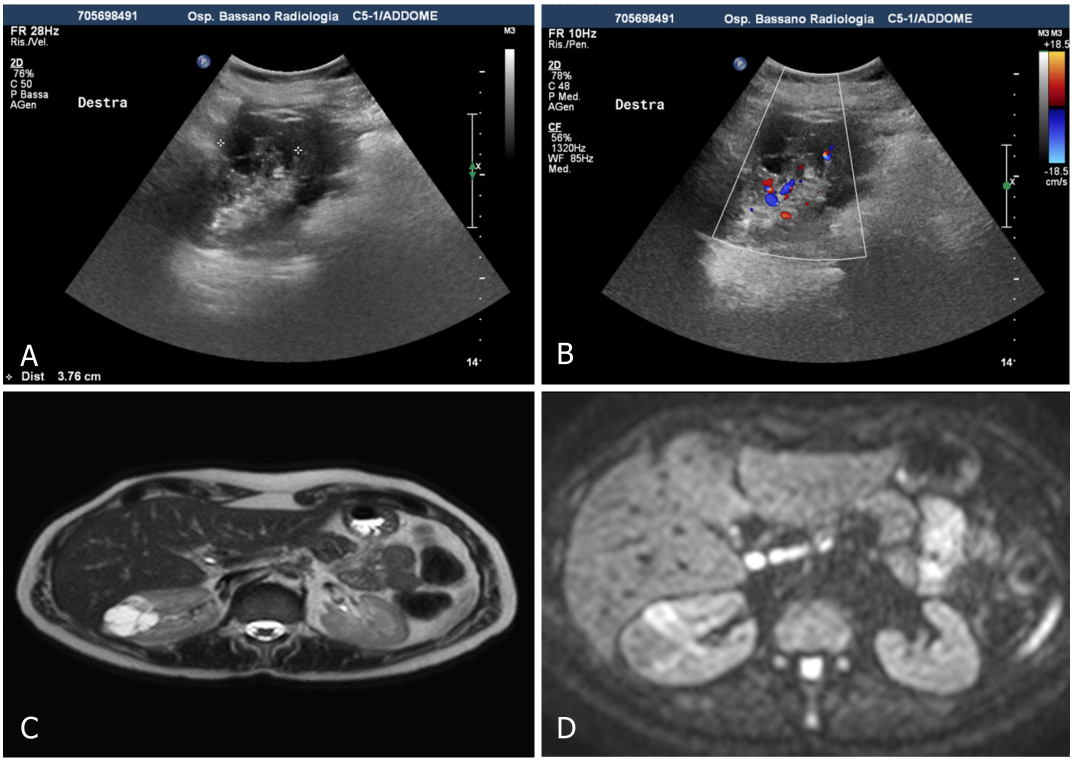


Figure 9. MRI with DWI. Greyscale sonography shows right midportion complex cystic, without vascularization at color-Doppler analysis (A, B). MR reveals on T2 weighted images complex cystic lesion (Bosniak III-IV) with multiple thin septa and hypointense intramural nodule (C). DWI weighted images show restriction of the intramural nodule: it was a papillary RCC (D). DWI: diffusion weighted imaging; RCC: renal cell carcinoma

parameters, such as DWI and dynamic contrast-enhanced imaging, in order to obtain a complete and precise lesion characterization[21] [Figure 9].

Hence, using those parameters could be helpful to differentiate benign from malignant SRMs, but also have a role in distinguishing the different subtypes of RCC and tumor's grade[22,23].

IMAGING MODALITIES - FOLLOW-UP

The aim of ablation therapy of SRMs is to obtain a complete necrosis of the lesion with an obligatory damage to adjacent healthy renal tissue to achieve a negative tumor margin and decrease the liability of residual disease near the ablation zone. The absence of contrast enhancement at the site of treatment, indicates success after procedure. The importance of imaging is both to evaluate technique success and to follow up the ablated mass.

Historically there has been different debate regarding the definitions of recurrence after ablation for SRMs. The literature has a not unique definition of recurrence after treatment for RCC and particularly after ablation there are different controversy also in the definition of progression, treatment success, and treatment efficacy. As opposed to surgery, the ablation efficacy is based typically on radiological findings[24].

Literature lacks of good quality data about long-term efficacy of percutaneous ablation treatment for SRMs. Regarding radiofrequency ablation several studies report short-term outcomes. In a limited period of follow up: (1) tumors with a diameter < 4 cm have a low probability of residual disease after a single procedure[25,26]; (2) central located tumors have lower rates of residual disease when compared with

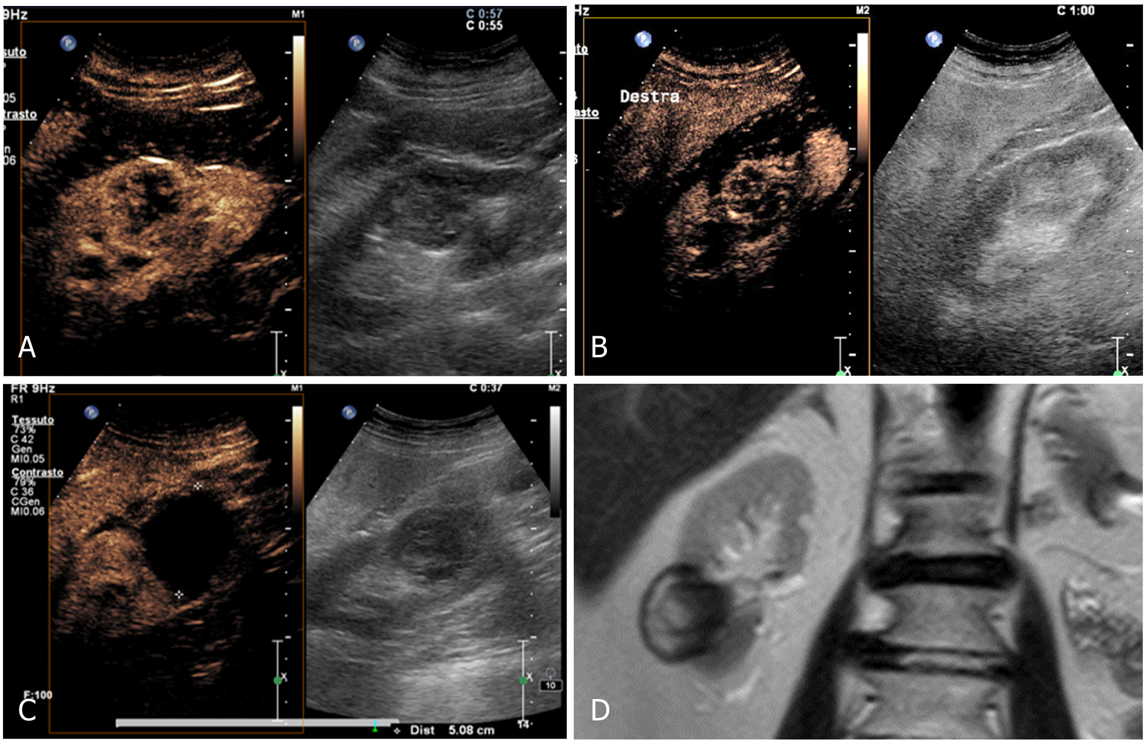


Figure 10. Follow-up after cryoablation. A: 84 years old patient with 5 cm RCC; B: Postoperative day 1 and enhancement; C: no tumor persistence and often a repeated CEUS after 1 month is recommended in lesions that maintain vascularity on postoperative to exclude residual tumor; D: MR after 6 months confirms the success of the cryoablation treatment. CEUS: contrast enhancement ultrasonography; RCC: renal cell carcinoma

exophytic tumors[27]; and (3) tumors with a diameter > 3 cm compared with smaller tumors, have an higher rates of residual disease after the first treatment[27].

Anyway, follow-up can be performed by CEUS, CT or MRI. CT and MRI are the best options for the patient because of their high resolution and chance to detect recurrences. However, as for the diagnostic pathway, the cumulative radiation dose could be very high. Another problem is that the CT scan requires iodine contrast, which is a well-known nephrotoxic substance.

The current guidelines don't explain the tyme and duration imaging follow up after ablation treatment. The AUA recommends cross-sectional imaging at 3 months and 6 months after ablation, then annually for 5 years. After ablation treatments, the timing of initial follow up varies according to operator's preference; the range is from day 0 to 1 month post operatively[28-30]. Generally, the majority of residual tumor is detected within the first 3 months after ablation, the urge for early short interval follow-up. According to Matin *et al.*[26], the most frequent timing of recidive is within the first 3 months after treatment: this is important in order to programme an early follow up.

CEUS is increasingly used during follow-up and particularly on close postoperative time: day 1 to 1 month. The main aim is looking complications.

The first imaging sign of tumor persistence after ablation treatment, is the persistence of vascularization in enhancement to imaging. This signal is the first post operative day not allow to diagnose a failure of the procedure. For this reason, it is important to perform a CEUS at 30 days to evaluate a successful or uncessful ablation [Figure 10][8].

This is particularly true in cryoablated lesions (15%-20% of cases) that can exhibit post-ablation contrast enhancement on initial postoperative imaging and also for the first few months, which resolves in 45% of patients in a period from 1 up to 14 months. Most recurrent lesions develop after the first year therefore, different authors suggest surveillance protocol based on CT or MRI with short interval for the first year (1, 3, 6, and 12 months respectively after treatment), and then every 6 months for the second year and then annually thereafter[31].

DISCUSSION

The role of imaging in the diagnosis and decision-making of management of SMRs has been crucial over the last years. Firsty, the development of new technology and the acquisition of extremely sophisticated machines has allowed a better quality and better precision in the characterization and diagnosis of SRMs. Hence, the quality in the diagnosis allowed a better decision-making process, tailored for each patients. NSS is performed for SMRs, but as many 30% of the lesions prove benign nature; for this reasons, there is increased interest in preoperative study of SMRs subtypes[27]. Secondary the imaging modalities have changed the treatment process itself: ablation modalities are performed nowadays often via imaging-guide mode and in 2017 AUA Guidelines has recommended a percutaneous approach as the best choice if possible, in the ablation treatment of SRMs[28]. Percutaneous biopsy results were shown to be discordant with surgical pathology from resected specimens in 8% of cases: is a safe procedure, Hemorrhage, if it occurs, is usually subclinical and needle tract seeding is exceedingly rare. A renal tumor biopsy before ablative therapy and systemic therapy without previous pathology must be considered in select patients who are considered for AS, in order to obtaining a histological diagnosis preoperative[32]. Third, the success of a treatment of a kidney tumor is not only in the diagnosis and management but also in the follow-up of that lesions. For this reason, the real success of ablation therapy is evaluated by routinely imaging follow up. The surveillance with CT and/or MRI is crucial and indispensable for determining initial treatment success, detecting recurrence disease at the ablation site, or new metachronous lesions. The introduction of multidisciplinary team with urologists and radiologists could improve the follow up after ablation therapy[33]. As concerning the first diagnosis, frequently pathologic features are observed in RCC like hemorrhage, necrosis and cystic change. CT scan correlates these features with the existence of necrotic degeneration or intratumoral cystis: the washout and LE pattern of CEUS might relate to the pathologic features of RCC such as intratumoral blood flow, thin-walled blood vessels and hemorrhage. CEUS could be used for US diagnosis of pseudocapsules like a useful sign both in the differential diagnosis of RCC and in the choice of NSS[34].

CONCLUSION

The ablation procedure for SRMs is increasing worldwide together with an evolution of imaging assessment. Multiple combination of different technology and modalities is offering different opportunity for a more precisely diagnosis of SRMs. Furthermore, this real cutting-edge imaging protocols might be more effective and crucial in the patient management. However, there is a need of more precisely evidence-based algorithms for diagnostic and treatment pathway that could be the glue that integrate the imaging for diagnosis with the imaging for treatment.

DECLARATIONS

Authors' contributions

Made contributions to conception and design of the study/review and performed data analysis and interpretation: Cicero C, Casarin A

Performed data acquisition: Currò F, Campo I

Made substantial contributions to conception and design of the study/review, performed an entire revision of data analysis, re-interpretation and the revision for editors: Silvestri T, Bada M

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Kane CJ, Mallin K, Ritchey J, Cooperberg MR, Carroll PR. Renal cell cancer stage migration: analysis of the National Cancer Data Base. Cancer 2008;113:78-83.
2. Uzosike AC, Patel HD, Alam R, Schwen ZR, Gupta M, et al. Growth Kinetics of Small Renal Masses on Active Surveillance:Variability and Results from the DISSRM Registry. J Urol 2018;199:641-8.
3. Bertolotto M, Catalano O. Contrast-enhanced ultrasound: past, present, and future. Ultrasound Clin 2009;4:339-67.
4. Oh TH, Lee YH, Seo IY. Diagnostic efficacy of contrast-enhanced ultrasound for small renal masses. Korean Journal of Urology. Diagnostic Efficacy of Contrast-Enhanced Ultrasound for Small Renal Masses. Korean J Urol 2014;55:587-92.
5. Bertolotto M, Derchi LE, Cicero C, Iannelli M. Renal Masses as Characterized by Ultrasound Contrast. Ultrasound Clin 2013;8:581-92.
6. Barozzi L, Valentino M, Bertolotto M, Pavlica P. Contrast enhanced ultrasound of renal diseases. Arch Ital Urol Androl 2010;82:232-7.
7. Sidhu PS, Cantisani V, Dietrich CF, Gilja OH, Saftoiu A, et al. The EFSUMB Guidelines and Recommendations for the Clinical Practice of Contrast-Enhanced Ultrasound (CEUS) in Non-Hepatic Applications: Update 2017. Ultraschall Med 2018;39:e2-44.
8. Bertolotto M, Siracusano S, Cicero C, Iannelli M, Silvestri T, et al. Cryotherapy of Renal Lesions: Enhancement on Contrast-Enhanced Sonography on Postoperative Day 1 Does Not Imply Viable Tissue Persistence. J Ultrasound Med 2017;36:301-10.
9. Correas JM, Claudon M, Tranquart F, Hélénon AO. The kidney: imaging with microbubble contrast agents. Ultrasound Q 2006;22:53-66.
10. Mazziotti S, Zimbaro F, Pandolfo A, Racchiusa S, Settineri N, et al. Usefulness of contrast-en-hanced ultrasonography in the diagnosis of renal pseudotumors. Abdom Imaging 2010;35:241-5.
11. Barr RG, Peterson C, Hindi A. Evaluation of indeterminate renal massess with contrast-enhanced US: a diagnostic performance study. Radiology 2014;271:133-42.
12. Sanz E, Hevia V, Gomez V, Álvarez S, Fabuel JJ, et al. Renal complex cystic masses: usefulness of contrast-enhanced ultrasound (CEUS) in their assessment and its agreement with computed tomography. Curr Urol Rep 2016;17:89.
13. Quaia E, Bertolotto M, Cioffi V, Rossi A, Baratella E, et al. Comparison of contrast-enhanced sonography with unenhanced sonography and contrast-enhanced CT in the diagnosis of malignancy in complex renal masses. AJR Am J Roentgenol 2008;191:1239-49.
14. Clevert DA, Minaifar N, Weckbach S, Jung EM, Stock K, et al. Multislice computed tomography versus contrast-enhanced ultrasound in evaluation of complex cystic renal masses using the Bosniak classification system. Clin Hemorheol Micro 2008;39:171-8.
15. Park BK, Kim B, Kim SH, Ko K, Lee HM, et al. Assessment of cystic renal masses based on Bosniak classification: comparison of CT and contrast-enhanced US. Eur J Radiol 2007;61:310-4.
16. Harkanyi Z. Potential applications of contrast-enhanced ultrasound in pediatric patients. Ultrasound Clin North Am 2013;8:403-22.
17. Ascenti G, Mazziotti S, Zimbaro G, Settineri N, Magno C, et al. Complex Cystic Renal Masses: Characterization with Contrast-enhanced US. Radiology 2007;243:158-65.
18. Bertolotto M, Cicero C, Perrone R, Degrassi F, Cacciato F, et al. Renal masses with equivocal enhamcement at CT: characterization with contrast-enhanced ultrasound. AJR Am J Roentgenol 2015;205:W557-65.
19. Di Vece F, Tombesi P, Ermili F, Sartori S. Management of incidental renal masses: time to consider contrast-enhanced ultrasonography. Ultrasound 2016;24:34-40.
20. Helck A, D'Anastasi M, Notohamiprodjo M, Thieme S, Sommer W, et al. Multimodality imaging using ultrasound image fusion in renal lesions. Clin Hemorheol Micro 2012;50:79-89.
21. Heilbrun ME, Remer EM, Casalino DD, Beland MD, Bishoff JT, et al. ACR appropriateness criteria indeterminate renal mass. J Am

Coll Radiol 2015;12:333-41.
22. Kreft BP, Muller-Miny H, Sommer T, Steudel A, Vahlensieck M, et al. Diagnostic value of MR imaging in comparison to CT in the detection and differential diagnosis of renal masses: ROC analysis. Eur Radiol 1997;7:542-7.
23. Pedrosa I, Chou MT, Ngo L, H Baroni R, Genega EM, et al. MR classification of renal masses with pathologic correlation. Eur Radiol 2008;18:365-75.
24. Pedrosa I, Alsop DC, Rofsky NM. Magnetic resonance imaging as a biomarker in renal cell carcinoma. Cancer 2009;115(10 Suppl):2334-45.
25. Kay FU, Pedrosa I. Imaging of Solid Renal Masses. Urol Clin North Am 2018;45:311-30.
26. Matin SF, Ahrar K, Cadeddu JA, Gervais DA, McGovern FJ, et al. Residual and Recurrent Disease Following Renal Energy Ablative Therapy: A Multi-Institutional Study. J Urol 2006;176:1973-7.
27. Del Cura JL, Zabala R, Iriarte JI, Unda M. Treatment of renal tumors by percutaneous ultrasound-guided radiofrequency ablation using a multitined electrode: effectiveness and complications. Eur Urol 2010;57:459-65.
28. Farrell MA, Charboneau WJ, DiMarco DS, Chow GK, Zincke H, et al. Imaging-guided radiofrequency ablation of solid renal tumors. AJR Am J Roentgenol 2003;180:1509-13.
29. Ferakis N, Bouropoulos C, Granitsas T, Mylona S, Poulias I. Longterm results after computed-tomography-guided percutaneous radiofrequency ablation for small renal tumors. J Endourol 2010;24:1909-13.
30. Donat SM, Diaz M, Bishoff JT, Coleman JA, Dahm P, et al. Follow-up for clinically localized renal neoplasms: AUA guideline. J Urol 2013;190:407-16.
31. Campbell S, Uzzo RG, Allaf ME, Bass EB, Cadeddu JA, et al. Renal Mass and Localized Renal Cancer: AUA Guideline. J Urol 2017;198:520-9.
32. Caoili EM, Davenport MS. Role of Percutaneous Needle Biopsy for Renal Masses. Semin Intervent Radiol 2014;31:20-6.
33. Rutherford EE, Cast J EI, Breen DJ. Immediate and long-term CT appearances following radiofrequency ablation of renal tumours. Clin Radiol 2008;63:220-30.
34. Tanagho YS, Bhayani SB, Kim EH, Figenshau RS. Renal Cryoablation Versus Robot-Assisted Partial Nephrectomy: Washington University Long-Term Experience. J Endourol 2013;27:1477-86.

Fukunaga. *Mini-invasive Surg* 2019;3:26
DOI: 10.20517/2574-1225.2019.32

Mini-invasive Surgery

Editorial

Open Access

Check for updates

Advances in the minimally invasive management of gastric and esophagogastric junction cancer

Tetsu Fukunaga

Department of Gastroenterology and Minimally Invasive Surgery, Juntendo University Hospital, Tokyo 113-8421, Japan.

Correspondence to: Prof. Tetsu Fukunaga, Department of Gastroenterology and Minimally Invasive Surgery, Juntendo University Hospital, Tokyo 113-8421, Japan. E-mail: t2fukunaga@juntendo.ac.jp

How to cite this article: Fukunaga T. Advances in the minimally invasive management of gastric and esophagogastric junction cancer. *Mini-invasive Surg* 2019;3:26. http://dx.doi.org/10.20517/2574-1225.2019.32

Received: 2 Sep 2019 **First Decision:** 2 Sep 2019 **Revised:** 10 Sep 2019 **Accepted:** 11 Sep 2019 **Published:** 19 Sep 2019

Science Editor: Tetsu Fukunaga **Copy Editor:** Jia-Jia Meng **Production Editor:** Tian Zhang

It is a great honor and pleasure to act as guest editor for this special issue where many of these key international opinion leaders have generously contributed to help coalesce the goal for the topic of advances in the minimally invasive management of gastric and esophagogastric junction (EGJ) cancer.

Gastrointestinal (GI) cancers are aggressive diseases and ranks the most common diagnosed cancer and death causes worldwide[1]. Surgical resection with lymph node dissection (LND) is still the only potentially curative therapy. Minimally invasive surgeries including laparoscopy and robot are widely used in the treatment of GI cancers.

The operation procedures for gastric cancer base on the location of tumor and include distal, proximal or total gastrectomy. Introduction of laparoscopic gastrectomy (LG) has shown promising results and therefore gained popularity worldwide. Van den Berg *et al.*[2] outlined the current state of LG for gastric cancer and its future perspective. Laparoscopic LND is preferred for early gastric cancer now[3]. However, the safety and oncologic validity for advanced gastric cancer (AGC) are still being debated. Some clinical trials have been gradually performed focusing AGC treated by LG recently and reported no inferior short-term outcomes compared with open surgery[4]. Shimada *et al.*[5] discussed the clinical indications and limitations dealing with LND for AGC, and also the technical tips. LG may be not suitable for all AGC patients, but the role for AGC cannot be underestimated. The authors also discussed the value of LND combined with neo-adjuvant chemotherapy, conversion surgery and other treatments. It is believed that after the long-term outcomes of many ongoing large-scaled phase III trials released in the near future, we can get more powerful evidences. As society ages, older gastric cancer patients are increasing. It is indicated that age may be an independent predictor of increased morbidity and mortality. Few studies about older gastric cancer patients are reported and even fewer on older patients with AGC. Yuu *et al.*[6] reported their study to show elderly patients with AGC may benefit from laparoscopic distal gastrectomy (LDG).

More and more GI reconstruction can be performed intracorporeally especially in LDG. Ohmura *et al.*[7] reported a new reconstruction method named hemi-hand-sewn (HHS) technique. The HHS technique combines linear stapler in posterior wall with hand sewn in anterior wall to create Billroth-I anastomosis. They reported the better surgical results with HHS in comparison with extracorporeal total hand-sewn. An optimal technique of digestive tract reconstruction after distal gastrectomy has not yet been consensus. Zhang and Fukunaga[8] describe the different Billroth-I reconstruction techniques that can be proposed after total LDG. As mentioned by the authors, the ideal reconstruction should be not only for doctors but also for patients. From the review article, readers can understand that the developing reconstruction techniques covering from using hand-sewn anastomosis, circular stapler to linear stapler method, which reflect the wisdom of the surgeon and the pursuit the minima invasive to patients.

There has been a recent increase in the use of totally laparoscopic total gastrectomy (TLTG) for gastric cancer. TLTG usually needs higher laparoscopic techniques and longer learning process. Mazzola *et al.*[9] reported their results of TLTG. Their results showed TLTG was a feasible and safe option in the treatment of gastric cancer.

Robotic surgery for gastric cancer is a relatively new research field. With high-resolution three-dimensional and articulated devices, surgeons are able to perform difficult techniques more comfortably and meticulously. Makuuchi *et al.*[10] reviewed the development of surgical robotics, and describe the advantages and disadvantages of robot gastrectomy for gastric cancer compared to LG. Although robotic gastrectomy has theoretical advantages over LG, evidences are still lacking. Well-designed prospective randomized controlled trials are needed and awaited to obtain conclusive results on this issue.

The incidence of EGJ cancer has shown an upward trend over the past several decades both in the West and East[11]. The management is challenging and there is no one-size-fit-all strategy[12]. Siewert classification is the standard classification for EGJ cancer. Surgery remains the fundamental treatment and a lot of detail during surgery are reported recent years. Oo and Ahmed[13] discussed the epidemiology, risk factors and the management of EGJ tumors. Readers can get the general of this disease from this review article. Shibao *et al.*[14] introduced minimally invasive approach for EGJ cancer and listed evidences for various surgical strategies. The authors discussed different technique according to Siewert type classification and listed advantages and disadvantages.

Most studies focus on Siewert type II cancer, since it is considered the true EGJ tumor. The treatment for type II cancer is still debated. Li and Zang[15] focused on the surgical strategies for type II EGJ cancer in recent year. The Ivor Lewis esophagectomy is the universally accepted technique to resect cancers situated in the middle and distal esophagus and EGJ. de Pascale *et al.*[16] and Parthasarathi *et al.*[17] introduced their experiences and results of totally minimally invasive Ivor Lewis (TMIIL) esophagectomy. Both of their results showed better surgical outcomes in TMIL esophagectomy.

All of published articles are well written and meaningful. Articles published in this present special issue have highlighted the outline of minimally invasive management of gastric and EGJ cancer. We can study al lot from these studies. In the future, still a lot need to be researched and higher evidences are needed to support the conclusions.

DECLARATIONS

Authors' contributions

The author contributed solely to this preface.

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

The author declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.
2. Van den Berg JW, Shilton H, Cheong E. Gastrectomy: the expanding role of minimally invasive surgery in gastric cancer. Mini-invasive Surg 2019;3:23.
3. Katai H, Mizusawa J, Katayama H, Takagi M, Yoshikawa T, et al. Short-term surgical outcomes from a phase III study of laparoscopy-assisted versus open distal gastrectomy with nodal dissection for clinical stage IA/IB gastric cancer: Japan Clinical Oncology Group Study JCOG0912. Gastric Cancer 2017;20:699-708.
4. Yu J, Huang C, Sun Y, Su X, Cao H, et al. Effect of Laparoscopic vs Open Distal Gastrectomy on 3-Year Disease-Free Survival in Patients With Locally Advanced Gastric Cancer: The CLASS-01 Randomized Clinical Trial. JAMA 2019;321:1983-92.
5. Shimada M, Amaya S, Munemoto Y, Mitsui T. Laparoscopic lymph nodes dissection for advanced gastric cancer: the current status and the perspective. Mini-invasive Surg 2019;3:7.
6. Yuu K, Tsuchihashi K, Toyoda S, Kawasaki M, Kameyama M. Laparoscopic vs. open distal gastrectomy for advanced gastric cancer in elderly patients: a retrospective study. Mini-invasive Surg 2019;3:6.
7. Ohmura Y, Suzuki H, Kotani K, Teramoto A. Intracorporeal hemi-hand-sewn technique for Billroth-I gastroduodenostomy after laparoscopic distal gastrectomy: comparative analysis with laparoscopy-assisted distal gastrectomy. Mini-invasive Surg 2019;3:4.
8. Zhang S, Fukunaga T. Current status of technique for Billroth-I anastomosis in totally laparoscopic distal gastrectomy for gastric cancer. Mini-invasive Surg 2019;3:2.
9. Mazzola M, Gualtierotti M, Martini PD, Bertoglio CL, Morini L, et al. Totally laparoscopic total gastrectomy: challenging but feasible: a single center case series. Mini-invasive Surg 2019;3:12.
10. Makuuchi R, Kamiya S, Tanizawa Y, Bando E, Terashima M. Robotic surgery for gastric cancer. Mini-invasive Surg 2019;3:11.
11. Imamura Y, Watanabe M, Toihata T, Takamatsu M, Kawachi H, et al. Recent Incidence Trend of Surgically Resected Esophagogastric Junction Adenocarcinoma and Microsatellite Instability Status in Japanese Patients. Digestion 2019;99:6-13.
12. Zhang S, Orita H, Fukunaga T. Current surgical treatment of esophagogastric junction adenocarcinoma. World J Gastrointest Oncol 2019;11:567-78.
13. Oo AM, Ahmed S. Overview of gastroesophageal junction cancers. Mini-invasive Surg 2019;3:1-9.
14. Shibao K, Mitsuyoshi M, Matayoshi N, Sato N, Hirata K. Minimally invasive approach for cancer of the esophagogastric junction. Mini-invasive Surg 2019;3:16
15. Li SC, Zang L. Siewert type II adenocarcinoma of esophagogastric junction: treatment status. Mini-invasive Surg 2019;3:15.
16. de Pascale S, Ghidinelli F, Piccioli AN, Borin S, Romario UF. Totally minimally invasive Ivor-Lewis esophagectomy: initial single center experience. Mini-invasive Surg 2019;3:18.
17. Parthasarathi R, Gupta GR, Sabnis SC, Raj PP, Senthilnathan P, et al. Thoraco-laparoscopic Ivor-Lewis esophagectomy: the most extensive Indian experience. Mini-invasive Surg 2019;3:20.

M'Harzi *et al. Mini-invasive Surg* 2019;3:27
DOI: 10.20517/2574-1225.2019.22

Mini-invasive Surgery

Technical Note

Open Access

Check for updates

One anastomosis gastric bypass and esojejunostomy in rats: surgical techniques

Leila M'Harzi[1,2], Matthieu Bruzzi[1,2,3], Jean-Marc Chevallier[1,2,3], Richard Douard[1,2,3]

[1]General and Digestive Surgery Unit, Georges Pompidou, AP-HP University Hospital, Paris 75908, France.
[2]INSERM 970, Équipe 2, PARCC, HEGP, Paris 75015, France.
[3]Paris Descartes Faculty of Medicine, Paris 75006, France.

Correspondence to: Dr. Matthieu Bruzzi, Service de chirurgie digestive, Hôpital européen Georges Pompidou, 20 Rue Leblanc, Paris 75908, France. E-mail: matthieu.bruzzi@aphp.fr

How to cite this article: M'Harzi L, Bruzzi M, Chevallier JM, Douard R. One anastomosis gastric bypass and esojejunostomy in rats: surgical techniques. *Mini-invasive Surg* 2019;3:27. http://dx.doi.org/10.20517/2574-1225.2019.22

Received: 16 Jul 2019 **First Decision:** 27 Aug 2019 **Revised:** 12 Sep 2019 **Accepted:** 17 Sep 2019 **Published:** 23 Sep 2019

Science Editor: Wah Yang **Copy Editor:** Cai-Hong Wang **Production Editor:** Tian Zhang

Abstract

One anastomosis gastric bypass (OAGB) is a popular bariatric procedure, but controversies remain regarding biliary reflux and the potential risk of cancer. Esophagojejunostomy (EJ) in rats is a validated and reproducible model for the development of metaplasia [Barett's esophagus (BE)] and esophageal adenocarcinoma (EA) with a minimal exposure of 12 to 20 weeks. We are analyzing the risks of BE and EA in an OAGB rat model and comparing these with the EJ rat model. The purpose of this study is to describe our OAGB and EJ techniques in rats that we used to evaluate biliary reflux and share our experience with scientists and the bariatric community. These operations are short and simple procedures with acceptable morbidity.

Keywords: Mini-gastric bypass, biliary reflux, cancer

INTRODUCTION

One anastomosis gastric bypass (OAGB), or mini-gastric bypass, is a popular bariatric surgery procedure in humans[1-3], but controversies remain regarding the risks of biliary reflux and potential complications as metaplasia, dysplasia and cancer[4].

No studies on the risks of these for humans are currently available and research, including experimental studies, is needed to help answer this important question[4,5]. The risk of developing metaplasia [Barett's esophagus (BE)] or esophageal adenocarcinoma (EA) after omega loop montage mainly exists because of

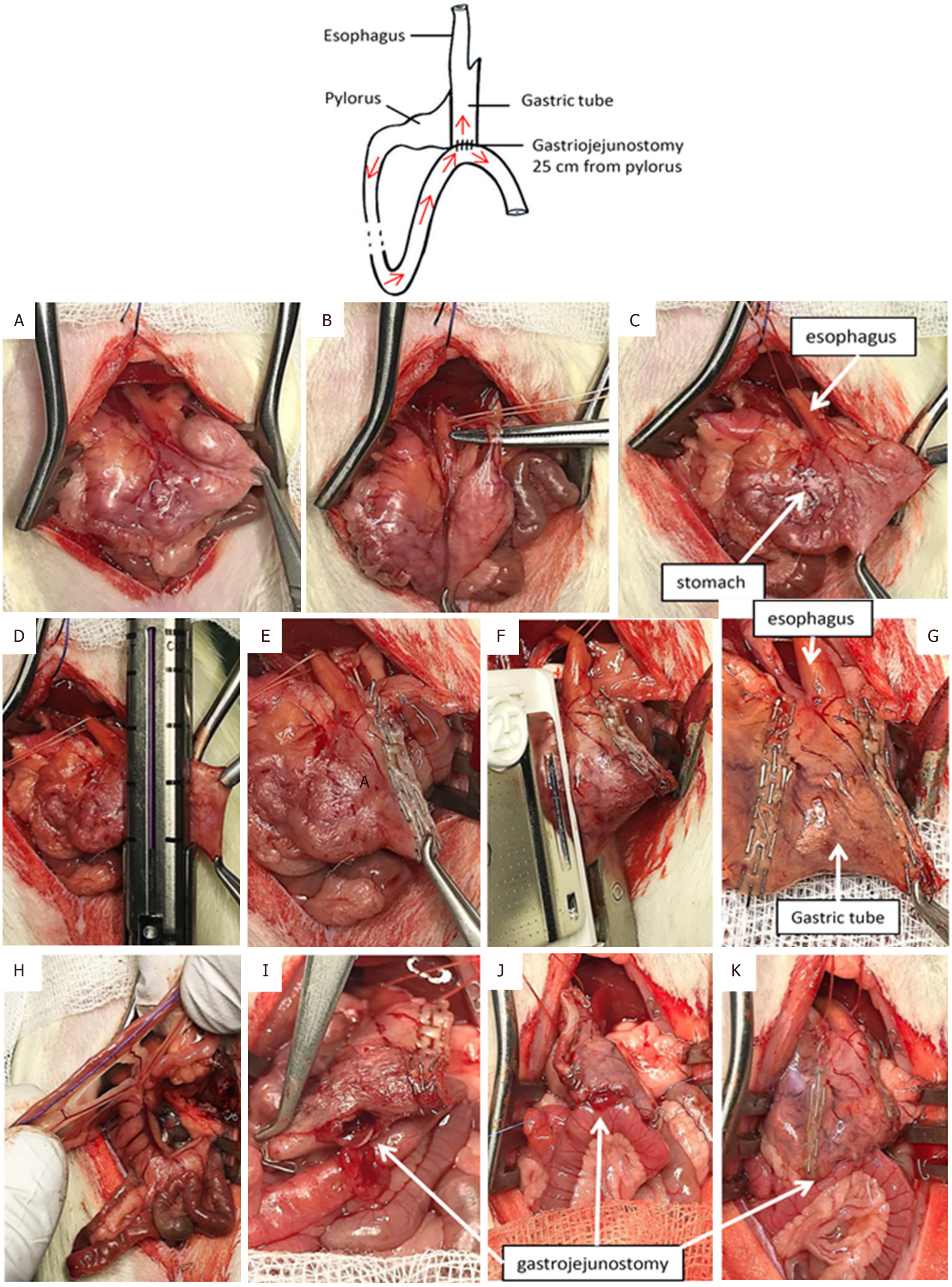


Figure 1. One-anastomosis gastric bypass

studies that analyzed surgical models in rats in which the gastro-duodenal or enteral contents were placed in direct contact with the esophageal mucosa [esophagojejunostomy (EJ))][6,7]. EJ in rats is a validated and reproducible model for the development of BE and EA with a minimal exposure of 12 to 20 weeks.

We are analyzing and comparing the risk of metaplasia (BE) and/or EA in OAGB and EJ rat models with a follow-up of 30 weeks[8]. The study is currently in progress but we decided to communicate the different surgical techniques that we used to share our experience with scientists and the bariatric community.

METHODS

The study complied with European Community guidelines and was approved by the ethics committee (Comité d'éthique en expérimentation animale n°18-115). Female and male Wistar rats aged 7 weeks and weighing 250 g were used.

Preoperative care and anesthesia

Rats were fasted overnight before operation. Anesthesia was given by inhalation with isoflurane. Standard aseptic procedures were used throughout[9].

Materials

Our equipment included an anesthesia workstation, Prolene 7/0 and Vicryl 3/0 sutures, a self-retaining retractor, curve dressing forceps, curved scissors, a micro needle order and needle order, scalpel handle, crile and an optical magnification system, an endo GIA 45-mm staple gun with purple cartridge (Medtronic) and a TA-DST 30-mm-3.5-mm stapler (Covidien).

Rat position and exposition

The rat was positioned supine, feet spread apart, abdomen shaved. After laparotomy, the lateral banks were removed with a self-retaining retractor and a suture was suspended at the xyphoid.

OAGB surgeries

After retraction of the liver, the stomach was isolated [Figure 1A]. Loose gastric connections to the spleen were released along the greater curvature, and the suspensory ligament supporting the upper fundus was severed [Figure 1B]. A vicryl suture was passed behind the esophagus. Then, the gastric artery and the esophagus were separated[5,10].

The gastric pouch

The forestomach was resected using an endo GIA 45-mm staple gun with purple cartridge (Medtronic; Figure 1C-E). The esogastric junction was then dissected and the vascular supply isolated in this region. The stapler TA-DST 30 mm-3.5 mm (Covidien) position was delimited between the esophagus and the left gastric artery using the wire previously placed positioned in a parallel line with the transection line of the forestomach, and the gastric pouch created [Figures 1F and G].

Omega limb

The small intestines were run distally from the pylorus for 25 cm. We recommend using a premeasured suture for this [Figure 1H]. Curved scissors were used to create a 3-mm jejunostomy on the anti-mesenteric margin of bowel. The jejunum was then anastomosed to the gastric pouch 25 cm from the pylorus [Figure 1I].

Hand-sewn gastro-jejunostomy

The loop of bowel was identified was moved gently to the gastric pouch. A 3-to-4-mm gastrostomy was made on the gastric pouch [Figure 1I]. The anastomosis was performed manually with 7-0 Prolene running sutures. We began with the corner points on both sides of the anastomosis [Figure 1J]. When the anterior running suture was complete, we turned the gastrojejunal block and then completed the posterior running suture. The suture took serosa on the esophagus and the gastric tube. After replacing the gastrojejunal block [Figure 1K], we wrapped the anastomosis in the omentum. One milliliter of saline was then poured intraperitoneally.

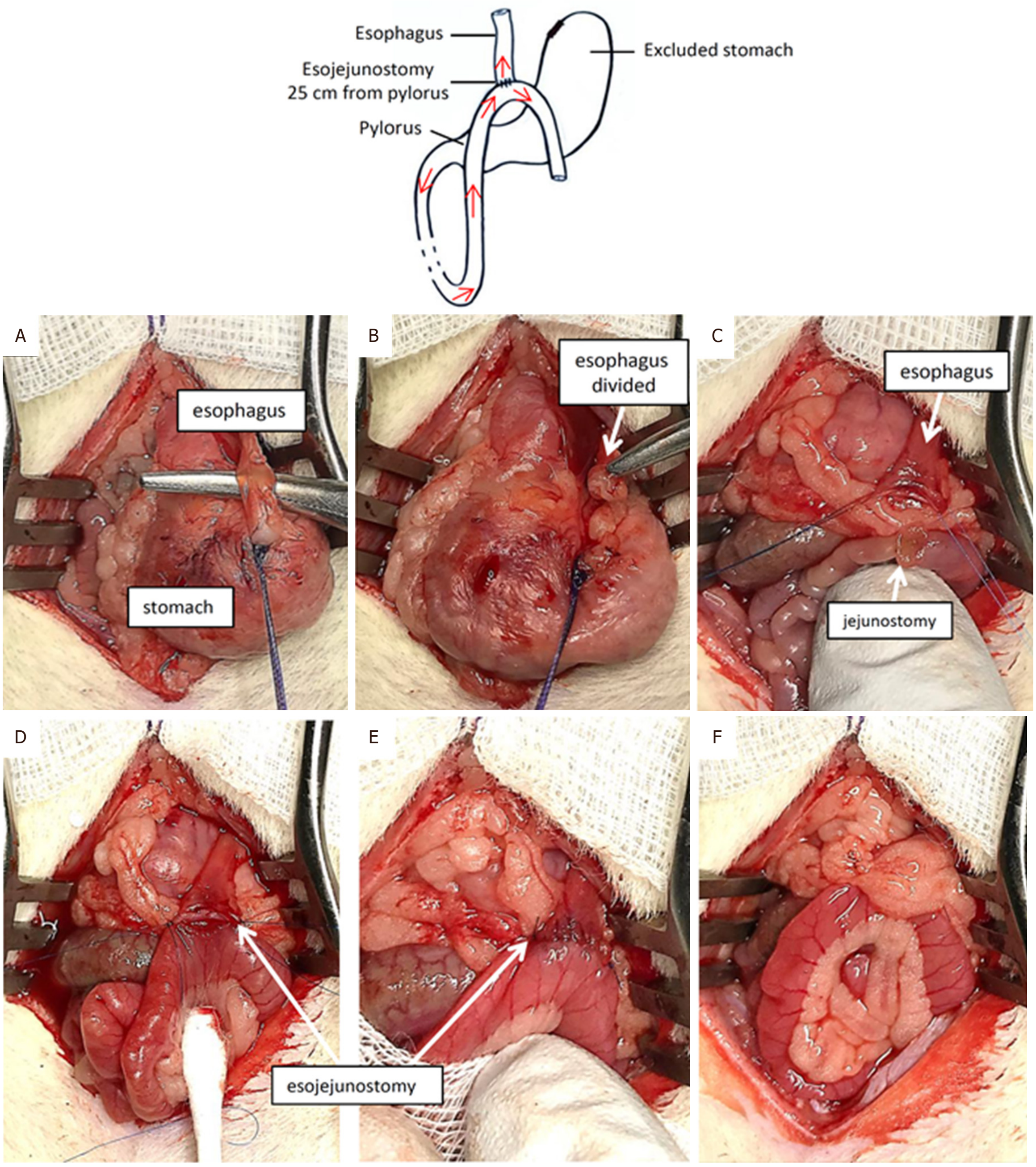


Figure 2. Esojejunostomy

EJ surgeries

The liver was retracted and the stomach isolated. Loose gastric connections to the spleen and liver were released along the greater curvature, and the suspensory ligament supporting the upper fundus was severed. A vicryl wire was passed behind the esophagus.

Section of the esophagus

The wire behind the esophagus was placed at the base of this one. It was tied and pulled down. The esophagus was cut with a scalpel, as close to the esogastric junction as possible [Figure 2A and B].

Before it was retracted, two Prolene 7/0 tractors were placed on both side of the esophagus, taking care to remove mucosa and serosa (total points). The knot of the stomach was reinforced with a running suture completed with Prolene 7.0 [Figure 2C].

Omega limb

The small intestines were run distally from the pylorus for 25 cm. We recommend using a premeasured wire (as described in OAGB surgeries, Figure 1H). Curved scissors were used to create a 3-mm jejunostomy on the anti-mesenteric margin of the bowel [Figure 2C].

Hand-sewn EJ

The loop of the bowel was identified and moved gently to the esophagus in a precolic position [Figure 2D]. Anastomosis was performed manually using 7-0 Prolene running sutures. We started with the corner points on both sides of the anastomosis [Figure 2E]. When the anterior running suture was complete, we turned the esojejunal block and completed the posterior running suture. There are approximately 5 to 6 passes for each running suture. The suture took mucosa and serosa on the esophagus and only serosa on the jejunum.

After replacing the esojejunal block, we wrapped the anastomosis in the omentum [Figure 2F]. One milliliter of saline was poured intraperitoneally.

RESULTS AND DISCUSSION

Postoperative care and mortality

OAGB and EJ rats were maintained without food for 24 h after surgery. They received subcutaneous injections of 10 mL Bionolyte G5 (Baxter) on the first postoperative day (POD). From POD 2 to POD 3, they had access to a liquid diet ad libitum. Free access to a normal diet was allowed from POD 4. Pain and distress were carefully monitored twice a day with scoring. Rats showing signs of pain or not eating were maintained on antalgics and euthanized if there was no improvement after 24 h. In our experience, major morbidity in OAGB rat surgeries was due to anastomotic leakage and gastric tube necrosis and major morbidity in EJ surgeries was due to anastomotic stenosis. Gastric necrosis was due to an inadequate stapling of the left gastric artery at the level of the lesser curvature in our first surgeries. With increased experience, we improved the dissection of this artery to decrease these ischemic complications.

We operated on 40 rats: 16 with EJ surgery, 16 with OAGB, and 8 with sham surgery (laparotomy without any digestive suture). Of the 16 EJ rats, acute mortality occurred in four (25%) on mean postoperative day 6. This was due to anastomotic stenosis in all cases.

To prevent stenosis, we recommend doing the anastomosis carefully with very tiny passages on the esophageal mucosa and the jejunal serous. Second, the running suture must be tightened with low pressure. Of the 16 OAGB rats, we had 3 deaths (19%) on mean postoperative day 4. Mortality was due to anastomotic leakage in one rat and gastric pouch necrosis followed by peritonitis in two. To prevent these ischemic complications, we recommend carefully preserving the left gastric artery during TA stapling. In fact, this artery must be well dissected and isolated to avoid its stapling during the confection of the right side on the gastric tube.

Risk of cancer after OAGB and the need for experimental studies

Analysis of the prevalence of cancer and BE after EJ surgeries must be performed after sufficient esophageal exposure to bile and enteral juices, at least 12 to 20 weeks[6,7]. In our experience of OAGB surgeries, no dysplasia, metaplasia or cancer were observed after a 16-week follow-up[5]. The lack of follow-up and control group prompts us to now evaluate OAGB and its consequences using 30-week and 50-week follow-ups[8] and compare these results to EJ surgeries (control group).

On the day of sacrifices, histology and molecular analysis on esophageal and gastric mucosae can be performed to analyze the prevalence of BE and cancer[5].

Concerning the esophagus, the absence of metaplasia, dysplasia or cancer in the OAGB group compared with the EJ group will suggest confer a real protective effect of the long gastric tube used in the OAGB model. Conversely, the presence of precancerous or cancerous lesions in the esogastric blocs of OAGB rats gives additional arguments to detractors of the technique to decrease its diffusion.

This short communication is a simple contribution for researchers interested in the topic of biliary reflux after OAGB because there is an urgent need to answer this specific issue, especially for patients who have already undergone surgery.

DECLARATIONS

Acknowledgments
We thank the assistance of INSERM U970, ERI in the study.

Authors' contributions
Project development: Bruzzi M, Chevallier JM, Douard R
Surgery and data Collection: M'Harzi L, Bruzzi M
Wrote the manuscript: M'Harzi L, Bruzzi M
Comment: Chevallier JM, Douard R

Availability of data and materials
Not applicable.

Financial support and sponsorship
None.

Conflicts of interest
All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate
All applicable institutional and/or national guidelines for the care and use of animals were followed. All experiments were performed in compliance with the European Community guidelines and approved by the Institutional Animal Care and Use Committee.

Consent for publication
Not applicable.

REFERENCES

1. Deitel M. Letter to the editor: bariatric surgery worldwide 2013 reveals a rise in mini-gastric bypass. Obes Surg 2015;25:2166-8.
2. Mahawar KK, Kumar P, Carr WR, Jennings N, Schroeder N, et al. Current status of mini-gastric bypass. J Minim Access Surg 2016;12:305-10.
3. Rutledge R. The mini-gastric bypass: experience with the first 1,274 cases. Obes Surg 2001;11:276-80.

4. Bruzzi M, Chevallier JM, Czernichow S. One-Anastomosis gastric bypass: why biliary reflux remains controversial? Obes Surg 2017;27:545-7.
5. Bruzzi M, Duboc H, Gronnier C, Rainteau D, Couvelard A, et al. Long-term evaluation of biliary reflux after experimental one-anastomosis gastric bypass in rats. Obes Surg 2017;27:1119-22.
6. Greene CL, Worrell SG, DeMeester TR. Rat reflux model of esophageal cancer and its implication in human disease. 2015;262:910-24.
7. Gronnier C, Bruyere E, Piessen G, Briez N, Bot J, et al. Operatively induced chronic reflux in rats: a suitable model for studying esophageal carcinogenesis? Surg 2013;154:955-67.
8. Quinn R. Comparing rat's to human's age: How old is my rat in people years? Nutrition 2005;21:775-7.
9. Pritchett-Corning KR, Luo Y, Mulder GB, White WJ. Principles of rodent surgery for the new surgeon. J Vis Exp 2011; doi: 10.3791/2586.
10. Cavin JB, Couvelard A, Lebtahi R, Ducroc R, Arapis K, et al. Differences in alimentary glucose absorption and intestinal disposal of blood glucose after Roux-en-Y gastric bypass vs sleeve gastrectomy. Gastroenterology 2016;150:454-64.

Mini-invasive Surgery

Preface

Open Access

Preface to special issue on "Minimally Invasive Surgery of the Thymus Gland"

Piergiorgio Solli

Department of Thoracic Surgery, Ospedale Maggiore Largo Nigrisoli, Bologna 2 - 40133, Italy.

Correspondence to: Dott. Piergiorgio Solli, Department of Thoracic Surgery, Ospedale Maggiore Largo Nigrisoli, Bologna 2 - 40133, Italy. E-mail: piergiorgio.solli@gmail.com

How to cite this article: Solli P. Preface to special issue on "Minimally Invasive Surgery of the Thymus Gland". *Mini-invasive Surg* 2019;3:28. http://dx.doi.org/10.20517/2574-1225.2019.37

Received: 23 Sep 2019 **Accepted**: 24 Sep 2019 **Published**: 30 Sep 2019

Science Editor: Giulio Belli **Copy Editor**: Jia-Jia Meng **Production Editor**: Jing Yu

I am thrilled to introduce this *Minimally Invasive Surgery Journal* special issue dedicated to surgery of the thymus gland.

The recently published international MGTX trial[1] has confirmed the effectiveness of thymectomy in myasthenia gravis and although many unanswered questions still remain in the treatment of these patients, the positive results of the trial combined with a variety of available minimally invasive surgical techniques today available, could potentially lead to a much wider acceptance and utilization of thymectomy.

This issue is intended to offer an up-to date review of the several available technical surgical options and cover details of minimally invasive surgical approaches, presented by champions of those techniques, offering valuable lessons and practical tricks for experienced surgeons.

We are aware that the optimal surgical approach is only a part of the whole pathway for these patients, in fact only ongoing and future trials leaded by next generation of surgeons potentially will clarify the immunologic role of the thymus, the best medical strategy to myasthenic patients and eventually the best surgical approach to these patients. Nevertheless surgeons must be fully conscious of current concepts and focused on clear definitions that should be shared among our community, in order to effectively integrate our treatment in a multidisciplinary approach.

Each article has been written by prominent respected physicians in the fields and this issue has been possible only thanks to the efforts of such eminent colleagues: to all of them I would like to express my personal words of gratitude.

DECLARATIONS

Authors' contributions

The author contributed solely to this preface.

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

The author declared that there is no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Wolfe GI, Kaminski HJ, Aban IB, Minisman G, Kuo HC, et al. Randomized Trial of Thymectomy in Myasthenia Gravis. N Engl J Med 2016;375:511-522.

Mini-invasive Surgery

Original Article

Open Access

Check for updates

The difference of intraoperative free-run electromyography monitoring between percutaneous endoscopic lumbar discectomy via a transforaminal and via an interlaminal

Jun-Ichiro Nakamura, Tomoyuki Setoue, Jun Hara

Orthopedic surgery, Kawasaki-saiwai hospital, Kawasaki city, Kanagawa-ken 212-0014, Japan.

Correspondence to: Dr. Jun-Ichiro Nakamura, Orthopedic surgery, Kawasaki-saiwai hospital, 31-27 Ohmiya-cho, Saiwai-ku, Kawasaki city, Kanagawa-ken 212-0014, Japan. E-mail: nakajun16@yahoo.co.jp

How to cite this article: Nakamura JI, Setoue T, Hara J. The difference of intraoperative free-run electromyography monitoring between percutaneous endoscopic lumbar discectomy via a transforaminal and via an interlaminal. *Mini-invasive Surg* 2019;3:29. http://dx.doi.org/10.20517/2574-1225.2019.28

Received: 26 Aug 2019 **First Decision:** 26 Sep 2019 **Revised:** 2 Oct 2019 **Accepted:** 10 Oct 2019 **Published:** 15 Oct 2019

Science Editor: Giulio Belli **Copy Editor:** Cai-Hong Wang **Production Editor:** Tian Zhang

Abstract

Aim: Transforaminal percutaneous endoscopic lumbar discectomy (TF-PELD) is usually performed under local anesthesia because the patient should be conscious to prevent nerve root injury. However, some patients cannot tolerate intraoperative pain and require intravenous analgesia, or must be converted to surgery under general anesthesia (GA). If PELD under GA can be performed safely, it is more convenient and comfortable for both the patient and surgeon.

Methods: A total of 49 cases (mean age, 53 years) were examined. PELD was performed under GA with free-run electromyography (f-EMG) monitoring. Clinical outcomes were assessed according to the visual analogue scale score (VAS) and the Oswestry disability index (ODI). All patients were monitored with f-EMG.

Results: VAS decreased from 7.7 to 1.1 and ODI from 62.3% to 20.5%. A true-positive was observed in one of 27 TF-PELD cases. Care during the procedure is necessary to avoid the risk of severe neurological injury. A false-negative was observed in one of 22 interlaminar (IL)-PELD cases. This patient complained of aggravated numbness for 6 months after surgery. False-positives were recorded in 2 cases of IL-PELD with a train wave just after removal of the herniated discs.

Conclusion: F-EMG monitoring during PELD under GA was useful to identify nerve root damage. TF-PELD under GA requires f-EMG to ensure safety. On the contrary, IL-PELD does not necessitate f-EMG.

Keywords: Free-run electromyography, general anesthesia, iatrogenic nerve injury, percutaneous endoscopic lumbar discectomy

INTRODUCTION

Transforaminal percutaneous endoscopic lumbar discectomy (TF-PELD) is usually performed on an outpatient basis under local anesthesia (LA). The procedure is neurologically safe and avoids injury to the exiting nerve root (ENR) since the patient is conscious and able to notify the surgeon of any pain[1-6].

However, some patients cannot tolerate intraoperative pain and may acquire intravenous analgesia, sedative agents, or conversion to epidural or general anesthesia (GA) on another day.

PELD under GA is considered neurologically safe since the patient is unconscious. Recently, the efficacy of free-run electromyography (f-EMG) has been reported in neurosurgery and spine surgery[7-12], but not for PELD. Therefore, the aim of this study was to evaluate the efficacy of f-EMG monitoring during PELD under GA.

METHODS

Anesthesia

Propofol and remifentanil hydrochloride-based GA were administered. A muscle relaxant (rocuronium bromide) was only used at the initial stage for intubation, and sugammadex sodium was used for reversal of neuromuscular blockade. The stimulation pattern (i.e., train-of-four) was confirmed as more than 90% before starting of f-EMG monitoring.

F-EMG

Continuous f-EMG activity was recorded using a NVM5® monitoring system (NuVasive Inc., San Diego, CA, USA) with surface electrode patches placed at 6 positions (i.e., the bilateral vastus mediaris, tibialis anterior, and gastrocnemius). Before affixing the patches, the skin was scraped with sandpaper to ensure impedance was less than 10 kΩ. The threshold of electrical impact was set at 80 μV. All instances of f-EMG activity were immediately reported to the surgeon.

Neurotonic, burst, and train waves that occurred in response to a surgical maneuver to the affected nerve were considered to be abnormal. A small amplitude, low frequency, and isolated discharge were not considered pathologic[10]. Any of these instances automatically sounded an alarm to notify the surgeon.

Surgical procedure

TF-PELD

With the patient in the prone position on a radiolucent table, an 8-mm incision was made to the entry points of the skin at about 9-11 cm lateral to the midline and then an 18-gauge needle was inserted into the annulus fibrosus. Discography with 2 mL of liquid indigo carmine contrast agent (1:1) was performed using the same needle. A guide wire and sleeve were inserted for endoscopy with a VERTEBRIS lumbar-thoracic® instrument (Richard Wolf GmbH, Knittlingen, Germany). A bipolar radio-frequency electrode system (Elliquence, Baldwin, NY, USA) was used for hemostasis and a high-speed Primado 2® drill with a super slim hand piece 200® (NSK-Nakanishi medical, Tochigi, Japan) was used for foraminoplasty.

IL-PELD

With the patient in the prone position on a radiolucent table, an 8-mm incision was made to the entry points of the skin at about 1 cm lateral to the midline. Once the entry point and the direction of the sleeve were confirmed by image intensifier, a 8-mmsleeve was inserted. A VERTEBRIS lumbar-thoracic® instrument was used for endoscopy and a bipolar radio-frequency electrode system was also used for hemostasis. The ligamentum flavum was resected piece-by-piece using a micro punch. A high-speed Primado 2® drill was used for laminotomy and medial facetectomy. Partial laminotomy was necessary in almost all cases, particularly at L4-L5, to remove the laminae and ligamentum flavum and confirm the

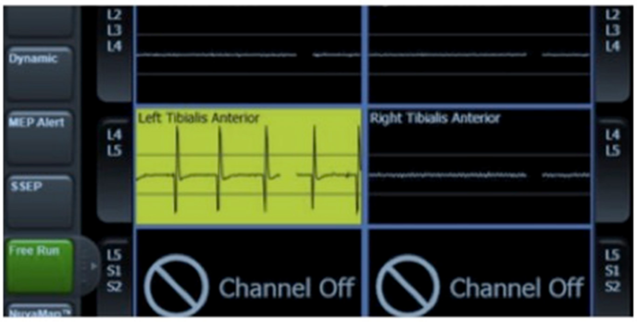


Figure 1. Train wave of free-run electromyogram. This wave was observed in TF-PELD at L4-L5 case when the sleeve was manipulated hand-down. Same waves were also observed in IL-PELD at L5-S1. TF-PELD: transforaminal percutaneous endoscopic lumbar discectomy; IL: interlaminar

lateral edge of the nerve root. Then, after the sleeve was rotated and thecal sac was retracted, the herniated disc was removed.

Statistical analysis

Descriptive analysis of group characteristics was performed using JMP version 11.2 software for Macintosh (SAS Institute Inc., Cary, NC, USA). The independent two-sample *t*-test and Wilcoxon test were used to compare the clinical outcomes. A probability value of $P < 0.05$ was considered to be statistically significant.

RESULTS

There were 49 patients (43 men, 6 women) with a mean age of 52.9 (range, 17-88) years. The mean follow-up period was 10 (range, 6-14) months. The affected level was L2-L3 in one patient (TF-PELD), L3-L4 in 9 (TF-PELD), L4-L5 in 17 [TF-PELD, 14; interlaminar (IL)-PELD, 3], and L5-S1 in 22 (TF-PELD, 3; IL-PELD, 19) patients.

The mean operative time was 63 ± 29 (range, 30-143) min and intraoperative blood loss was negligible in all cases. The mean hospital stay was 3.2 ± 1.5 (range, 1-5) days. The mean numerical rating scale score for the affected leg improved significantly from 7.7 to 1.1 at follow-up, and the mean Oswestry disability index had improved from 62.3 to 20.5. Two patients experienced recurrence of the herniated nucleus pulposus.

In all cases, single waves were observed but were not considered to be clinically significant. A true-positive was observed in one case during TF-PELD at L4-L5 [Figure 1]. When the sleeve was manipulated downward by hand, an alarm sounded. Careful performance of the procedure will prevent ringing of the alarm, which indicates a postoperative motor deficit. However, this patient complained of dysesthesia for 3 weeks postoperatively. The numbness gradually improved with the use of pregabalin and disappeared by the final follow-up.

False-positives were observed in 2 patients following IL-PELD at L5-S1. No alarm sound was observed when the nerve root was retracted by rotating the sleeve. Train waves appeared with the alarm several seconds after the herniated disc material was removed. At that time, no surgical maneuver was performed. In these 2 cases, no neurological deficit was observed after surgery. Including these 2 cases, no alarm sounded during IL-PELD when the nerve root and dura were retracted.

A false-negative was observed in one patient following IL-PELD at L5-S1, but no abnormal wave was observed. However, this patient complained of severe numbness for 6 months postoperatively.

The sensitivity of f-EMG for neurological deficits was 50% in all cases, 100% for TF-PELD, and 0% for IL-PELD. The specificity was 95.8%, 100%, and 90.4%, respectively.

DISCUSSION

F-EMG's effectiveness has been reported for cranial nerve tumor resection and spinal surgery[7-11]. Any irritation to the nerve, by stretching or compression, causes trains of motor unit potential discharge in the corresponding muscle[7]. F-EMG is reported to have high sensitivity and relatively low specificity[8]. However, monitoring in real-time would improve specificity when confirming that the related nerve was correctly manipulated during surgery[7]. Therefore, application of f-EMG in PELD surgery is considered to be efficient.

One of the most important complications in TF-PELD is ENR injury, which reportedly occurs at a relatively high rate of 2%-8.9% under LA[3,4,13-16]. A large LA dosage may increase the risk of ENR injury because of complete nerve blockage. Furthermore, some patients cannot tolerate surgery because of pain and, thus, had to be converted to GA on another day. Therefore, we believe that PELD under LA is not necessarily safe or comfortable for the patient.

In this study, there was one true-positive case with detectable nerve irritation during surgery. This patient complained of severe numbness without motor deficit after surgery. Train waves appeared when the sleeve was manipulated by hand. Hence, caution is required during surgery to avoid motor deficits.

Conversely, we carefully monitored f-EMG during IL-PELD while rotating the sleeve when retracting the dural sac and nerve root. No alarm sounded when performing IL-PELD. However, 2 false-positives were observed during IL-PELD. An alarm sounded after herniated disc material was removed. F-EMG sensitivity during IL-PELD was low. Hence, f-EMG may be inappropriate for monitoring the nerve root during IL-PELD.

F-EMG monitoring cannot detect damage to sensory nerves, but it can potentially prevent injury to motor and sensory fibers. PELD under GA, without the use of a muscle relaxant with f-EMG monitoring, can reduce neural injury.

This study was limited by the small number of patients. Therefore, future studies with larger numbers of patients will be necessary to evaluate the efficacy of f-EMG for PELD.

In conclusion, PELD was performed safely under GA using f-EMG monitoring. Patients who cannot tolerate pain are good candidates for PELD under GA.

DECLARATIONS

Acknowledgments
The authors would like to thank Enago (www.enago.jp) for the English language review.

Authors' contributions

Wrote and reviewed the manuscript: Nakamura JI, Setoue T, Hara J

Availability of data and materials
Not applicable.

Financial support and sponsorship
None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Copyright

REFERENCES

1. Kambin P, Schaffer JL. Percutaneous lumbar discectomy. Review of 100 patients and current practice. Clin Orthop Rel Res 1989;238:24-34.
2. Yeung AT, Tsou PM. Posterolateral endoscopic excision for lumbar disc herniation. Surgical technique, outcome, and complications in 307 consecutive cases. Spine 2002;27:722-31.
3. Yeung AT, Yeung CA. Minimally invasive techniques for the management of lumbar disc herniation. Orthop Cl North Am 2007;38:363-72.
4. Choi G, Lee SH, Raiturker PP, Lee SS, Chae YS. Percutaneous endoscopic interlaminar discectomy for intracanalicular disc herniations at L5-S1 using a rigid working channel endoscope. Neurosurg 2006;58:59-68.
5. Ruetten S, Komp M, MerkH, Godolias G. Full-endoscopic interlaminar and transforaminal lumbar discectomy versus conventional microsurgical technique: a prospective randomized, control study. Spine 2008;33:931-9.
6. Sairyo K, Egawa H, Matsuura T, Takahashi M, Higashino K, et al. State of the art: transforaminal approach for percutaneous endoscopic lumbar discectomy under local anesthesia. J Med Invest 2014;61:217-25.
7. Pajewski TN, Arlet V, Phillips LH. Current approach on spinal cord monitoring: the point of view of the neurologist, the anesthesiologist and the spine surgeon. Eur Spine J 2007;16:S115-29.
8. Holmes JT, Chappuis JL. Monitoring of lumbosacral nerve roots during spinal instrumentation. Spine 1993;18:2059-62.
9. Skinner SA, Nagib M, Bergman TA, Maxwell RE, Msangi G. The initial use of free-running electromyography to detect early motor tract injury during resection of intramedullary spinal cord lesions. Neurosurg 2005;56:299-314; discussion 299-314.
10. Gunnarsson T, Krassioukov AV, Sarjeant R, Fehlings MG. Real-time continuous intraoperative electromyographic and somatosensory evoked potential recordings in spinal surgery: correlation of clinical and electrophysiologic findings in a prospective, consecutive series of 213 cases. Spine 2004;29:677-84.
11. Chung I, Grigorian A. EMG and evoked potentials in the operating room during spinal surgery. In: Schwartz M, editor. EMG methods for evaluating muscle and nerve function. InTech; 2011. pp. 325-40.
12. Nakamura JI, Yoshihara K. Initial clinical outcomes of percutaneous full-endoscopic lumbar discectomy using an interlaminar approach at the L4-L5. Pain Physician 2017;20:E507-12.
13. Sairyo K, Matsuura T, Higashino K, Sakai T, Takata Y, et al. Surgery related complications in percutaneous endoscopic lumbar discectomy under local anesthesia. J Med Invest 2014;61:264-9.
14. Sakane M. Anatomical relationship between Kambin's triangle and exiting nerve root. Mini-invasive Surg 2017;1:99-102.
15. Fang G, Ding Z, Song Z. Comparison of the effects of epidural anesthesia and local anesthesia in lumbar transforaminal endoscopic surgery. Pain Physician 2016;19:E1001-4.
16. Choi I, Ahn JO, So WS, Lee SJ, Choi IJ, et al. Exiting root injury in transforaminal endoscopic discectomy: preoperative image considerations for safety. Eur Spine J 2013;22:2481-7.

Sebastián-Tomás *et al*. *Mini-invasive Surg* 2019;3:30
DOI: 10.20517/2574-1225.2019.29

Mini-invasive Surgery

Review

Open Access

Robotic total mesorectal excision: state of the art

Juan Carlos Sebastián-Tomás[1], Sandra Santarrufina-Martínez[1], Sergio Navarro-Martínez[1], Paula Gonzálvez-Guardiola[1], Elías Martínez-López[1], Carmen Payá-Llorente[1], Eduardo García-Granero[2], Aleix Martínez-Pérez[1]

[1]Department of General and Digestive Surgery, Hospital Universitario Doctor Peset, Valencia 46017, Spain.
[2]Department of General and Digestive Surgery, Hospital Universitario y Politécnico La Fe, Valencia 46026, Spain.

Correspondence to: Dr. Aleix Martínez-Pérez, Department of General and Digestive Surgery, Hospital Universitario Doctor Peset, Avenida Gaspar Aguilar 90, Valencia 46017, Spain. E-mail: aleix.martinez.perez@gmail.com

How to cite this article: Sebastián-Tomás JC, Santarrufina-Martínez S, Navarro-Martínez S, Gonzálvez-Guardiola P, Martínez-López E, Payá-Llorente C, García-Granero E, Martínez-Pérez A. Robotic total mesorectal excision: state of the art. *Mini-invasive Surg* 2019;3:30. http://dx.doi.org/10.20517/2574-1225.2019.29

Received: 27 Aug 2019 **First Decision**: 23 Sep 2019 **Revised**: 3 Oct 2019 **Accepted**: 11 Oct 2019 **Published**: 15 Oct 2019

Science Editor: Nicola de'Angelis **Copy Editor**: Cai-Hong Wang **Production Editor**: Jing Yu

Abstract

Minimally-invasive conventional up-to-down laparoscopic approach is a widespread alternative for rectal cancer resection. Its potential benefits towards open surgery have been shown to rely, however, at secondary clinical outcomes, and its oncological non-inferiority compared with the traditional open approach has not been demonstrated yet. In this scenario, robotic-assisted minimally-invasive rectal resection has gained increasing popularity and promising expectancies. This narrative review aims to assemble the most updated evidence available and to discuss the future perspectives and challenges for this emergent surgical tool. The main benefit over conventional laparoscopy appears to be a reduction of conversion rates to open surgery, whereas the oncologic and functional outcomes seem similar than the other alternatives. Increased costs are the main limitation of the widespread of robotic technology. Low quality of the current evidence is remarkable.

Keywords: Rectal cancer, total mesorectal excision, robotic surgery, minimally-invasive surgery

INTRODUCTION

In 2018, colorectal cancer (CRC) was the third most commonly diagnosed cancer (10.2%), and the second leading cause of cancer death (9.2%). Nearby two million of new CRC cases and more than 800,000 deaths were estimated to occur worldwide in 2018[1]. Surgery remains as the mainstay treatment for rectal cancer, improvements on the outcomes have been observed since the introduction and widespread of the principles of total mesorectal excision (TME)[2]. Preoperative radiotherapy and chemotherapy have a major role in the treatment of locally advanced rectal tumors[3]. To perform an accurate mesorectal dissection achieving clean margins is mandatory for rectal resections. Obtaining both negative circumferential resection margin (CRM-) and a complete mesorectal excision is associated with lower recurrence rates an improved long-term survival[4-10].

Laparoscopic rectal surgery was introduced shortly after 1990. The earliest large randomized controlled trials (RCT) comparing conventional laparoscopic and open approaches for rectal cancer showed that the use of laparoscopy was associated with a lower blood loss, an earlier return of bowel movement, and a shorter length of hospital stay[11-14]. Further studies questioned the oncological safety of the approach, by means of obtaining a complete mesorectal quality or a composite pathologic outcome associating also free circumferential and distal margins[15-17]. Remarkably, the observed impairment should be reflected in the long-term oncologic prognosis in order to reach any clinical interest. The question remains still open after the publication of the mid-term (2-year) results of the latest trials[18-20]. Conventional laparoscopic instruments may not be appropriate for assuring the achievement of the best plane of dissection in all patients, especially in those with the narrow or irradiated pelvis[21]. Due to this, TME seems to be one of the procedures in which the robotic assistance will have a critical role[22-25].

At the time of the present review, the ROLARR study was the largest RCT comparing robotic-assisted *vs*. conventional laparoscopic surgery for patients with rectal cancer[26]. Two recent systematic reviews with meta-analyses summarized the outcomes from 7 and 5 RCTs with a similar design[27,28]. Other meta-analyses have been published including also non-randomized clinical trials[29,30]. No guidelines are now available suggesting the true role of robotics in colorectal surgery, high-quality clinical data is similarly lacking. In the present review, we dissected the current status of robotic TME, with special emphasis on surgical outcomes and near future perspectives.

BACKGROUND

A robot is a device that can be programmed to carry out a task, being controlled by mechanical and computing systems[31]. The concept of robotic surgery appeared in the 1970s as a military project of the Defense Advanced Research Project Administration endorsed by the National Aeronautics and Space Administration aiming to keep the surgeon from the battlefield[32]. In 1985, a robot was introduced into an operating theatre, an industrial robotic arm (PUMA 200) was modified to perform a preprogrammed intracranial biopsy. Shortly thereafter, the PROBOT® and ROBODOC® systems were developed, designed for transurethral prostatic resections and total hip arthroplasties, respectively[33,34]. The earliest systems required prior task programming, implying longer procedure duration and poor response to unexpected events. At the end of the 20th century, the way of conceiving abdominal surgery changed by the introduction of laparoscopy. The first laparoscopic colorectal surgery was performed in 1990 by Fowler[35]. In 1994, the automated endoscopic system for optimal positioning was the first real-time surgical manipulation system being commercialized. It consisted of an endoscope attached to a voice-controlled mechanical arm that modified its position following surgeon's orders. It allowed greater image stability and sometimes dispensed the need for an assistant but provided longer operative time compared with conventional laparoscopy[36,37].

In 2000, ZEUS® (Computer Motion, Goleta, California, USA), a three-armed robot mounted on the operating table; and the da Vinci® robot (Intuitive Surgical, Sunnyvale, California, USA) were developed. In 2003 Computer Motion was incorporated into Intuitive Surgical. The da Vinci® system provided a fourth arm and an independent console where the surgeon has a three-dimensional view of the field. Specifically designed devices with Endowrist® technology allow for 7º of freedom, 180º articulation and 540º rotation[38].

The latest release to date, the Xi version, appeared in 2014. It offers the possibility of adjusting the operating table without undocking the system, shortening the procedure length and allowing multi-quadrant single-docking procedures. Augmented-reality software allows the assessment of intestinal perfusion or real-time three-dimensional (3D) anatomical simulation of abdominal structures[39-41]. Senhance® Surgical Robotic System and the REVO-I® Robot Platform are the two other systems commercially available nowadays. Competitive industry players like Medtronic and Verb surgical (powered by GOOGLE® and Johnson & Johnson®) platforms are expected soon[42].

LEARNING CURVE OF ROBOTIC TME

The learning curve for robotic TME, from the beginning to the higher expertise, should include at least 20-23 cases, which is faster than for conventional laparoscopy[43,44]. Contrasting results have been reported regarding the impact of the previous proficiency on laparoscopy on the duration of the period[45,46]. Most of the publications evaluated the expertise with variables as "operative time", "bleeding" or "conversion" which may not be the most critical outcomes[47]. There is a wide agreement on the fact that operative times are longer during a learning curve, but a recent study on robotic rectal resection showed no relationship between extended operative time and morbidity[48]. The evaluation of the experience in oncologic surgery should also focus on the quality of the resected specimen, especially for rectal cancer resection. Only a recent meta-analysis showed no significant differences in CRM involvement between learning and competent surgeons. The authors did not found significant differences in the other clinic and pathologic variables, without evaluating the quality of the TME[49].

A learning curve is unavoidable, and robotic surgery requires special training and the development of new skills. The companies responsible for robotic systems are compelled by the Food and Drug Agency to develop technical training for the surgeons. The European Association of Endoscopic Surgeons (EAES) recommended a training officially-certified and based on a formal curriculum for skills and procedures[50]. The lack of standardization in robotic rectal surgery was specifically noted, this is critical to assure the safety and success of training surgeons in their future practice. Recent resources aim to provide an objective assessment of the acquired surgical skills to produce future standards for robotic surgeons on basic knowledge and procedural safety[50]. If any superiority favouring robotic TME is proven soon, the learning curve should not be an obstacle, but a necessary step for novel surgeons to reach the standards of quality. Noteworthy, there is an underlying and not despicable risk if surgeons abandon conventional laparoscopic surgery learning in favour of robotics. We may have soon a generation of surgeon incapable of performing laparoscopic surgery, with unclear but potentially serious consequences.

BENEFITS AND LIMITATIONS OF ROBOTIC RECTAL SURGERY

Technical advantages

Current robotic platforms display a 3D image, enhancing the visualization of the anatomical structures by improving the surgeon's depth perception and image quality. Compared to conventional laparoscopy, robotic surgery also allows to control a stable camera[47]. The system has recently incorporated the EndoWrist® technology, which improves dexterity and eliminates physiological tremor reducing the challenge of laparoscopic intra-corporeal suturing[51]. These technical advantages are expected to allow a better mesorectal dissection, preserving the integrity of the fascia and decreasing the odds of autonomic nerve injury resulting in sexual dysfunction, anterior resection syndrome, or urinary retention[38].

The use of robotic platforms is associated with better surgeon's ergonomics than those provided by conventional laparoscopy. Robotic assistance results in lesser activation of the upper-body mussels reducing musculoskeletal discomfort[52]. Berguer *et al.*[53] reported that robotic help makes less stressful performing complex tasks. Previous laparoscopic experience has a complex influence on the adaptation to the new approach[53]. Tele-surgery is the latest potential advantage of robotic surgery, allowing real-time international collaborations and mentoring[54].

Technical disadvantages

The loss of haptic feedback is still the main technical limitation of the available robotic platforms. A multi-modal pneumatic feedback system offering tactile, kinesthetic, and vibrotactile feedback was incorporated in the da Vinci® Surgical System[55]. Other platforms, as Senhance® Surgical Robotic System and the REVO-I® Robot Platform, also incorporated haptic feedback assistance[56].

Costs

Increased costs attributed to robotic surgery are the most important current impediment for the widespread of this technology. The economic impact is an important point to assess in the setting of increasing demands on limited health resources. To accurately measure costs has a particular difficulty at economic evaluations. Total costs rely on direct, indirect and intangible costs. Direct costs can be divided into fixed costs (to buy and maintain the robotic system), and variable costs (consumable instruments). The cost of a robotic platform is $1-$2.3 million[47]. Cost-analysis studies determined that robotic is more expensive than open and laparoscopic surgeries[57,58]. Baek *et al*.[58] in 2012, reported that robotic rectal surgery charges were between $7,150-10,700, and $1,240 for laparoscopic surgery[58]. The ROLARR trial showed that health-care costs in the robotic-assisted laparoscopic group (£11 853 or $13 668) were higher than in the conventional laparoscopic group (£10 874 or $12 556). The higher costs were attributed to longer theater occupation and the use of specific instruments. Conversely, Ielpo *et al*.[59] found that the mean overall costs were similar between robotic and laparoscopic approach, excluding the initial purchase of the robotic system[59].

Few studies have assessed the cost-effectiveness of robotic rectal surgery, it is difficult to assign a monetary value to the measured outcomes in this particular scenario[60]. Morelli *et al*.[61] observed that excluding fixed costs and comparing experienced phase of robotic surgery with the laparoscopic approach, the variable operative costs were similar[61]. Therefore, robotic expertise has a critical role in the operative costs, similar to the procedures standardization, the surgical team's consistency, and the institution's volume[62]. Robotic surgery could mitigate increased expenditures whether provide lesser risk of conversion and shorter hospitalization[29,63]. Indirect costs have not been deeply evaluated for robotic rectal resections. Only Bertani *et al*.[57] found a faster physical recovery after 1 month in the robotic group compared with open surgery[57]. The ROLARR did not found differences between laparoscopic and robotic surgery in bladder and sexual dysfunction rates[26]. No cost-utility study aiming to determine indirect costs has been reported to date. Further research is needed to evaluate the quality of life; including sexual, stool, and urinary functions, using utility measures like the disability-adjusted life-year and the quality-adjusted life-year, to accurately compare the outcomes of the different surgical alternatives. For the latest 20 years, da Vinci® System has dominated robotic surgery, the lack of adversaries led to rising costs and maybe slowed the evolution of the technology[42]. In the near future, with the introduction of new robotic platforms, this situation is expected to change dramatically.

OUTCOMES OF ROBOTIC SURGERY FOR RECTAL CANCER

Intraoperative outcomes

Some authors suggested the potential advantage of robotic TME over conventional laparoscopy decreasing the conversion rates to open surgery: Prete *et al*.[28] [Risk Ratio (RR), 0.58; 95%CI: 0.35-0.97; $P = 0.04$], Jones *et al*.[29] [Odds Ratio (OR), 0.40; 95%CI: 0.29-0.55; $P < 0.00001$], Ohtani *et al*.[64] (OR, 0.30; 95%CI: 0.19-0.46; $P < 0.00001$), and Lee *et al*.[65] (RR, 0.28; 95%CI: 0.15-0.54; $P < 0.0001$)[28,29,64,65]. The benefit has been related to the use of three-dimensional vision and articulated instruments, facilitating the dissection during TME.

The ROLARR study, however, only found benefits in the men subgroup[26]. Although the study found no significant differences in the rest of the short-term outcomes being evaluated, trial's sample estimation, and the varying expertise on robotics of the participating surgeons assured the debate after its publication[26]. Existing research demonstrated longer operative time for robotics compared with open and laparoscopic rectal resections[28,65,66]. Ohtani *et al.*[64] reported an operative time 44 minutes greater than laparoscopy [weighted mean difference (MD), 44.80; 95%CI: 28.44-61.15; $P < 0.00001$][64]. Lee *et al.*[67] showed no differences in operative time between robotic and transanal-TME[67]. Other studies reported less blood loss for robotic TME, compared with the open and laparoscopic approaches[68,69]. Intraoperative complications were found similar for robotic surgery when compared with the open and laparoscopic approaches[26,66].

Postoperative outcomes

Anastomotic leak rate was not significantly different for robotics compared with open and laparoscopic operations[28,69]. Laparoscopic, transanal, and robotic TME also showed similar leak and reoperation rates[67,70]. Postoperative ileus, wound infection, and urinary retention were similar between open, laparoscopic, transanal procedures in comparison with robotic approach[30,65,69]. Length of hospital stay was shorter after robotic surgery compared with open (7.5 days *vs.* 13.24 days)[66,69], but no difference was found when comparing it with conventional laparoscopy[28,70]. Perioperative complications and mortality rates appear to be similar for all four approaches[28,30,69]. Mortality is low in elective rectal surgery, with only 2 cases in each arm among 466 patients (0.9%) in the ROLARR study[26].

Pathologic outcomes

As robotic assistance seems to facilitate mesorectal dissection, particularly in mid and low rectal tumours, a reduced rate of positive CRM+ was presupposed to be one of the major benefits conferred by the novel technology. However, different studies showed that CRM+ is similar when compared with the other techniques. Jayne *et al.*[26] reported no statistically significant differences in the odds of CRM+ between robotic and laparoscopic groups (OR, 0.78; 95%CI: 0.35-1.76; $P = 0.56$)[26]. Accordingly, a propensity adjusted analysis of 7616 patients support both for the resection of locally advanced rectal cancer, with equivalent CRM- rates (93% *vs.* 94%; 95%CI: 0.69-1.06)[71].

The completeness of the mesorectal resection became a valuable item to assess the oncologic safety of a rectal resection and predicts tumor recurrence in the pelvis[72]. Rausa *et al.*[30] showed no significant differences in complete, near-complete or incomplete mesorectal excision between laparoscopic and robotic approaches (complete RR, 0.8; 95%CI: 0.7-1.0; nearly-complete RR, 1.6; 95%CI: 0.9-2.7; incomplete RR, 1.5; 95%CI: 0.8-2.5)[30].

Liao *et al.*[27] associated the robotic approach with a longer distance to the distal margin in comparison with laparoscopy (MD, 0.83 cm, 95%CI: 0.29-1.37; $P = 0.003$)[27]. When comparing robotic and open surgeries, no differences were found (MD, 0.17; 95%CI: -0.14 to 0.48; $P = 0.27$)[69].

Truong *et al.*[73] analysed a retrospective cohort of patients looking at successful resections, defined as a circumferential and distal resection margins < 1 mm and complete mesorectal resection, which were similar between the robotic (75%) and open (76%) approaches[73]. There were no differences in the studies comparing all four approaches for rectal cancer regarding the number of lymph nodes retrieved[26,27,30,69].

Long-term oncologic outcomes

Local recurrence rates were similar between laparoscopic *vs.* robotic (RR, 1.4; 95%CI: 0.7-2.4) and transanal-TME *vs.* robotic (RR, 1.4; 95%CI: 0.5-3.4) in the meta-analysis performed by Rausa *et al.*[30]. Moreover, Ohtani *et al.*[64] also reported no differences in terms of local, metastatic, and overall recurrences, 3-year OS and 3-year DFS between robotic and laparoscopic approaches[64]. In their recent meta-analysis, Liao *et al.*[27]

described the OS and DFS after a mean follow-up of 29.2 months in the robotic group and 18.7 months in the laparoscopic group. The OS was 100% in the robotic group and 94.1% in the laparoscopic group. The DFS was 100% in the robotic group and 88.2% in the laparoscopic group. Studies comparing robotic and open resections also found non-significant long-term outcomes between them. Five-year DFS was 73.2% and 69.5% in the robotic and open groups, respectively. Five-year OS was 85.0% in the robotic and 76.1% in the open approach[69].

Functional outcomes

Two trials evaluated the urinary function of using the International Prostate Symptom Score (I-PSS) comparing robotic and laparoscopy TME. Lee *et al.*[65] showed improved urinary continence for robotic surgery at 3 months, but there was no statistical difference on I-PSS at 6 or 12 months after surgery[65]. Erectile dysfunction rates did not differ between robotic and laparoscopic groups (OR, 0.54; 95%CI: 0.19-1.58; P = 0.26)[64]. Somashekhar *et al.*[66] analyzed erectile dysfunction and retrograde ejaculation using the European Organization for Research and Treatment of Cancer questionnaire QLQ-C38. A total of 18 % of male patients in the robotic group and 26% in the open group had sexual dysfunction[66]. Li *et al.*[70] published a meta-analysis reporting lesser incidence of urinary retention using robotic TME[70]. The ROLARR trial evaluated bladder function, male sexual function and female sexual function separately by using I-PSS, International Index of Erectile Function and Female Sexual Function Index, respectively. This study did not find any differences between laparoscopic and robotic surgery after 6-months follow-up[26].

FUTURE PERSPECTIVES

Fluorescence-guided robotic rectal resection

Near-infrared (NIR) light (650-900 nm) has optimum characteristics for *in vivo* imaging[74], resulting in higher penetration depth and minimum background auto-fluorescence[75]. Indocyanine green (ICG) is the only available fluorophore in the NIR window, it is confined into the vascular compartment through binding plasmatic proteins presenting low toxicity[76]. The applications of ICG are increasing, especially at colorectal cancer surgery. NIR has been used for assessing tissue perfusion and to detect sentinel nodes, peritoneal carcinomatosis, or liver metastases[77-80]. Anastomotic leak remains as the main complication in colorectal surgery, ischemia of intestinal stumps constitutes a major risk factor[81,82]. To determine the viability of the intestinal stumps when performing the anastomosis may decrease the odds of leak development. The earliest RCT on the subject just showed a reduction (9% *vs*. 5%), but non-significant, of the anastomotic leak rate in the fluorescence arm after colorectal resection[83]. Only two retrospective studies have been conducted using robotic technology[84,85].

The "enhanced permeability and retention" effect is the mechanism involved. It reflects the affinity of ICG towards tumoral and near-tumoral tissue due to neovascularization. Few studies are trying to elucidate the role of ICG in carcinomatosis, with contrasting results[79,86]. Neoadjuvant therapy with bevacizumab decreases the sensitivity of ICG to detect peritoneal metastases of colorectal cancer[87]. Mucinous metastases cannot be identified with ICG. A recent RCT comparing the use of white light versus NIR and ICG showed increasing sensitivity from 80% to 96%[88]. ICG can be alternatively used to improve surgical safety when marking important structures, as the ureters or the hepatic ducts, and even for tattooing colonic neoplasms instead of ink[89].

Robotic-assisted transanal TME

Over the last few years, the transanal approach gained popularity as seemed to facilitate complex pelvic dissections. Several studies reported that Ta-TME achieved similar technical success and perioperative outcomes than laparoscopic TME, with a lower conversion rate[90]. Recent studies also showed that serious complications secondary to wrong down-to-up dissection planes were not despicable, same for anastomotic leaks[91]. To improve the accuracy of the transanal dissection, robotic technology could also be helpful[92]. Two surgical teams (abdominal and perineal) can work together with the new platforms[93]. At present, however, further investigations are still needed to assure the long-term functional, and more critically, the oncological outcomes of the transanal approach for resecting rectal tumors[94].

CONCLUSION

The use of robotic assistance provides interesting improvements that may overcome some of the technical limitations of conventional laparoscopic instruments. Acceptable oncologic outcomes have been similarly reported. Increased costs, poor availability, and special training requirements are still important barriers to be overcome. Surgeons and health-care providers should notice that no important benefits have been yet demonstrated for robotic TME compared with the other available surgical alternatives. The combination of emerging technology, technical refinements, and an optimal trainee learning system may allow robotic surgery to be a gold standard for rectal cancer in the near future.

DECLARATIONS

Authors' contributions

Concept and design: Sebastián-Tomás JC, García-Granero E, Martínez-Pérez A
Collection and assembly of data: Sebastián-Tomás JC, Santarrufina-Martínez S, Navarro-Martínez S, Gonzálvez-Guardiola P, Martínez-López E, Payá-Llorente C
Provision of study materials or patients, data analysis and interpretation, manuscript writing and final approval: All authors

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.
2. Heald RJ, Husband EM, Ryall RD. The mesorectum in rectal cancer surgery--the clue to pelvic recurrence? Br J Surg 1982;69:613-6.
3. De Caluwe L, Van Nieuwenhove Y, Ceelen WP. Preoperative chemoradiation versus radiation alone for stage II and III resectable rectal cancer. Cochrane Database Syst Rev 2013;(2):CD006041.
4. Quirke P, Steele R, Monson J, Grieve R, Khanna S, et al. Effect of the plane of surgery achieved on local recurrence in patients with operable rectal cancer: a prospective study using data from the MRC CR07 and NCIC-CTG CO16 randomised clinical trial. Lancet 2009;373:821-8.

5. Leonard D, Penninckx F, Laenen A, Kartheuser A; Procare. Scoring the quality of total mesorectal excision for the prediction of cancer-specific outcome. Colorectal Dis 2015;17:O115-22.
6. Kitz J, Fokas E, Beissbarth T, Strobel P, Wittekind C, et al. Association of plane of total mesorectal excision with prognosis of rectal cancer: secondary analysis of the CAO/ARO/AIO-04 Phase 3 randomized clinical trial. JAMA Surg 2018;153:e181607.
7. Kusters M, Marijnen CA, van de Velde CJ, Rutten HJ, Lahaye MJ, et al. Patterns of local recurrence in rectal cancer; a study of the Dutch TME trial. Eur J Surg Oncol 2010;36:470-6.
8. Nagtegaal ID, Quirke P. What is the role for the circumferential margin in the modern treatment of rectal cancer? J Clin Oncol 2008;26:303-12.
9. Birbeck KF, Macklin CP, Tiffin NJ, Parsons W, Dixon MF, et al. Rates of circumferential resection margin involvement vary between surgeons and predict outcomes in rectal cancer surgery. Ann Surg 2002;235:449-57.
10. Garcia-Granero E, Faiz O, Munoz E, Flor B, Navarro S, et al. Macroscopic assessment of mesorectal excision in rectal cancer: a useful tool for improving quality control in a multidisciplinary team. Cancer 2009;115:3400-11.
11. van der Pas MH, Haglind E, Cuesta MA, Furst A, Lacy AM, et al. Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. Lancet Oncol 2013;14:210-8.
12. Kang SB, Park JW, Jeong SY, Nam BH, Choi HS, et al. Open versus laparoscopic surgery for mid or low rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): short-term outcomes of an open-label randomised controlled trial. Lancet Oncol 2010;11:637-45.
13. Guillou PJ, Quirke P, Thorpe H, Walker J, Jayne DG, et al. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. Lancet 2005;365:1718-26.
14. Martinez-Perez A, Carra MC, Brunetti F, de'Angelis N. Short-term clinical outcomes of laparoscopic vs open rectal excision for rectal cancer: A systematic review and meta-analysis. World J Gastroenterol 2017;23:7906-16.
15. Fleshman J, Branda M, Sargent DJ, Boller AM, George V, et al. Effect of laparoscopic-assisted resection vs open resection of Stage II or III rectal cancer on pathologic outcomes: the ACOSOG Z6051 randomized clinical trial. JAMA 2015;314:1346-55.
16. Stevenson AR, Solomon MJ, Lumley JW, Hewett P, Clouston AD, et al. Effect of laparoscopic-assisted resection vs open resection on pathological outcomes in rectal cancer: the ALaCaRT randomized clinical trial. JAMA 2015;314:1356-63.
17. Martinez-Perez A, Carra MC, Brunetti F, de'Angelis N. Pathologic outcomes of laparoscopic vs open mesorectal excision for rectal cancer: a systematic review and meta-analysis. JAMA Surg 2017;152:e165665.
18. Fleshman J, Branda ME, Sargent DJ, Boller AM, George VV, et al. Disease-free survival and local recurrence for laparoscopic resection compared with open resection of Stage II to III rectal cancer: follow-up results of the ACOSOG Z6051 randomized controlled trial. Ann Surg 2019;269:589-95.
19. Stevenson ARL, Solomon MJ, Brown CSB, Lumley JW, Hewett P, et al. Disease-free survival and local recurrence after laparoscopic-assisted resection or open resection for rectal cancer: the australasian laparoscopic cancer of the rectum randomized clinical trial. Ann Surg 2019;269:596-602.
20. Martinez-Perez A, de'Angelis N. Comment on "Mid-term results of ACOSOG Z6051 trial sustain the unresolved debate". Ann Surg 2019;270:e52-3.
21. Petrucciani N, Martinez-Perez A, Bianchi G, Memeo R, Brunetti F, et al. The use of laparoscopy for locally advanced rectal cancer. Minerva Chir 2018;73:77-92.
22. de'Angelis N, Lizzi V, Azoulay D, Brunetti F. Robotic versus laparoscopic right colectomy for colon cancer: analysis of the initial simultaneous learning curve of a surgical fellow. J Laparoendosc Adv Surg Tech A 2016;26:882-92.
23. Ahmed J, Nasir M, Flashman K, Khan J, Parvaiz A. Totally robotic rectal resection: an experience of the first 100 consecutive cases. Int J Colorectal Dis 2016;31:869-76.
24. de'Angelis N, Portigliotti L, Azoulay D, Brunetti F. Robotic surgery: a step forward in the wide spread of minimally invasive colorectal surgery. J Minim Access Surg 2015;11:285-6.
25. de'Angelis N, Portigliotti L, Brunetti F. Robot-assisted rectal cancer surgery deserves a fair trial. Colorectal Dis 2015;17:824-5.
26. Jayne D, Pigazzi A, Marshall H, Croft J, Corrigan N, et al. Effect of robotic-assisted vs conventional laparoscopic surgery on risk of conversion to open laparotomy among patients undergoing resection for rectal cancer: the ROLARR randomized clinical trial. Jama 2017;318:1569-80.
27. Liao G, Zhao Z, Deng H, Li X. Comparison of pathological outcomes between robotic rectal cancer surgery and laparoscopic rectal cancer surgery: A meta-analysis based on seven randomized controlled trials. Int J Med Robot 2019;15:e2027.
28. Prete FP, Pezzolla A, Prete F, Testini M, Marzaioli R, et al. Robotic versus laparoscopic minimally invasive surgery for rectal cancer: a systematic review and meta-analysis of randomized controlled trials. Ann Surg 2018;267:1034-46.
29. Jones K, Qassem MG, Sains P, Baig MK, Sajid MS. Robotic total meso-rectal excision for rectal cancer: a systematic review following the publication of the ROLARR trial. World J Gastrointest Oncol 2018;10:449-64.
30. Rausa E, Bianco F, Kelly ME, Aiolfi A, Petrelli F, et al. Systemic review and network meta-analysis comparing minimal surgical techniques for rectal cancer: quality of total mesorectum excision, pathological, surgical, and oncological outcomes. J Surg Oncol 2019;119:987-98.
31. Diana M, Marescaux J. Robotic surgery. Br J Surg 2015;102:e15-28.
32. George EI, Brand TC, LaPorta A, Marescaux J, Satava RM. Origins of robotic surgery: from skepticism to standard of care. JSLS 2018;22:e2018.00039.
33. Bargar WL, Bauer A, Borner M. Primary and revision total hip replacement using the robodoc system. Clin Orthop Relat Res

1998;(354):82-91.
34. Harris SJ, Arambula-Cosio F, Mei Q, Hibberd RD, Davies BL, et al. The probot--an active robot for prostate resection. Proc Inst Mech Eng H 1997;211:317-25.
35. Fowler DL, White SA. Laparoscopy-assisted sigmoid resection. Surg Laparosc Endosc 1991;1:183-8.
36. Kraft BM, Jager C, Kraft K, Leibl BJ, Bittner R. The AESOP robot system in laparoscopic surgery: increased risk or advantage for surgeon and patient? Surg Endosc 2004;18:1216-23.
37. Cheng CL, Rezac C. The role of robotics in colorectal surgery. BMJ 2018;360:j5304.
38. Nozawa H, Watanabe T. Robotic surgery for rectal cancer. Asian J Endosc Surg 2017;10:364-71.
39. Gorpas D, Phipps J, Bec J, Ma D, Dochow S, et al. Autofluorescence lifetime augmented reality as a means for real-time robotic surgery guidance in human patients. Sci Rep 2019;9:1187.
40. Atallah S, Parra-Davila E, Melani AGF, Romagnolo LG, Larach SW, et al. Robotic-assisted stereotactic real-time navigation: initial clinical experience and feasibility for rectal cancer surgery. Tech Coloproctol 2019;23:53-63.
41. Porpiglia F, Checcucci E, Amparore D, Autorino R, Piana A, et al. Augmented-reality robot-assisted radical prostatectomy using hyper-accuracy three-dimensional reconstruction (HA3D) technology: a radiological and pathological study. BJU Int 2019;123:834-45.
42. Andolfi C, Umanskiy K. Appraisal and current considerations of robotics in colon and rectal surgery. J Laparoendosc Adv Surg Tech A 2019;29:152-8.
43. Huang CW, Yeh YS, Ma CJ, Choy TK, Huang MY, et al. Robotic colorectal surgery for laparoscopic surgeons with limited experience: preliminary experiences for 40 consecutive cases at a single medical center. BMC Surg 2015;15:73.
44. Jimenez-Rodriguez RM, Rubio-Dorado-Manzanares M, Diaz-Pavon JM, Reyes-Diaz ML, Vazquez-Monchul JM, et al. Learning curve in robotic rectal cancer surgery: current state of affairs. Int J Colorectal Dis 2016;31:1807-15.
45. Odermatt M, Ahmed J, Panteleimonitis S, Khan J, Parvaiz A. Prior experience in laparoscopic rectal surgery can minimise the learning curve for robotic rectal resections: a cumulative sum analysis. Surg Endosc 2017;31:4067-76.
46. Foo CC, Law WL. The learning curve of robotic-assisted low rectal resection of a novice rectal surgeon. World J Surg 2016;40:456-62.
47. Mohd Azman ZA, Kim SH. A review on robotic surgery in rectal cancer. Transl Gastroenterol Hepatol 2016;1:5.
48. Duchalais E, Machairas N, Kelley SR, Landmann RG, Merchea A, et al. Does prolonged operative time impact postoperative morbidity in patients undergoing robotic-assisted rectal resection for cancer? Surg Endosc 2018;32:3659-66.
49. Gachabayov M, You K, Kim SH, Yamaguchi T, Jimenez-Rodriguez R, et al. Meta-analysis of the impact of the learning curve in robotic rectal cancer surgery on histopathologic outcomes. Surg Technol Int 2019;34:139-55.
50. Szold A, Bergamaschi R, Broeders I, Dankelman J, Forgione A, et al. European association of endoscopic surgeons (EAES) consensus statement on the use of robotics in general surgery. Surg Endosc 2015;29:253-88.
51. Baek SJ, Kim SH. Robotics in general surgery: an evidence-based review. Asian J Endosc Surg 2014;7:117-23.
52. Zihni AM, Ohu I, Cavallo JA, Cho S, Awad MM. Ergonomic analysis of robot-assisted and traditional laparoscopic procedures. Surg Endosc 2014;28:3379-84.
53. Berguer R, Smith W. An ergonomic comparison of robotic and laparoscopic technique: the influence of surgeon experience and task complexity. J Surg Res 2006;134:87-92.
54. Choi PJ, Oskouian RJ, Tubbs RS. Telesurgery: past, present, and future. Cureus 2018;10:e2716.
55. Abiri A, Pensa J, Tao A, Ma J, Juo YY, et al. Multi-Modal haptic feedback for grip force reduction in robotic surgery. Sci Rep 2019;9:5016.
56. Rao PP. Robotic surgery: new robots and finally some real competition! World J Urol 2018;36:537-41.
57. Bertani E, Chiappa A, Biffi R, Bianchi PP, Radice D, et al. Assessing appropriateness for elective colorectal cancer surgery: clinical, oncological, and quality-of-life short-term outcomes employing different treatment approaches. Int J Colorectal Dis 2011;26:1317-27.
58. Baek SJ, Kim SH, Cho JS, Shin JW, Kim J. Robotic versus conventional laparoscopic surgery for rectal cancer: a cost analysis from a single institute in Korea. World J Surg 2012;36:2722-9.
59. Ielpo B, Duran H, Diaz E, Fabra I, Caruso R, et al. Robotic versus laparoscopic surgery for rectal cancer: a comparative study of clinical outcomes and costs. Int J Colorectal Dis 2017;32:1423-9.
60. Kim CW, Baik SH, Roh YH, Kang J, Hur H, et al. Cost-effectiveness of robotic surgery for rectal cancer focusing on short-term outcomes: a propensity score-matching analysis. Medicine (Baltimore) 2015;94:e823.
61. Morelli L, Guadagni S, Lorenzoni V, Di Franco G, Cobuccio L, et al. Robot-assisted versus laparoscopic rectal resection for cancer in a single surgeon's experience: a cost analysis covering the initial 50 robotic cases with the da Vinci Si. Int J Colorectal Dis 2016;31:1639-48.
62. Biffi R, Luca F, Bianchi PP, Cenciarelli S, Petz W, et al. Dealing with robot-assisted surgery for rectal cancer: Current status and perspectives. World J Gastroenterol 2016;22:546-56.
63. Cleary RK, Mullard AJ, Ferraro J, Regenbogen SE. The cost of conversion in robotic and laparoscopic colorectal surgery. Surg Endosc 2018;32:1515-24.
64. Ohtani H, Maeda K, Nomura S, Shinto O, Mizuyama Y, et al. Meta-analysis of robot-assisted versus laparoscopic surgery for rectal cancer. In Vivo 2018;32:611-23.
65. Lee SH, Lim S, Kim JH, Lee KY. Robotic versus conventional laparoscopic surgery for rectal cancer: systematic review and meta-analysis. Ann Surg Treat Res 2015;89:190-201.
66. Somashekhar SP, Ashwin KR, Rajashekhar J, Zaveri S. Prospective randomized study comparing robotic-assisted surgery with traditional laparotomy for rectal cancer-Indian study. Indian J Surg 2015;77:788-94.

67. Lee L, de Lacy B, Gomez Ruiz M, Liberman AS, Albert MR, et al. A multicenter matched comparison of transanal and robotic total mesorectal excision for mid and low-rectal adenocarcinoma. Ann Surg 2018; doi: 10.1097/SLA.0000000000002862.
68. Yang Y, Wang F, Zhang P, Shi C, Zou Y, et al. Robot-assisted versus conventional laparoscopic surgery for colorectal disease, focusing on rectal cancer: a meta-analysis. Ann Surg Oncol 2012;19:3727-36.
69. Liao G, Li YB, Zhao Z, Li X, Deng H, et al. Robotic-assisted surgery versus open surgery in the treatment of rectal cancer: the current evidence. Sci Rep 2016;6:26981.
70. Li X, Wang T, Yao L, Hu L, Jin P, et al. The safety and effectiveness of robot-assisted versus laparoscopic TME in patients with rectal cancer: A meta-analysis and systematic review. Medicine (Baltimore) 2017;96:e7585.
71. Hopkins MB, Geiger TM, Bethurum AJ, Ford MM, Muldoon RL, et al. Comparing pathologic outcomes for robotic versus laparoscopic surgery in rectal cancer resection: a propensity adjusted analysis of 7616 patients. Surg Endosc 2019; doi: 10.1007/s00464-019-07032-1.
72. Martinez-Perez A, de'Angelis N. Oncologic results of conventional laparoscopic TME: is the intramesorectal plane really acceptable? Tech Coloproctol 2018;22:831-4.
73. Truong A, Lopez N, Fleshner P, Zaghiyan K. Preservation of pathologic outcomes in robotic versus open resection for rectal cancer: can the robot fill the minimally invasive gap? Am Surg 2018;84:1876-81.
74. Owens EA, Henary M, El Fakhri G, Choi HS. Tissue-specific near-infrared fluorescence imaging. Acc Chem Res 2016;49:1731-40.
75. Frangioni JV. In vivo near-infrared fluorescence imaging. Curr Opin Chem Biol 2003;7:626-34.
76. Alander JT, Kaartinen I, Laakso A, Patila T, Spillmann T, et al. A review of indocyanine green fluorescent imaging in surgery. Int J Biomed Imaging 2012;2012:940585.
77. Liberale G, Bourgeois P, Larsimont D, Moreau M, Donckier V, et al. Indocyanine green fluorescence-guided surgery after IV injection in metastatic colorectal cancer: a systematic review. Eur J Surg Oncol 2017;43:1656-67.
78. Degett TH, Andersen HS, Gogenur I. Indocyanine green fluorescence angiography for intraoperative assessment of gastrointestinal anastomotic perfusion: a systematic review of clinical trials. Langenbecks Arch Surg 2016;401:767-75.
79. Liberale G, Bohlok A, Bormans A, Bouazza F, Galdon MG, et al. Indocyanine green fluorescence imaging for sentinel lymph node detection in colorectal cancer: A systematic review. Eur J Surg Oncol 2018;44:1301-6.
80. Lieto E, Auricchio A, Cardella F, Mabilia A, Basile N, et al. Fluorescence-guided surgery in the combined treatment of peritoneal carcinomatosis from colorectal cancer: preliminary results and considerations. World J Surg 2018;42:1154-60.
81. Kang CY, Halabi WJ, Chaudhry OO, Nguyen V, Pigazzi A, et al. Risk factors for anastomotic leakage after anterior resection for rectal cancer. JAMA Surg 2013;148:65-71.
82. Vignali A, Gianotti L, Braga M, Radaelli G, Malvezzi L, et al. Altered microperfusion at the rectal stump is predictive for rectal anastomotic leak. Dis Colon Rectum 2000;43:76-82.
83. De Nardi P, Elmore U, Maggi G, Maggiore R, Boni L, et al. Intraoperative angiography with indocyanine green to assess anastomosis perfusion in patients undergoing laparoscopic colorectal resection: results of a multicenter randomized controlled trial. Surg Endosc 2019; doi: 10.1007/s00464-019-06730-0.
84. Jafari MD, Lee KH, Halabi WJ, Mills SD, Carmichael JC, et al. The use of indocyanine green fluorescence to assess anastomotic perfusion during robotic assisted laparoscopic rectal surgery. Surg Endosc 2013;27:3003-8.
85. Kim JC, Lee JL, Park SH. Interpretative guidelines and possible indications for indocyanine green fluorescence imaging in robot-assisted sphincter-saving operations. Dis Colon Rectum 2017;60:376-84.
86. Barabino G, Klein JP, Porcheron J, Grichine A, Coll JL, et al. Intraoperative near-infrared fluorescence imaging using indocyanine green in colorectal carcinomatosis surgery: proof of concept. Eur J Surg Oncol 2016;42:1931-7.
87. Filippello A, Porcheron J, Klein JP, Cottier M, Barabino G. Affinity of Indocyanine green in the detection of colorectal peritoneal carcinomatosis. Surg Innov 2017;24:103-8.
88. Sluiter NR, Vlek SL, Wijsmuller AR, Brandsma HT, de Vet HCW, et al. Narrow-band imaging improves detection of colorectal peritoneal metastases: a clinical study comparing advanced imaging techniques. Ann Surg Oncol 2019;26:156-64.
89. Lee SJ, Sohn DK, Han KS, Kim BC, Hong CW, et al. Preoperative tattooing using indocyanine green in laparoscopic colorectal surgery. Ann Coloproctol 2018;34:206-11.
90. Penna M, Hompes R, Arnold S, Wynn G, Austin R, et al. Transanal total mesorectal excision: international registry results of the first 720 cases. Ann Surg 2017;266:111-7.
91. Roodbeen SX, Penna M, Mackenzie H, Kusters M, Slater A, et al. Transanal total mesorectal excision (TaTME) versus laparoscopic TME for MRI-defined low rectal cancer: a propensity score-matched analysis of oncological outcomes. Surg Endosc 2019;33:2459-67.
92. Gomez Ruiz M, Parra IM, Palazuelos CM, Martin JA, Fernandez CC, et al. Robotic-assisted laparoscopic transanal total mesorectal excision for rectal cancer: a prospective pilot study. Dis Colon Rectum 2015;58:145-53.
93. Protyniak B, Jorden J, Farmer R. Multiquadrant robotic colorectal surgery: the da Vinci Xi vs Si comparison. J Robot Surg 2018;12:67-74.
94. Larsen SG, Pfeffer F, Kørner H; Norwegian Colorectal Cancer Group. Norwegian moratorium on transanal total mesorectal excision. Br J Surg 2019;106:1120-1.

Mini-invasive Surgery

Systematic Review

Open Access

Check for updates

Robotic synchronous treatment of colorectal cancer and liver metastasis: state of the art

Anita Sammarco[1], Nicola de'Angelis[2], Mario Testini[1], Riccardo Memeo[3]

[1]Department of Biomedical Sciences and Human Oncology, Unit of Endocrine, Digestive and Emergency Surgery, University Medical School of Bari, Bari 70121, Italy.
[2]Department of Digestive and Hepato-Pancreato-Biliary Surgery, Henri Mondor University Hospital, AP-HP, Université Paris-Est Créteil (UPEC), Créteil 94010, France.
[3]Department of Emergency and Organ Transplant, Institute of General Surgery and Liver Transplantation, University of Bari, Bari 70124, Italy.

Correspondence to: Dr. Riccardo Memeo, Department of Emergency and Organ Transplant, Policlinico di Bari, Bari 70100, Italy. E-mail: drmemeo@yahoo.it

How to cite this article: Sammarco A, de'Angelis N, Testini M, Memeo R. Robotic synchronous treatment of colorectal cancer and liver metastasis: state of the art. *Mini-invasive Surg* 2019;3:31. http://dx.doi.org/10.20517/2574-1225.2019.33

Received: 2 Sep 2019 **First Decision**: 2 Sep 2019 **Revised**: 9 Oct 2019 **Accepted**: 9 Oct 2019 **Published**: 25 Oct 2019

Science Editor: Giulio Belli **Copy Editor**: Cai-Hong Wang **Production Editor**: Jing Yu

Abstract

Aim: To analyze the series in literature of pure robotic surgery.

Methods: A complete review of the literature was performed to identify papers with data concerning robotic synchronous treatment of colorectal liver metastases.

Results: Three papers demonstrate the feasibility of this kind of synchronous treatment.

Conclusion: Robotic synchronous treatment of primary tumor and colorectal liver metastasis is feasible and safe.

Keywords: Robotic liver surgery, minimally invasive liver surgery, liver surgery, hepatectomy, colorectal liver metastasis

INTRODUCTION

Colorectal cancer (CRC) remains the third cause of cancer in the United States, and liver is considered the most common site of metastasis. Surgical management of patients with primary CRC with liver metastasis is still controversial with different opinion on the subject[1]. In patients with resectable disease, surgical resection can be considered the only potentially curative treatment even if operative sequence on the management of CRC and liver metastasis (CLM) still remain unclear[2]. Considering that 20%-40% of all patients with CRC presents at the time of diagnosis, two main strategies are available for patients with synchronous metastasis, treating primarily the liver (liver first) or the colon (colon first). In some cases, especially in case of oligometastatic lesion of the liver, considering the spread of parenchymal sparing surgery[3], it has been demonstrated that synchronous treatment could be considered a safe option, with acceptable morbidity and mortality[2]. Initially, the introduction of minimally invasive surgery (MIS) has probably limited synchronous metastasis treatment due to the technical difficulties of two different kind of resection. Despite this, nowadays, various studies have demonstrated the feasibility of MIS for synchronous liver and CRC[4]. With the introduction of robotic surgery, it represent a valid alternative lo laparoscopic surgery achieve optimal surgical and oncological outcomes. Considering robotic surgery, The well-known advantages of for laparoscopic surgery are preserved (shorter length of stay, reduced blood loss and postoperative morbidity) adding the advantages of robotic[5-8] (magnified 3d dimensional vision, a very good access allowed for posterosuperior segment's lesions or in contact with main liver vessels, less development of adhesions, tremor suppression, flexibility of the instruments).

The aim of this study is to present a systematic review of the literature to present the results of robotic surgery for colorectal liver metastasis in terms of short and long terms results.

METHODS

The present study was designed following the PRISMA guidelines.

A systematic literature search was performed by two authors (Sammarco A, Memeo R) using PubMed, EMBASE, Scopus and Cochrane Library Central restricting to papers in English language, finding studies and articles published from 1998 to 2018, focusing the study on the synchronized treatment of the liver metastasis and the CRC. All studies including patients who underwent robotic liver resection for colorectal liver metastasis were considered as eligible for the study, especially studies who considered synchronous pure robotic resection of CLM and CRC.

The following MESH search in heading were used: "robotic", "robot-assisted", "minimally invasive", "liver metastasis", "colorectal cancer", "stage 4", "combined resection", "simultaneous resection", and "synchronous resection".

All series containing other liver resection for different pathologies were excluded.

RESULTS

We retrospectively reviewed collected data included OT, perioperative blood loss, disease free, overall survival. We identified 16 relevant articles, to analyse the role of the MIS in patients with colorectal liver metastases (CRLM) and previous or synchronous surgery, focusing our attention on robotic assisted surgery (RAS). Just three of this 16 concerned CRLM only.

CRLM and RAS

Actually in literature, due to the reduced number of series describing RAS liver resection, most series comprehend different kind of pathology, mostly hepatocellular carcinoma and CRLM. Only 3 series described detailed results with only CRLM [Table 1][9-11]: 2 were retrospective and 1 prospective The number of patients ranged from 6 to 59. No data were available on number of resected lesions. Only one series presented major resection: 1 left hepatectomy, 3 right hepatectomy in a total of 82 resected patients

Table 1. Current state of the art of series with syncronous treatment of colorectal liver metastases and primary cancer

Author, type study	Period	No. of Patient	Syncronous resection	Major resection, *n* (%)	OT (min)	Perop BL (mL)	Conv (%)	Morbidity (%)	Major morb, *n* (%)	Mortality (90 days), *n* (%)	Length of stay	R0, *n* (%)	Disease free	Overall survival
Guerra *et al.*[9]	01/2008 - 02/2018	59	4	13.55%	210	200	12%	27%	n.a.	0%	6	92%	1-year DFS 83.5% 3-year DFS 41.9%	1-year OS 90.4% 3-year OS 66.1
Guadagni *et al.*[10]	05/ 2012 - 04/2018	20	3	0%	198.5 ± 98	250	0%	25%	n.a.	0%	4.7 ± 1.8	100%	1-year 89.5% 3-year 35.8%	100%
Dwyer *et al.*[11]	02/2013 - 06/2014	6	3	0%	401	316	0%	66.5%	Pelvic abscess (33.3%)	0%	4.5	100%	9.5 months (media)	5-year survival ranges from 25% to 40%

for CRLM. Operative time ranged from 198.5 min to 401 min. Perioperative Blood loss ranged from 200 mL to 316 mL. Conversion tax ranged from 0% to 12%. Complications and major morbidity included delayed wound healing after an abdominal perineal resection (APR) and a delayed rectal anastomotic failure after ileostomy reversal in synchronous resection[11], 1 postoperative bile leak, 2 heart failure[9]. 90 days mortality was 0%. The length of stay ranged from 4.5 days to 6 days. The rate of R0 resections ranged from 92% to 100%.

Synchronous treatment

The role of synchronous treatment was largely described in literature. In these three papers included in the review, we have different attitude. In the more extensive series described by Guerra *et al.*[9], 59 patients underwent robotic CLMR, describing only 4 cases of synchronous colorectal resection (3 right colectomy and 1 left colectomy). No data are available on postoperative outcome colorectal resection. Guadagni *et al.*[10] described 20 cases of CRLM resection but only three synchronous RAS, performing 2 right colectomies, 1 APR. Dwyer *et al.*[11] described 3 low anterior resection, 1 right colectomy and 2 APR. Only in 2 cases colorectal anastomosis was performed, describing 1 anastomotic leakage. In these paper authors describe only minor liver resection associated with colorectal resection.

DISCUSSION

This systematic review confirmed the benefits of robotic approach with satisfying results, even if more extensive series and long-term results are still unclear, they are expected to be reported in the future studies.

Robotic surgery has been considered as an alternative to laparoscopic surgery to reduce the technical difficulties of laparoscopic procedure, maintaining the benefit of minimally invasive surgery. In this idea, simultaneous resection of liver and CRC could be considered a good indication for robotic surgery, due the possibility to perform both surgery in the same surgical procedure in two different surgical fields. Synchronous MIS resection has been well described in laparoscopic surgery[12], but this strategy needs to be confirmed in robotic surgery in future, considering the increased diffusion Da Vinci robot and the progressive reduction of procedure related costs.

One of the main data available reading this review, is the pauperism of cases of synchronous resection. Only few series described resection for colorectal liver metastasis, most of them described as wedge resection. In all literature, only 8 case on 85 describe simultaneous resection, demonstrating that the synchronous approach still remains limited to few cases, despite the technical advantage of robotic surgery. As described in our paper, few synchronous procedure were performed, with two main limitations evidenced by the data, evidencing the difficulties to perform synchronous resection with major hepatectomies (only one series describe 13.5% of major resection) and to perform colorectal anastomosis, due to the higher risk of anastomotic leak in patients who underwent pedicle clamping for control of bleeding during liver resection.

In synchronous resection, usually liver resection anticipates colon resection. The management of bleeding remains a priority in this kind of resection and prolonged portal vein occlusion should be avoided in order to reduce the risk of damage the colonic anastomosis[6,13]: the prolonged vascular clamping leads to the transient portal hypertension with edema of the intestinal mucosa, responsible of the colorectal anastomotic failure[14], so the use of the intermittent Pringle's maneuver has to be carefully shrewd.

Another important data evidenced by review is that despite an augmented duration of surgery due to the necessity to perform synchronous operation, operative time still remains acceptable and comparable to laparoscopic, non-impacting the length of stay.

Conversion rate still remains low, comparable to laparoscopic series[15], confirming how the augmented dexterity probably associated to the high selection of patients guarantee a reduced rate of conversion.

Postoperative morbidity and mortality are acceptable, confirming the data reported by minimally invasive surgery. In the series of Dwyer *et al*.[11], an anastomotic leakage is described, and this event strongly impact postoperative course due to the necessity of reoperation, questioning the risk of performing the colorectal anastomosis during synchronous resection.

Even if more studies are still required to define the oncologic outcome, RAS seems also expendable in a one-stage minimally invasive approach for the treatment of the simultaneous resection of primary colorectal neoplasm with synchronous liver metastases, showing advantages over conventional surgery in terms of postoperative short-term couse[14].

Nowadays, the benefit of the robotic approach on the laparoscopic one is still a matter of debate, because of the heterogeneity of patients and the lack of long-term outcomes. This paucity of data makes difficult to draw a conclusion but, based on the few data available in this review, synchronous robotic liver and colic resection seems feasible in highly selected cases.

DECLARATIONS

Authors' contributions

Contributed to the concept and writing of the paper: Sammarco A
Contributed to the writing and revision of the paper: de'Angelis N, Testini M
Contributed to the writing and editing of the paper: Memeo R

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Copyright

REFERENCES

1. Zhang XL, Liu RF, Zhang D, Zhang YS, Wang T. Laparoscopic versus open liver resection for colorectal liver metastases: a systematic review and meta-analysis of studies with propensity score-based analysis, Int J Surg 2017;44:191-203.
2. Fretland ÅA, Dagenborg VJ, Bjørnelv GMW, Kazaryan AM, Kristiansen R, et al. Laparoscopic versus open resection for colorectal liver metastases: the OSLO-COMET randomized controlled trial. Ann Surg 2018;267:199-207.
3. Memeo R, De Blasi V, Adam R, Goéré D, Azoulay D, et al. Parenchymal-sparing hepatectomies (PSH) for bilobar colorectal liver metastases are associated with a lower morbidity and similar oncological results: a propensity score matching analysis. HPB (Oxford) 2016;18:781-90.
4. Thome S, Goswami J, Han K, Chidi AP, Geller DA, et al. Minimally invasive resection of colorectal carcer liver metastases leads to an earlier initation of chemotherapy compared to open surgery. J Gastrointest Surg 2015;19:2199-206.
5. Giulianotti PC. Totally robotic right hepatectomy. Arch Surg 2011;146:844.
6. Casciola L, Patriti A, Ceccarelli G, Bartoli A, Ceribelli C, et al. Robot-assisted parenchymal-sparing liver surgery including lesions located in the posterosuperior segments. Surg Endosc 2011;25:3815-24.
7. Croner RS, Perrakis A, Brunner M, Matzel KE, Hohenberger W. Pioneering robotic liver surgery in germany: first experiences with liver malignancies. Front Surg 2015;2:18.
8. Lai EC, Tang CN, Li MK. Robot-assisted laparoscopic hemi-hepatectomy: technique and surgical outcomes. Int J Surg 2012;10:11-5.
9. Guerra F, Guadagni S, Pesi B, Furbetta N, Di Franco G, et al. Outcomes of robotic liver resections for colorectal liver metastases. A multi-institutional analysis of minimally invasive ultrasound-guided robotic surgery. Surg Oncol 2019;28:14-8.
10. Guadagni S, Furbetta N, Di Franco G, Palmeri M, Gianardi D, et al. Rpbotic-assisted surgery for colorectal liver metastasis: a single-centre experience. J Minim Access Surg 2019; doi: 10.4103/jmas.JMAS_265_18.
11. Dwyer RH, Scheidt MJ, Marshall JS, Tsoraides SS. Safety and efficacy of synchronous robotic surgery for colorectal cancer with liver metastases. J Robot Surg 2018;12:603-6.
12. Cipriani F, Rawashdeh M, Stanton L, Armstrong T, Takhar A, et al. Propensity score-based analysis of outcomes of laparoscopic versus open liver resection for colorectal metastases, Br J Surg 2016;103:1504-12.
13. Patriti A, Ceccarelli G, Bartoli A, Spaziani A, Lapalorcia LM, et al. Laparoscopic and robot-assisted one-stage resection of colorectal cancer with synchronous liver metastases: a pilot study. J Hepatobiliary Pancreat Surg 2009;16:450-7.
14. Garritano S, Selvaggi F, Spampinato MG. Simultaneous minimally invasive treatment of colorectal neoplasm with synchronous liver metastasis. Biomed Res Int 2016;2016:9328250.
15. Qiu J, Chen S, Chengyou D. A systematic review of robotic-assisted liver resection and meta-analysis of robotic versus laparoscopic hepatectomy for hepatic neoplasms. Surg Endosc 2016;30:862-75.

Cosgun *et al. Mini-invasive Surg* 2019;3:32
DOI: 10.20517/2574-1225.2019.024

Mini-invasive Surgery

Original Article

Open Access

Factors on nodal up-staging in clinical N0 adenocarcinoma patients who had minimally invasive anatomic lung resections

Tugba Cosgun[1], Erkan Kaba[1], Kemal Ayalp[2], Alper Toker[2]

[1]Department of Thoracic Surgery, Demiroglu Bilim University, Istanbul 34381, Turkey.
[2]Department of Thoracic Surgery, Istanbul Florence Nightingale Hospital, Istanbul 34381, Turkey.

Correspondence to: Dr. Tugba Cosgun, Sisli Florence Nightingale Hospital, Merkez Mah, Abide-i Hurriyet Cd No:164, Sisli/Istanbul 34387, Turkey. E-mail: tugba_cosgun@hotmail.com

How to cite this article: Cosgun T, Kaba E, Ayalp K, Toker A. Factors on nodal up-staging in clinical N0 adenocarcinoma patients who had minimally invasive anatomic lung resections. *Mini-invasive Surg* 2019;3:32. http://dx.doi.org/10.20517/2574-1225.2019.024

Received: 17 Aug 2019 **First Decision**: 15 Oct 2019 **Revised**: 27 Oct 2019 **Accepted**: 5 Nov 2019 **Published**: 15 Nov 2019

Science Editor: Noriyoshi Sawabata **Copy Editor**: Jing-Wen Zhang **Production Editor**: Jing Yu

Abstract

Aim: The incidence of adenocarcinoma among lung cancer patients has increased in recent years. We identified the factors affecting lymph node status in patients with primary lung adenocarcinoma who underwent minimally-invasive anatomic resection.

Methods: We retrospectively analyzed the medical records of primary lung adenocarcinoma patients who underwent minimally-invasive anatomic lung resections and mediastinal lymph node dissection between January 2012 and December 2017. We evaluated lymph node positivity and nodal status in each T and histologic subgroup, tumoral prognostic characteristics, minimally-invasive surgical methods and resection type.

Results: Of 473 patients who underwent anatomic resection for lung cancer between January 2012 and December 2017, 274 underwent minimally-invasive anatomic lung resections for primary lung cancer, 158 adenocarcinoma patients were analyzed in this study. Nodal status and number of positive lymph nodes were similar in the stages T1, T2, T3. Lymphovascular invasion (n : 78) and micropapillary predominance tended to be significant predisposing factors for lymph node metastasis. Mean dissected lymph node number was significantly higher in patients who underwent Robot-assisted thoracoscopic surgery compared to Video-assisted thoracoscopic surgery ($P < 0.05$), and in those who underwent lobectomy compared to segmentectomy ($P < 0.05$).

Conclusion: We were unable to demonstrate a relationship between T stage and N status. Factors contributing to unexpected N positivity were tumor characteristics that could not be identified in the preoperative period. We recommend performing systematic mediastinal lymph node dissection regardless of the size and histopathologic type of adenocarcinoma. In our study, robotic surgery and lobectomy operation showed superiority in dissecting more lymph nodes.

Keywords: Adenocarcinoma, robot-assisted thoracoscopic surgery, lymphovascular invasion, micropapillary predominance

INTRODUCTION

Lung cancer is one of the leading causes of death worldwide. Anatomic lung resections with systematic lymph node dissection have become the recommended treatment for early stage nonsmall lung cancer (NSCLC)[1]. Many investigators and clinicians recommend systematic nodal dissection to all lung cancer patients except those with clinical stage I disease[2].

The Guidelines of the European Society for Medical Oncology (2014) recommend that preoperative invasive mediastinal staging (fine-needle aspiration with endobronchial ultrasonography/endoscopic ultrasonography guidance, or mediastinoscopy) should be used only if positive hilar nodes (stage N1 or N2) are suspected or tumor is located centrally on chest computed tomography (CT) or positron emission tomography (PET)/CT scan[3]. However, clinically diagnosed cN0 disease preoperatively may sometimes be upstaged to N1 (pN1) or N2 (pN2) postoperatively[4]. Debate continues over whether systematic lymph node dissection is necessary for all patients with T1 or T2 tumors without signs of metastatic disease on preoperative clinical staging studies, such as CT-PET/CT, endobronchial ultrasound (EBUS), and endoscopic ultrasonography (EUS)[5,6]. Watanabe *et al.*[7] advocated that mediastinal nodal dissection would be unnecessary in patients with peripheral small lung cancers (≤ 1 cm for adenocarcinomas and 2 cm for tumors other than adenocarcinoma). We speculated that adenocarcinoma subtypes are heterogeneous groups of lung cancers, and may even consist of mixed subtypes with different metastatic characteristics[8]. We also speculated that upstaging may be related to surgical technique and may change in the hands of the same surgeons with different surgical techniques.

Many studies have shown that the incidence of nodal upstaging postoperatively is a quality measure of surgery[4]. However, we speculated that upstaging may also be related to other characteristics of tumor in adenocarcinoma.

In this study, we tried to identify the relationships between tumor size, sub-histology, prognostic factors, and postoperative nodal upstaging in patients with clinical stage N0 adenocarcinoma who underwent minimally-invasive surgery.

METHODS

Of 274 patients who underwent minimally-invasive anatomic lung resections for primary lung cancer between January 2012 and December 2017, 158 (102 male, 56 female; mean age, 62.3 ± 8.4 years; range, 42-92 years) had clinical stage N0 primary lung adenocarcinoma and underwent minimally-invasive anatomic lung resections and systematic mediastinal lymph node dissections robotic assisted surgery (RATS; n = 83) and video thoracoscopic surgery (n = 75). We retrospectively analyzed their prospectively collected medical records. A total of 17 patients were excluded because of insufficient data. Patients with positive mediastinal lymph nodes on mediastinoscopy and EBUS were underwent neoadjuvant treatment and excluded from the study. Patients who were diagnosed to have positive mediastinal lymph nodes preoperatively were excluded. Forty-one patients who underwent mediastinoscopy or EBUS preoperatively and patients who were reported as negative were included in this study. A total number of 158 patients without PET/CT, Mediastinoscopy, EBUS- evident stage N1 or N2 disease and those who underwent anatomic lung resections with systemic mediastinal and hilar complete lymph node dissections were analyzed. Mediastinal lymph node dissections yielded 1242 (mean, 18.8 ± 10.6) lymph nodes with complete dissection of stations 5, 6, 7, 8, 9, 10, 11, 12 on the left, and 1919 lymph nodes (mean 20.9 ± 11.8) with complete dissection of stations 2R, 4R, 7, 8, 9, 10, 11 on the right hemithorax.

Surgical technique

Patients were intubated and single-lung ventilation was placed via fiberoptic bronchoscopy. A lateral decubitus position was used. A two-port technique was used for videoassited thoracoscopic surgery (VATS) lobectomy. For RATS, three ports were opened, keeping 10 cm between each port and 10-15 cm from the target. We preferred to use the VATS-based approach for our RATS technique. When a fourth arm was used, it was placed lateral to the posterior arm. The technique we described here was used for Da Vinci SI systems (Da Vinci System Intuitive Surgical, Sunnyvale, CA, USA)[9]. The Da Vinci robotic system was used in 83 patients, while 75 underwent biportal VATS. Postoperative nodal status and number of positive lymph nodes were evaluated in each group and compared with each other.

Segmentectomy was preferred for tumors smaller than 2 cm and negative lymph nodes or for larger tumors in patients with poor pulmonary function who could not tolerate lobectomy, especially those who do not have visceral pleural invasion in our center. But if the tumor invaded visceral pleura or especially hilar lypmh node positivity could change the surgeon's decision. Also if the remaining tissue after segmentectomy seems not have a good ventilation or blood supply, we decided to perform completion lobectomy during the operation.

Lymph node dissection

Mediastinal and N1-level lymph node dissections were performed in similar manners on all patients regardless of whether they underwent RATS or VATS. Typically dissected mediastinal lymph node stations were 2R, 4R, and 7-9 for patients with right-sided tumors, and 5-9 *en bloc* with perinodal fatty tissue for those with left-sided tumors. Segmentectomy became an operation option for peripheral, clinical T1N0M0, and 2 cm or smaller in size tumors. N1-level lymph nodes, and stations 10 and 11 for lobectomies, and additionally, station 12 were dissected completely and separately during segmentectomies. For segmentectomy, stations 11 and 12 nodes were dissected completely and evaluated by frozen section analysis[10]. If either of them was positive, we preferred to perform lobectomy instead of segmentectomy.

Lymph node status and number of positive lymph nodes were evaluated for each patient. Rate of positive lymph nodes was calculated as the ratio of positive lymph nodes to the number of dissected lymph nodes.

Histopathology

Tumors were classified histologically as well (grade 1), medium (grade 2), and poorly (grade 3) differentiated. Histopathologic types of tumors also were analyzed. In 134 patients, the tumor could be categorized according to predominance of acinar, solid, lepidic, and micropapillary patterns.

Lymphovascular and visceral pleural invasion of tumors was analyzed according to positive lymph nodes and possible effects on N upstaging.

Statistical analysis

Lymph node positivity and nodal status were evaluated in each subgroup, comparing stages T1 *vs.* T2, T1 *vs.* T3, and T2 *vs.* T3. T stage subgroups, such as T1a, Tb, T1c, T2a, T2b, and T3, also were compared using

Table 1. Characteristics of patients, tumors and operations

Patients' characteristics	*n* = 158 (%)
Gender	
Male	102 (64.5%)
Female	56 (35.5%)
Side	
Left	66 (41.7%)
Right	92 (58.3%)
Type of operation	
Segmentectomy	32 (20.25%)
Segment 6	3
Segment 3	1
Segment 1	1
Segment 1-2 (left)	5
Common basal segmentectomy (7.8.9.10.)	2
Lingulectomy	1
Lingula sparing LUL	11
Segment 2 (right)	8
Lobectomy	126 (79.7%)
LUL	27
LLL	21
RUL	53
RML	8
RLL	16
Bilobectomy	1

LUL: left upper lobectomy; LLL: left lower lobectomy; RUL: right upper lobectomy; RML: right middle lobectomy; RLL: right lower lobectomy

the Mann-Whitney *U* and analysis of variance (ANOVA) tests. Regression of histopathologic subtypes and lymph node positivity, and nodal status were analyzed with ANOVA. Resection types (lobectomy, segmentectomy) and operative technique (VATS, RATS) also were analyzed with the Mann-Whitney *U* test.

RESULTS

There were 158 patients in the study group with a mean age of 62.36 ± 8.4 (range 42-92). There were 102 male and 56 female patients. Characteristics of the patients, tumors and operations are noted in Table 1.

Operative techniques

Of the patients, 83 underwent RATS and 75 underwent VATS. Mean number of dissected lymph nodes was 23.3 ± 11.3 (range, 1-57) in the RATS group and 16.3 ± 10.2 (range, 2-49) in the VATS group. Robotic surgery showed higher numbers of lymph node dissections ($P < 0.05$). Mean number of positive lymph nodes was 1.2 ± 2.6 (range, 0-11) in RATS group and 0.3 ± 0.8 (range, 0-4) in the VATS group ($P = 0.06$). In final pathology 14 patients were staged as N2, 7 patients were N1, and 62 were N0 in RATS group; 7 patients were N2, 4 patients were N1 and 64 were N0 in the VATS group ($P = 0.13$; Table 2).

The mean number of dissected lymph nodes was 22.5 ± 11.05 in patients who underwent lobectomy, which was significantly higher than that in patients who underwent segmentectomy (14.5 ± 10.5; $P < 0.05$). However, the numbers of positive lymph nodes were comparable between the groups (0.75 ± 1.9 *vs.* 0.6 ± 1.9, respectively; $P = 0.36$).

Tumor size

According to the 8th Tumor, Nodes, and Metastases (TNM) classification, 108 patients had pathologic stage T1 (11 T1a, 69 T1b, 28 T1c), 34 stage T2 (23 T2a, 11 T2b), and 16 stage T3 tumors. A total of 26 patients

Table 2. Type of minimal invasive surgery and effects of surgical technique on lymph nodes

	RATS 83	VATS 75	*P* value
N of dissected LN/patients	23.3 ± 11.3	16.3 ± 10.2	$P < 0.05$
N of positive LN/patients	1.2 ± 2.6	0.3 ± 0.8	$P = 0.06$
N status			
N2	14 (17%)	7 (9.3%)	
N1	7 (8.4%)	4 (5.3%)	$P = 0.13$
N0	62 (74.7%)	64 (85.3%)	

N: number; LN: lymph node; RATS: robot assisted thoracoscopic surgery; VATS: videoassited thoracoscopic surgery; N status: nodal status (*P* value was derived from ANOVA test)

Table 3. Effects of T factor on nodal status and positivity of lymph nodes

	T1			T2		T3	*P* value
	T1a	T1b	T1c	T2a	T2b	T3	
Number of patients	11	69	28	23	11	16	
N0	8%-72.7%	56%-81.2%	22%-78.6%	18%-78.26%	10%-90.1%	12%-75%	
N1	1%-9%	5%-7.3%	1%-3.6%	3%-13%	1%-9%	0	$P > 0.05$
N2	2%-18%	8%-13.3%	5%-17.8%	2%-8.6%	0	4%-25%	
Number of positive lymph nodes	6	46	23	20	1	21	$P > 0.05$
Rate of positive lymph nodes	0.03	0.045	0.034	0.03	0.033	0.042	$P > 0.05$

P value was derived from ANOVA test

had multifocal tumors. Mean tumor size was 2.8 ± 1.9 cm (range, 0.6-11; 2.9 ± 2 in the RATS and 2.6 ± 1.8 in the VATS groups; $P = 0.4$).

Lymph nodes

The most commonly dissected lymph nodes were those at stations 5-7, 10, and 11 for left-sided tumors, and at stations 2R, 4R, and 7-11 for right-sided tumors. Mean number of dissected lymph nodes was 20.0 ± 11.3 (range, 1-57).

Among all patients, the nodal status was N2 in 21 (13.3%), N1 in 11 (7%), and N0 in 126 (79.%). Total upstaging rate in all groups was 20.3%.

Nodal status and number of positive lymph nodes were evaluated with the Mann-Whitney *U* test for stages T1 *vs.* T2 ($P = 0.79$, $P = 0.77$), T1 *vs.* T3 ($P = 0.32$, $P = 0.36$), and T2 *vs.* T3 ($P = 0.29$, $P = 0.39$) disease. All differences were statistically insignificant. Nodal status and number of positive lymph nodes also were not statistically significant when comparing the three stage (T1, T2, T3) groups via ANOVA [Table 3].

Subgroups of T status (T1a, T1b, T1c, T2a, T2b, and T3) were compared and they had similar numbers of positive lymph nodes, positive lymph node ratios, and similar nodal status [Table 3].

Histopathology

Lymphovascular and visceral pleural invasions are the most commonly investigated histopathologic parameters. A total of 77 patients had lymphovascular and 34 had visceral pleural invasion. When analyzed, the effect of visceral pleural invasion on lymph node positivity was not significant ($P = 0.29$). However, lymphovascular invasion tended to be significantly related to lymph node positivity ($P = 0.08$).

Histologic tumor grade was classified according to differentiation: 16 patients had grade 1, 86 grade 2, and 41 grade 3 disease. There was no correlation between differentiation grade and lymph node positivity ($P = 0.86$) and N status ($P = 0.79$).

Histopathologic tumor types and their effect on lymph node positivity also were analyzed retrospectively. Of the patients, 134 could be categorized according to predominance of acinar, solid, lepidic, and micropapillary patterns. Micropapillary histologic subtype was associated with lymph node positivity. Other subtypes did not show significance (P = 0.65, P = 0.22, P = 0.78, P = 0.005, respectively).

DISCUSSION

Lymphatic dissemination is the major route of systematic metastasis, and it is the major determinant of long-term patient outcome. When a patient with clinical stage N0 disease has been demonstrated to have N1 or N2 positivity, not only prognosis, but also treatment modalities change. Larger consolidation size, central tumor location, and clinical N1-N2 stage have been defined as predictors of mediastinal lymph node metastasis[11]. A recent study demonstrated a significant increase in nodal upstaging to be related with the duration between radionuclear evaluation and surgery[12].

A current study shows that < 2 cm tumors may show occult nodal metastasis, so that dissection of lymph nodes during sublobar resection increases survival for patients underwent sublobar resection[13]. The same study claimed that nonanatomic resections without hilar lymphadenectomy may miss this upstaging. Preoperative radiographic tumor size, tumors not in the upper lobe, high carcinoembryonic antigen levels, and micropapillary predominant adenocarcinomas were identified as predictors for unexpected N1 or N2 node positivity in adenocarcinoma patients[14]. When two major types (squamous cell carcinoma and adenocarcinoma) were compared, lymph node metastasis occurred more frequently in adenocarcinomas than in squamous cell carcinomas and it was reported to be uncommon for mediastinal lymph node metastasis in tumors with a diameter < 3 cm. Poor differentiation grade may have an important role in lymph node metastasis[15]. Despite these findings, several investigators claim that mediastinal lymph node dissection may be unnecessary for adenocarcinomas ≥ 1 cm[7]. In our study, patients with clinicaly N0 disease, had postoperatively N stages (N1, N2) as high as 7.4% and 12.3% of cases, respectively, among all those with stages T1a and Tab cancer. Stage T1c group demonstrated similar upstaging (3.5% patient was N1 disease and 17.8% patient was N2 disease postoperatively). Our results contradicted the literature findings and recommendations. We recommended mediastinal and hilar systematic lymph node dissection to be performed for all stages, including stage 1A.

In another trial on adenocarcinomas ≤ 30 mm, solid pattern, maximum standardized uptake value, and lymphovascular invasion were independent predictors for lymph node metastasis[16].

Adenocarcinoma is a heterogeneous type of lung carcinoma and mostly consists of mixed subtypes. According to one study on solitary peripheral subsolid nodules; speculation, lesion size, vascular convergence and solid proportion are predictive parameters of invasive adenocarcinoma[17]. In another study that used nomogram for predicting risk of invasive pulmonary adenocarcinoma for pure ground-glass opacity nodules; lesion size, speculation, lobulation, air bronchogram, vascular convergence, pleural tag were risk factors for being invasive pulmonary adenocarcinoma[18].

Adenocarcinoma *in situ* and minimally-invasive adenocarcinoma, in which a lepidic pattern is a major component, may show very good prognosis without mediastinal and hilar lymph node metastasis[19]. Lepidic predominant, minimally-invasive adenocarcinoma, and adenocarcinoma *in situ* also are specified as safe tumors for lymph node invasion[20,21]. Since a lepidic pattern is known to be noninvasive and often appears as a ground glass opacity (GGO) on radiologic evaluation, and a patient with a GGO nodule on tomography is likely to be diagnosed with adenocarcinoma *in situ* or minimally-invasive adenocarcinoma pathologically, systematic lymph node dissection might not be considered[19]. Lepidic predominance has been shown to be the safest subtype in regard to mediastinal and hilar lymph nodes in our study (P = 0.78), similar to findings in the literature.

Moon *et al.*[19] claimed that mediastinal lymph node dissection may not be necessary for clinical stage N0 NSCLC presenting with a ≤ 3 cm GGO-predominant nodule. Segmentectomy can be a preferred technique if there is almost no lymph node metastasis at stations 12 and 11. In patients with adenocarcinoma and a micropapillary or solid component, lobectomy should be considered because of possible interlobar and intralobar lymph node metastasis[22], which may not be identified before and during surgery. A histologic component may be an important factor in patients with nodal upstaging of clinically N0 tumors[4]. It has been shown that micropapillary and solid tumor patterns significantly increase the risk of nodal upstaging[23,24]. Our study demonstrated that the micropapillary pattern is related to a higher rate of lymph node positivity. However, we were not able to identify solid predominance as a risk factor for lymph node positivity.

Spread through air spaces (STAS) was defined as spread of lung cancer tumor cells into air spaces in the lung parenchyma adjacent to the main tumor. Three morphologic patterns of STAS were identified: (1) micropapillary structures, consisting of papillary structures without central fibrovascular cores that occasionally form ring-like structures within air spaces; (2) solid nests or tumor islands, consisting of solid collections of tumor cells filling air spaces; and (3) single cells consisting of scattered discohesive single cells[25]. Lymphovascular invasion and high-grade morphologic pattern were identified more frequently in STAS-positive than STAS-negative tumors. Besides this, the risk of locoregional or distant recurrence was significantly higher in patients with STAS-positive than STAS-negative tumors who underwent limited resection. However, this association was not noted in the lobectomy group[26].

Another remarkable finding of this study was the number of dissected lymph nodes. The number of positive and total number of dissected lymph nodes were higher in the RATS compared to the VATS groups ($P = 0.06$, $P < 0.05$, respectively). These results were compatible with those of previous studies from our department[27]. We believed that RATS increases the capability of mediastinal dissection. On the other hand, our group has been performing VATS lobectomy consistently for more than a decade; we do not see this finding in VATS.

Limitation of our study are as follows: this study is performed in a single center with relatively small size population. We could not analyze the patients with preoperatively diagnosed N2 disease. Relatively a small number of patients underwent mediastinoscopy and/or or EBUS preoperatively in our series.

The number of positive lymph nodes and lymph node status were comparable between the T groups and subgroups in adenocarcinomas. These results may be related with heterogenous types and subgroups of adenocarcinoma. We demonstrated that lymphovascular invasion and micropapillary predominance could be considered candidates for nodal upstaging. Since these features of tumors cannot be identified preoperatively in most patients, we recommended performing systematic hilar and mediastinal lymph node dissection for an adenocarcinoma of any size considering minimally-invasive surgery; we preferred the robotic-assisted approach.

DECLARATIONS

Authors' contributions

Conceived and designed the study, wrote and reviewed the manuscript: Cosgun T
Collected and tabulated data, participated in manuscript writing: Kaba E, Ayalp K
Participated in manuscript writing and review: Toker A

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Yu X, Li Y, Shi C, Han B. Risk factors of lymph node metastasis in patients with non-small cell lung cancer ≤ 2 cm in size: A monocentric population-based analysis. Thorac Cancer 2018;9:3-9.
2. Takizawa H, Kondo K, Matsuoka H, Uyama K, Toba H, et al. Effect of mediastinal lymph nodes sampling in patients with clinical stage I non-small cell lung cancer. J Med Invest 2008;55:37-43.
3. Postmus PE, Kerr KM, Oudkerk M, Senan S, Waller DA, et al. Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2013;24:89-98.
4. Moon Y, Kim KS, Lee KY, Sung SW, Kim YK, et al. Clinicopathologic factors associated with occult lymph node metastasis in patients with clinically diagnosed N0 lung adenocarcinoma. Ann Thorac Surg 2016;101:1928-35.
5. Ettinger DS, Akerley W, Borghaei H, Akerley W, Bauman J, et al. Non-small cell lung cancer. J Natl Compr Canc Netw 2012;10:1236-71.
6. Gulack BC, Yang CF, Speicher PJ, Meza JM, Gu L, et al. The impact of tumor size on the association of the extent of lymph node resection and survival in clinical stage I non-small cell lung cancer. Lung Cancer 2015;90:554-60.
7. Watanabe S, Oda M, Go T, Ohta Y, Watanabe Y, et al. Should mediastinal nodal dissection be routinely undertaken in patients with peripheral small-sized (2 cm or less) lung cancer? Retrospective analysis of 225 patients. Eur J Cardiothorac Surg 2001;20:1007-11.
8. Travis WD, Brambilla E, Noguchi M, Nicholson AG, Geisinger K, et al. International association for the study of lung cancer/ American thoracic society/European respiratory society international multidisciplinary classification of lung adenocarcinoma. J Thorac Oncol 2011;6:244-85.
9. Toker A, Kaba E, Ayalp K, Ozyurtkan MO. Robotic lung resections: video-assisted thoracic surgery based approach. J Vis Surg 2017;3:15.
10. Toker A, Ozyurtkan MO, Demirhan O, Ayalp K, Kaba E, et al. Lymph node dissection in surgery for lung cancer: Comparison of open vs. video-assisted vs. robotic-assisted approaches. Ann Thorac Cardiovasc Surg 2016;22:284-90.
11. Zang RC, Qiu B, Gao SG, He J. A model predicting lymph node status for patients with clinical stage T1aN0-2M0 nonsmall cell lung cancer. Chin Med J (Engl) 2017;130:398-403.
12. Gard G, Voskoboynik M. Delay to Surgery May Upstage Patients With Non-Small Cell Lung Cancer. Chest 2019;156:633-4. doi: 10.1016/j.chest.2019.04.113.
13. Stiles BM, Mao J, Harrison S, Lee B, Port JL et al. Extent of lymphadenectomy is associated with oncological efficacy of sublobar resection for lung cancer ≤ 2 cm. J Thorac Cardiovasc Surg 2019;157:2454-65.
14. Bao F, Yuan P, Yuan X, Lv X, Wang Z, et al. Predictive risk factors for lymph node metastasis in patients with small size non-small cell lung cancer. J Thorac Dis 2014;6:1697-703.
15. Pan T, Zheng Z, Li J, Tang Y, Pan Y, et al. Relationship between tumor size and lymph node metastasis in squamous cell carcinoma and adenocarcinoma of the lung. Zhongguo Fei Ai Za Zhi 2006;9:267-9.
16. Seok Y, Yang HC, Kim TJ, Lee KW, Kim K, et al. Frequency of lymph node metastasis according to the size of tumors in resected pulmonary adenocarcinoma with a size of 30 mm or smaller. J Thorac Oncol 2014;9:818-24.
17. Jin C, Cao J, Cai Y, Wang L, Liu K, et al. A nomogram for predicting the risk of invasive pulmonary adenocarcinoma for patients with solitary peripheral subsolid nodules. J Thorac Cardiovasc Surg 2017;153:462-9.
18. Wang L, Shen W, Xi Y, Liu S, Zheng D, et al. Nomogram for predicting the risk of invasive pulmonary adenocarcinoma for pure ground-glass nodules. Ann Thorac Surg 2018;105:1058-64.
19. Moon Y, Sung SW, Namkoong M, Park JK. The effectiveness of mediastinal lymph node evaluation in a patient with ground glass opacity tumor. J Thorac Dis 2016;8:2617-25.
20. Yu Y, Jian H, Shen L, Zhu L, Lu S. Lymph node involvement influenced by lung adenocarcinoma subtypes in tumor size ≤ 3 cm disease: A study of 2268 cases. Eur J Surg Oncol 2016;42:1714-9.

21. Jiang L, Yin W, Peng G, Wang W, Zhang J, et al. Prognosis and status of lymph node involvement in patients with adenocarcinoma in situ and minimally invasive adenocarcinoma-a systematic literature review and pooled-data analysis. J Thorac Dis 2015;7:2003-9.
22. Wang L, Jiang W, Zhan C, Shi Y, Zhang Y, et al. Lymph node metastasis in clinical stage IA peripheral lung cancer. Lung Cancer 2015;90:41-6.
23. Yuan Y, Ma G, Zhang Y, Chen H. Presence of micropapillary and solid patterns are associated with nodal upstaging and unfavorable prognosis among patient with cT1N0M0 lung adenocarcinoma: a large-scale analysis. J Cancer Res Clin Oncol 2018;144:743-9.
24. Yu Y, Jian H, Shen L, Zhu L, Lu S. Lymph node involvement influenced by lung adenocarcinoma subtypes in tumor size ≤ 3 cm disease: A study of 2268 cases. Eur J Surg Oncol 2016;42:1714-9.
25. Onozato ML, Kovach AE, Yeap BY, Morales-Oyarvide V, Klepeis VE, et al. Tumor islands in resected early-stage lung adenocarcinomas are associated with unique clinicopathologic and molecular characteristics and worse prognosis. Am J Surg Pathol 2013;37:287-94.
26. Kadota K, Nitadori J, Sima CS, Ujiie H, Rizk NP, et al. Tumor spread through air spaces is an important pattern of invasion and impacts the frequency and location of recurrences after limited resection for small stage I lung adenocarcinomas. J Thorac Oncol 2015;10:806-14.
27. Toker A, Ozyurtkan MO, Demirhan O, Ayalp K, Kaba E, et al. Lymph node dissection in surgery for lung cancer: Comparison of open vs. video-assisted vs. robotic-assisted approaches. Ann Thorac Cardiovasc Surg 2016;22:284-90.

Kim *et al. Mini-invasive Surg* 2019;3:33
DOI: 10.20517/2574-1225.2019.23

Mini-invasive Surgery

Review

Open Access

Transanal total mesorectal excision: current East Asian perspectives for the future

Ho Seung Kim, Nam Kyu Kim

Division of Colorectal Surgery, Department of Surgery, Severance Hospital, Yonsei University College of Medicine, Seoul 03722, South Korea.

Correspondence to: Prof. Nam Kyu Kim, Division of Colorectal Surgery, Department of Surgery, Severance Hospital, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-Gu, Seoul 03722, South Korea. E-mail: namkyuk@yuhs.ac

How to cite this article: Kim HS, Kim NK. Transanal total mesorectal excision: current East Asian perspectives for the future. *Mini-invasive Surg* 2019;3:33. http://dx.doi.org/10.20517/2574-1225.2019.23

Received: 10 Aug 2019 **First Decision:** 24 Oct 2019 **Revised:** 6 Nov 2019 **Accepted:** 13 Nov 2019 **Published:** 22 Nov 2019

Science Editor: Giulio Belli **Copy Editor:** Cai-Hong Wang **Production Editor:** Tian Zhang

Abstract

Transanal total mesorectal excision (TaTME) is widely performed for the resection of rectal cancer around the world. However, due to lower body mass index and a lack of necessity, TaTMEs have not been accepted in East Asia as generally as in Western countries. In East Asia, conventional laparoscopic surgeries have been performed with lower rates of open conversions and robotic surgery has been considered as an acceptable option for patients with narrow pelvis. This review article discusses TaTMEs from an East Asian perspective.

Keywords: Transanal total mesorectal excision, East Asia, robotic surgery, laparoscopic surgery, difficult pelvis

INTRODUCTION

The evaluation and management of rectal cancer has evolved remarkably over the last few decades since Heald *et al.*[1] proposed and reported on total mesorectal excisions for rectal cancer in the reduction of local recurrences. Total mesorectal excision (TME) became the gold standard for curative resection from the standpoint of control and survival. In addition to increased anatomical knowledge, surgical instruments have also improved. In the early 1990s, laparoscopic surgery was introduced and gradually used in colon and rectal cancer treatments. Since several multicenter randomized trials reported potential short-term benefits with oncological outcomes comparable to open surgeries, laparoscopic TMEs were adopted for rectal cancer[2,3]. However, several prospective trials failed to prove the non-inferiority of laparoscopy, citing several reasons[4,5]. Most of the reasons were attributed to the difficulty in ensuring a sufficient surgical field in a narrow space. The three most common reasons for open conversions in the Colorectal Cancer

Laparoscopic or Open Resection (COLOR) II trial were a narrow pelvis (22%), obesity (10%), and tumor fixation (9%)[6].

To overcome the technical difficulties associated with laparoscopic TMEs, which resulted in poor visualization of the mesorectal planes and difficulty introducing instruments, the concept of a "bottom-up" alternative technique (from the distal to the proximal mesorectal plane), was proposed with the first transanal TME (TaTME) procedure performed in patients with rectal cancer in 2010 by Sylla *et al*.[7]. Before TaTME was introduced, new minimally invasive devices and innovations using the Natural Orifice Transluminal Endoscopic Surgery technique and the Transanal Endoscopic Microsurgery method were initiated, which made the concept possible[8]. The transabdominal transanal proctosigmoidectomy (TATA), which is similar to TaTMEs and was developed by Marks[9] in 1984, introduced the bottom-up technique, in contrast to the traditional top-down technique typically used in abdominal procedures.

In this review article, we focus on current and future East Asian perspectives. Since severely obese rectal cancer patients are still rare in East Asian countries, there is less need for TaTMEs compared to Western countries. The low rate of high body mass index (BMI) may be one of the reasons for the low conversion rate of laparoscopic surgery for rectal cancer and even for mid and low rectal cancers after neoadjuvant chemoradiotherapy compared to the high conversion rates in the COLOR II (16%) and the American College of Surgeons Oncology Group (ACOSOG) Z6051 (11.3%) trials.

ROBOTIC TME: EFFORTS TO OVERCOME THE DIFFICULTIES OF LAPAROSCOPIC TMES

Technical limitations exist with the laparoscopic approach, especially during the distal transection of the rectum due to limited visibility and working restrictions associated with the confined space of a narrow pelvis[10]. Recently, robotic surgery has been proposed as a solution to this problem. Although there is no concrete evidence that robotic surgery has an advantage in difficult cases, robotic-assisted surgery was introduced to address the limitations of laparoscopy, and gained acceptance due to improved visualization, lower conversion rates, better TME quality with lower positive circumferential resection margin (CRM) rates, and earlier recovery of genitourinary functions[11-13].

According to our experience at Severance Yonsei University Hospital in South Korea, the robotic group showed a lower conversion rate (0% *vs*. 7.1%, P = 0.003) when patients with upper rectal tumors were enrolled[14]. In addition, when we compared patients who only underwent robotic surgery *vs*. laparoscopic surgery with coloanal anastomosis, with or without intersphincteric resections, including patients with mean tumor heights of 5.5 cm and 4.4 cm from the anal verge, the conversion rates were 2.1% *vs*. 16.2%, P = 0.020, respectively[15]. The robotic groups showed better results in terms of open conversion rates. In addition, when we compared patients who had robotic TMEs according to pelvimetry, there were no differencess among easy, moderate, and difficult groups in terms of operative times, which were used as surrogate markers for TME difficulty[16].

In the Robotic *vs*. Laparoscopic Resection for Rectal Cancer (ROLARR) trial[17], the overall conversion rates were 12.2% and 8.1% for laparoscopic and robotic TME surgeries, respectively. However, 27.8% of obese patients undergoing laparoscopic TMEs and 18.9% in the robotic TME group required conversions. Although the robotic TME group showed better results than the laparoscopic TME group, the conversion rates were still high. In addition to high BMI, lower rectal cancers and the male gender were associated with increased conversion rates. Moreover, accurate identification of the distal margin and the application of the endoscope at right angles to the rectum can be challenging in a narrow pelvis.

TATME: EFFORTS TO OVERCOME THE DIFFICULTY OF LAPAROSCOPIC TMES

Risk factors in the ROLARR trial could be diminished using TaTMEs as constraints and challenges posed by anatomical features are minimized when approached from below. TaTMEs also showed lower conversion rates. Penna *et al.*[18] reported conversion rates from laparoscopic to open or transanal as 6.3% within the TaTME registry. Veltcamp Helbac *et al.*[19] reported a conversion rate of 5% for 80 TaTME cases. Moreover, Lacy *et al.*[20] reported no conversions in 140 cases. TaTME procedures overcome difficulties frequently encountered in trans-abdominal rectal transections and anastomosis-stapling techniques such as narrow pelvic anatomy, oblique stapling angles, rectal-tearing secondary to vigorous manipulation, and multiple staple firings.

Robotic surgery and transanal surgery have been developed to overcome some of the limitations of conventional laparoscopic surgery for rectal cancer. However, there are only a few studies comparing robotic and TaTME[21-23]. Those studies showed comparable results for robotic TME and TaTME. Among the studies, Lee *et al.*[21] compared, out of a total of 730 patients (277 TaTME and 453 robotic TME patients), matched groups of 226 TaTME and 370 robotic TME patients. The mean tumor height from the anal verge was 5.6 cm, and 70% received preoperative radiotherapy. There were no differences in TME specimen quality and CRM.

However, the evidence on TaTME is still lacking in many aspects with many still unanswered questions. Retrospective studies and meta-analysis showed that TaTME seems to achieve comparable technical success with acceptable oncologic and perioperative outcomes in comparison with laparoscopic TME[24]. However, there is no multicenter randomized controlled trial at present. The COLOR III trial, which compares TaTME and laparoscopic TME, is currently in the recruitment phase.

PREVIOUS EAST ASIAN STUDIES ON TATME

There have been a few reports describing the use of TaTMEs in Asian patients. One study from Taiwan[25] compared 50 patients with middle or lower rectal cancer and post-neoadjuvant chemoradiotherapy (nCRT) who underwent TaTMEs using 100 matched control cohorts who received conventional laparoscopic rectal surgeries. Seventy-six percent of the patients were male with a mean BMI of 24.2 kg/m^2 and had low (< 7 cm) tumor heights. There was only one conversion. Another prospective, single-arm phase II trial from Korea[26] enrolled 49 patients (65.3% male, a mean BMI of 23.3 kg/m^2, and a mean tumor height of 6.3 cm) with their rectal cancers located 3-12 cm from the anal verge and no conversions to open surgery. A study from Hong Kong[27] compared a TaTME group (n = 40) to a robotic group (n = 80) using propensity score matching. In the TaTME group, 72.5% of the patients were male and the median tumor height was 5.0 cm. There was a 5% conversion rate. All three of these studies concluded that TaTMEs were safe and feasible with acceptable results based on the perioperative and pathologic outcomes. Although conversion rates were higher than in the Comparison of Open *vs*. Laparoscopic Surgery for mid or low Rectal Cancer after Neoadjuvant Chemoradiotherapy (COREAN) trial, they are quite low compared to previous laparoscopic TME results.

Recently, studies by Chinese surgeons using TaTMEs have begun. After a preliminary study[28] with 20 patients that confirmed the safety and feasibility of the procedure, they began randomized controlled trial (RCT) enrollment in June 2019 to compare laparoscopic TMEs with TaTMEs (NCT03413930). They will only include patients with middle or lower rectal cancers similar to the East Asian studies.

ARE TATMES NECESSARY FOR EAST ASIA?

Presently, TaTMEs in East Asia are not as popular as in Western countries since few patients have BMIs above 30 kg/m^2. In females, even for those with lower rectal cancer, conventional laparoscopic TMEs can be accomplished without conversions. Additionally, robotic systems are used more frequently only in high volume centers. Another issue is the cost which patients should pay, especially in Korea where a two-team approach is not feasible due to the insurance system.

TATMES ARE NEEDED FOR EAST ASIA!

Even in East Asian patients, conventional laparoscopic TMEs are difficult for those with narrow pelvis. Several studies in Asia have found that a deep, narrow pelvis was an independent factor for intraoperative and postoperative outcomes[29-32]. Most studies using preoperative computed tomography and magnetic resonance pelvimetry have shown that the bones of the pelvis - the depth and length of sacrum, the pelvic inlet, and the pelvic outlet - are independent predictors for the operative times, which have been used as surrogate markers for determining TME difficulty[29,30,32]. Limited pelvic space impacts the quality of resected TME specimens[30,33]. Identifying the East Asian patients having normal BMIs with narrow pelvis before surgery has been beneficial for deciding if TaTMEs should be used. Often, we perform a transanal approach after transabdominal TMEs to ease resection and easily obtain quality resected TME specimens.

A study which utilized TaTMEs in challenging patients included a total of 12 patients (9 males and 3 females): 1 obese patient, 7 with large tumors, and 8 with threatened mesorectal fascias (four patients had multiple indications)[34]. The median tumor height was 5.5 cm from the anal verge, and all patients received preoperative chemoradiotherapy. There were no intraoperative complications. Only 1 patient required conversion to open surgery for ureterocystostomy after resection. Larger TaTME studies involving Asian patients are necessary to promote TaTMEs.

A CONCRETE INDICATION IS NECESSARY

Since TaTME has only just recently been introduced, the criteria of surgical candidates best suited for TaTME treatments are still evolving[35]. A recent consensus statement was published which listed the following indications for TaTME: (1) male gender; (2) narrow and/or deep pelvis; (3) visceral obesity and/or a BMI > 30 kg/m^2; (4) prostatic hypertrophy; (5) tumor height < 12 cm from the anal verge; (6) tumor diameter > 4 cm; (7) distortion of tissue planes secondary to neoadjuvant radiotherapy; and (8) an impalpable, lower primary tumor requiring accurate placement of the distal resection margin[36]. However, we believe that TaTMEs should be used in challenging cases to replace the transabdominal approach. In East Asia, challenging cases imply that patients are males with deep and narrow pelvis after preoperative chemotherapy. While TaTME was developed to assist in challenging middle to lower rectal cancer cases, its essential purpose should be initially adopted. In East Asia, a more concrete indication distinct from laparoscopic and robotic TMEs is required for transition to TaTMEs.

Moreover, the application of TaTMEs was recently extended to include benign tumor excisions, endopelvic surgeries, and pelvic exenterative surgeries[37]. In situations where robotic systems are used in high-volume centers, robotic TaTMEs can be a useful new technique as various robotic systems are developed.

PROBLEMS IN ADOPTING TATME IN EAST ASIA

The other issues for TaTME are the learning curve and training. The transition from laparoscopic TME to robotic TME is straightforward as the approach is the same. However, the technical complexity and unusual anatomy have led to the occurrence of rare complications such as urethral injury[38]. In terms of oncological outcome, Larsen *et al.*[39] reported 9.5% local recurrence, which led to a nationwide in norway halt of TaTME and thorough investigation. They suggested that the increase of local recurrences after TaTMEs might, to some extent, be due to the learning curve, which is inevitable in the introduction of a complex procedure. In addition, only a few centers in East Asia have accumulated much experience and have good results on TaTME. To adopt TaTME safely, a training strategy such as the detailed framework for a structured TaTME training curriculum proposed by the International TaTME Educational Collaborative Group is necessary[40].

CONCLUSION

TaTMEs are potential alternatives for East Asian male patients with rectal cancer who have deep and narrow pelvis. Many RCT and prospective studies (especially the RCT in China) are underway that could provide concrete indications for the usefulness and necessity of TaTMEs[41] in East Asia. To further promote TaTMEs in East Asia, further research with East Asian populations and training strategy are necessary.

DECLARATIONS

Authors' contributions

Conceptualized the topic and oversaw the direction and final edits: Kim NK
Drafted the manuscript: Kim HS

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Heald RJ, Husband EM, Ryall RD. The mesorectum in rectal cancer surgery--the clue to pelvic recurrence? Br J Surg 1982;69:613-6.
2. Kang SB, Park JW, Jeong SY, Nam BH, Choi HS, et al. Open versus laparoscopic surgery for mid or low rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): short-term outcomes of an open-label randomised controlled trial. Lancet Oncol 2010;11:637-45.
3. Jayne DG, Guillou PJ, Thorpe H, Quirke P, Copeland J, et al. Randomized trial of laparoscopic-assisted resection of colorectal carcinoma: 3-year results of the UK MRC CLASICC trial group. J Clin Oncol 2007;25:3061-8.
4. Fleshman J, Branda M, Sargent DJ, Boller AM, George V, et al. Effect of laparoscopic-assisted resection vs open resection of stage II or III rectal cancer on pathologic outcomes: the ACOSOG Z6051 randomized clinical trial. JAMA 2015;314:1346-55.
5. Stevenson AR, Solomon MJ, Lumley JW, Hewett P, Clouston AD, et al. Effect of laparoscopic-assisted resection vs open resection on pathological outcomes in rectal cancer: the ALaCaRT randomized clinical trial. JAMA 2015;314:1356-63.
6. Van der Pas MH, Haglind E, Cuesta MA, Furst A, Lacy AM, et al. Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. Lancet Oncol 2013;14:210-8.
7. Sylla P, Rattner DW, Delgado S, Lacy AM. NOTES transanal rectal cancer resection using transanal endoscopic microsurgery and laparoscopic assistance. Surg Endosc 2010;24:1205-10.
8. Atallah S, Albert M, Larach S. Transanal minimally invasive surgery: a giant leap forward. Surg Endosc 2010;24:2200-5.
9. Marks JH, Myers EA, Zeger EL, Denittis AS, Gummadi M. Long-term outcomes by a transanal approach to total mesorectal excision for rectal cancer. Surg Endosc 2017;31:5248-57.
10. Row D, Weiser MR. An update on laparoscopic resection for rectal cancer. Cancer Control 2010;17:16-24.
11. Young M, Pigazzi A. Total mesorectal excision: open, laparoscopic or robotic. Recent Results Cancer Res 2014;203:47-55.
12. Xiong B, Ma L, Huang W, Zhao Q, Cheng Y. Robotic versus laparoscopic total mesorectal excision for rectal cancer: a meta-analysis of eight studies. J Gastrointest Surg 2015;19:516-26.
13. Bianchi PP, Ceriani C, Locatelli A, Spinoglio G, Zampino MG, et al. Robotic versus laparoscopic total mesorectal excision for rectal cancer: a comparative analysis of oncological safety and short-term outcomes. Surg Endosc 2010;24:2888-94.
14. Park EJ, Cho MS, Baek SJ, Hur H, Min BS, et al. Long-term oncologic outcomes of robotic low anterior resection for rectal cancer: a comparative study with laparoscopic surgery. Ann Surg 2015;261:129-37.

15. Baek SJ, Al-Asari S, Jeong DH, Hur H, Min BS, et al. Robotic versus laparoscopic coloanal anastomosis with or without intersphincteric resection for rectal cancer. Surg Endosc 2013;27:4157-63.
16. Baek SJ, Kim CH, Cho MS, Bae SU, Hur H, et al. Robotic surgery for rectal cancer can overcome difficulties associated with pelvic anatomy. Surg Endosc 2015;29:1419-24.
17. Jayne D, Pigazzi A, Marshall H, Croft J, Corrigan N, et al. Effect of robotic-assisted vs conventional laparoscopic surgery on risk of conversion to open laparotomy among patients undergoing resection for rectal cancer: the ROLARR randomized clinical trial. JAMA 2017;318:1569-80.
18. Penna M, Hompes R, Arnold S, Wynn G, Austin R, et al. Transanal total mesorectal excision: international registry results of the first 720 cases. Ann Surg 2017;266:111-7.
19. Veltcamp Helbach M, Deijen CL, Velthuis S, Bonjer HJ, Tuynman JB. Transanal total mesorectal excision for rectal carcinoma: short-term outcomes and experience after 80 cases. Surg Endosc 2016;30:464-70.
20. Lacy AM, Tasende MM, Delgado S, Fernandez-Hevia M, Jimenez M, et al. Transanal total mesorectal excision for rectal cancer: outcomes after 140 patients. J Am Coll Surg 2015;221:415-23.
21. Lee L, de Lacy B, Gomez Ruiz M, Liberman AS, Albert MR, et al. A multicenter matched comparison of transanal and robotic total mesorectal excision for mid and low-rectal adenocarcinoma. Ann Surg 2018; doi: 10.1097/SLA.0000000000002862.
22. Law WL, Foo DCC. Comparison of early experience of robotic and transanal total mesorectal excision using propensity score matching. Surg Endosc 2019;33:757-63.
23. Perez D, Melling N, Biebl M, Reeh M, Baukloh JK, et al. Robotic low anterior resection versus transanal total mesorectal excision in rectal cancer: a comparison of 115 cases. Eur J Surg Oncol 2018;44:237-42.
24. Ma B, Gao P, Song Y, Zhang C, Zhang C, et al. Transanal total mesorectal excision (taTME) for rectal cancer: a systematic review and meta-analysis of oncological and perioperative outcomes compared with laparoscopic total mesorectal excision. BMC Cancer 2016;16:380.
25. Chen CC, Lai YL, Jiang JK, Chu CH, Huang IP, et al. Transanal total mesorectal excision versus laparoscopic surgery for rectal cancer receiving neoadjuvant chemoradiation: a matched case-control study. Ann Surg Oncol 2016;23:1169-76.
26. Park SC, Sohn DK, Kim MJ, Chang HJ, Han KS, et al. Phase II clinical trial to evaluate the efficacy of transanal endoscopic total mesorectal excision for rectal cancer. Dis Colon Rectum 2018;61:554-60.
27. Law WL, Foo DCC. Comparison of early experience of robotic and transanal total mesorectal excision using propensity score matching. Surg Endosc 2019;33:757-63.
28. Kang L, Chen WH, Luo SL, Luo YX, Liu ZH, et al. Transanal total mesorectal excision for rectal cancer: a preliminary report. Surg Endosc 2016;30:2552-62.
29. Zhou X, Su M, Hu K, Su Y, Ye Y, et al. Applications of computed tomography pelvimetry and clinical-pathological parameters in sphincter preservation of mid-low rectal cancer. Int J Clin Exp Med 2015;8:2174-81.
30. Kim JY, Kim YW, Kim NK, Hur H, Lee K, et al. Pelvic anatomy as a factor in laparoscopic rectal surgery: a prospective study. Surg Laparosc Endosc Percutan Tech 2011;21:334-9.
31. Zhou XC, Su M, Hu KQ, Su YF, Ye YH, et al. CT pelvimetry and clinicopathological parameters in evaluation of the technical difficulties in performing open rectal surgery for mid-low rectal cancer. Oncol Lett 2016;11:31-8.
32. Akiyoshi T, Kuroyanagi H, Oya M, Konishi T, Fukuda M, et al. Factors affecting the difficulty of laparoscopic total mesorectal excision with double stapling technique anastomosis for low rectal cancer. Surgery 2009;146:483-9.
33. Baik SH, Kim NK, Lee KY, Sohn SK, Cho CH, et al. Factors influencing pathologic results after total mesorectal excision for rectal cancer: analysis of consecutive 100 cases. Ann Surg Oncol 2008;15:721-8.
34. Oh JH, Park SC, Kim MJ, Park BK, Hyun JH, et al. Feasibility of transanal endoscopic total mesorectal excision for rectal cancer: results of a pilot study. Ann Surg Treat Res 2016;91:187-94.
35. Vignali A, Elmore U, Milone M, Rosati R. Transanal total mesorectal excision (TaTME): current status and future perspectives. Updates Surg 2019;71:29-37.
36. Yap R, Monson J. Transanal total mesorectal excision: current updates. Mini-invasive Surgery 2019;3:3.
37. Adegbola SO, Sahnan K, Pellino G, Warusavitarne J. Transanal minimal invasive surgery - pushing the boundaries of transanal surgery. Mini-invasive Surg 2018;2:40.
38. Sylla P, Knol JJ, D'Andrea AP, Perez RO, Atallah SB, et al. Urethral Injury and other urologic injuries during transanal total mesorectal excision: an international collaborative study. Ann Surg 2019; doi: 10.1097/SLA.0000000000003597.
39. Larsen SG, Pfeffer F, Korner H. Norwegian moratorium on transanal total mesorectal excision. Br J Surg 2019;106:1120-1.
40. Francis N, Penna M, Mackenzie H, Carter F, Hompes R. Consensus on structured training curriculum for transanal total mesorectal excision (TaTME). Surg Endos 2017;31:2711-9.
41. Yellinek S, Wexner SD. The role of transanal total mesorectal excision in rectal surgery. Mini-invasive Surg 2018;2:22.

Mini-invasive Surgery

Opinion

Open Access

Limits of transanal total mesorectal excision for low and middle rectal cancer

Mathilde Aubert, Diane Mege, Yves Panis

Department of Colorectal Surgery, Beaujon Hospital, Assistance Publique-Hôpitaux de Paris, Université Paris VII, Clichy 92110, France.

Correspondence to: Dr. Yves Panis, Département de Chirurgie Colorectale, Hôpital Beaujon, 100 Boulevard du Général Leclerc, Clichy 92110, France. E-mail: yves.panis@aphp.fr

How to cite this article: Aubert M, Mege D, Panis Y. Limits of transanal total mesorectal excision for low and middle rectal cancer. *Mini-invasive Surg* 2019;3:34. http://dx.doi.org/10.20517/2574-1225.2019.46

Received: 27 Oct 2019 **Accepted:** 19 Nov 2019 **Published:** 29 Nov 2019

Science Editor: Giulio Belli **Copy Editor:** Cai-Hong Wang **Production Editor:** Tian Zhang

Keywords: Transanal total mesorectal excision, rectal cancer, oncological results, laparoscopic total mesorectal excision, learning curve

Transanal total mesorectal excision (TaTME)[1] is now considered as a new standard of care in the surgical management of low and mid rectal cancer for many surgeons. The main argument is a supposed better visualization of the difficult anatomical area represented by the low third rectum (considered as "a rectal no man's land"), thus allowing better nerve preservation, better resection margins, and better functional outcomes than standard laparoscopic TME[2,3]. This transanal approach is particularly interesting in obese patients with narrow pelvis and/or bulky tumor. However, all the encouraging results are only based on retrospective and comparative studies. Two randomized trials comparing TaTME and standard laparoscopic TME from above are currently ongoing (GRECCAR 11 and COLOR III)[4,5], but their results are not yet available. In addition, the surgical community highlights some concerns about the safety of this procedure, especially regarding the occurrence of postoperative morbidity and some altered oncological and functional long-term outcomes.

An alarming report of the Norwegian Colorectal Cancer Group about oncologic results after TaTME has recently been published. This report was presented in January 2019 at the 9th Ahus Colorectal Symposium, University of Oslo in Norway and highlighted a higher rate of local recurrence after TaTME in the Norwegian national survey. Larsen *et al.*[6] published the Norwegian moratorium, which was decided after 110 TaTME procedures. The reason was that, after only 11 months, a local recurrence was observed in

9.5% of patients who underwent TaTME when compared with 3.4% of patients undergoing laparoscopic TME. Besides this increased rate, a new pattern of local recurrence in terms of its multifocality as well as its early timing after TaTME has been observed. Regarding these alarming data, the Norwegian surgical community decided to cease performing TaTME for low and middle rectal cancer[6]. Today, long-term results from the international registry of TaTME as well as those from the Dutch survey are not available. We can imagine that, according to the further results of these two registries, the opinion of the colorectal surgeon community will definitely be modified. In such an alarming situation, it will probably mean that TaTME should not be proceeded in non-expert centers.

However, possible problems of TaTME concern not only oncologic results, even if they are the most important. Some intraoperative adverse events have also been reported during the transanal phase, such as wrong dissection plane, organs injury (vagina, urethra, bladder, and rectum), and carbon dioxide embolism. In the international registry of TaTME including 1594 procedures[7], 31% of the patients presented with intraoperative adverse events during the transanal phase mainly represented by technical problems (18%), wrong dissection plane (6%), pelvic hemorrhage (4%), and organs (urethral, rectal, vaginal, or bladder) injuries (2%). As a new surgical procedure, the learning curve of TaTME is real, and its implementation seems to be possible only in high volume centers. In our experience of the 34 first TaTME cases, intraoperative complications occurred in 21% of patients (4 rectal, 1 bladder, and 1 vaginal perforations) *vs*. only 6% from control cases with standard laparoscopic TME (2 rectal perforations) (P = 0.07)[8]. In addition, Perdawood *et al*.[9] reported bladder and urethral injury in 2% and 1% of their patients, respectively, and bleeding in 8%. All these intraoperative adverse events occurred during the transanal phase. In our preliminary experience, when we compared the first 20 cases with the last 14 cases of TaTME, intra-operative complication rate, although not significant, decreased from 25% to 14% (P = 0.4)[8]. The American training program[10] reported the experience of surgeons after a two-day, cadaver-based training, with many concerns about wrong dissection plane in 60%, organ injury (especially urethral lesion) in 25%, and hemorrhage in 15% of cases. This cadaver-based training should be complemented by other training sessions to safely perform TaTME[10]. In addition, Koedam *et al*.[11] reported in their study that the learning curve is about 138 TaTME. At the beginning of their experience with their first 40 patients, the rate of major postoperative complications (Dindo III-IV) was 47.5% of patients, in whom 27.5% was leakage (anastomotic leakage after restorative surgery and presacral abscesses in patients with a colostomy). These rates decreased in the second part of the learning curve, but the procedure was still challenging. Forty procedures may be considered as a cut-off to appreciate an improvement in postoperative morbidity. In conclusion, the implementation of TaTME seems to be difficult, and the question remains of whether it can be done everywhere or only in high volume centers.

Carbon dioxide embolism is another intraoperative adverse event reported during TaTME in the literature. Even if this intraoperative complication is rare, it is well known during minimally invasive surgery[12,13]. The first description of carbon dioxide embolism during TaTME was made by Ratcliffe *et al*.[14] in 2017. More recently, Dickson *et al*.[15], considering the LOREC (The Low Rectal Cancer Development program) and OSTRiCh (Optimizing the Surgical Treatment of Rectal Cancer) TaTME registries, reported carbon dioxide embolism in 0.4% of patients (25/6375). Such occurrence required conversion into open surgery in 7 cases, conversion into abdominal laparoscopic approach in 13 cases, and surgical cessation in 4 cases. Moreover, postoperative readmission in intensive care unit was necessary in 60% of the cases. Among the 25 patients with carbon dioxide embolism, postoperative complications occurred in 12 patients (48%) including 10 major complications (Dindo III-IV: radiological or surgical management of pelvic collections, renal failure, and pulmonary embolism). Furthermore, carbon dioxide embolism seems to be associated with venous bleeding, which occurred in 84% of patients. Even if this complication is rare, it appears as a potentially life threatening complication during TaTME.

During the postoperative course, although the anastomotic leak rate was initially very low in the first TaTME reports, the rate is now similar to laparoscopic TME. In the international registry, anastomotic failure occurred in 15.7%[7], which is similar or even higher than those reported after laparoscopic TME: 13% in the COLOR II trial[16] and 10% in the CLASSIC trial[17]. The Dutch TaTME registry reported a quite similar rate of anastomotic leak: 16.5% after TaTME *vs*. 12.2% after laparoscopic TME[18]. Thus, the idea that leak rate would be lower after TaTME due to avoiding "dog ear" observed during stapled anastomosis performed from above might be wrong, and finally the risk of leak is probably unrelated to the technique used for performing TME.

Long-term functional result in rectal cancer surgery is an important endpoint. Concerning functional results, a comparative study[19] between TaTME and laparoscopic TME recently reported that functional outcomes after TaTME were significantly worse than those after laparoscopic TME. Indeed, anorectal symptoms, such as buttock pain (P = 0.011), diarrhea (P = 0.009), clustering of stools (P = 0.017), and urgency (P = 0.032), significantly disfavored TaTME, as did the mean low anterior resection syndrome score, which is worse after TaTME than laparoscopic TME: 26.18 *vs*. 20.61 (P = 0.054). These results suggest that the use of a transanal device during the entire operating time could lead to a worse functional result, which is already altered after standard colo-anal anastomosis.

To conclude, if TaTME appeared as an attractive alternative for mid and low rectal cancer surgery with encouraging results in the first retrospective studies, some concerns have recently emerged, especially regarding the oncological results and a higher rate of early and multifocal recurrence, leading the Norwegian colorectal cancer group to cease TaTME in their country. Results of ongoing randomized control trials are needed to consider or not TaTME as a standard of care in rectal cancer surgery.

DECLARATIONS

Authors' contributions

Made substantial contributions to conception and design of the study and performed literature review and interpretation: Aubert M, Mege D, Panis Y

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Sylla P, Rattner DW, Delgado S, Lacy AM. NOTES transanal rectal cancer resection using transanal endoscopic microsurgery and laparoscopic assistance. Surg Endosc 2010;24:1205-10.
2. de'Angelis N, Portigliotti L, Azoulay D, Brunetti F. Transanal total mesorectal excision for rectal cancer: a single center experience and

systematic review of the literature. Langenbeck's Arch Surg 2015;400:945-59.

3. Chen CC, Lai YL, Jiang JK, Chu CH, Huang IP, et al. Transanal total mesorectal excision versus laparoscopic surgery for rectal cancer receiving neoadjuvant chemoradiation: a matched case-control study. Ann Surg Oncol 2016;23:1169-76.
4. Lelong B, de Chaisemartin C, Meillat H, Cournier S, Boher JM, et al. A multicentre randomised controlled trial to evaluate the efficacy, morbidity and functional outcome of endoscopic transanal proctectomy versus laparoscopic proctectomy for low-lying rectal cancer (ETAP-GRECCAR 11 TRIAL): rationale and design. BMC Cancer 2017;17:1-8.
5. Deijen CL, Velthuis S, Tsai A, Mavroveli S, de Lange-de Klerk ES, et al. COLOR III: a multicentre randomised clinical trial comparing transanal TME versus laparoscopic TME for mid and low rectal cancer. Surg Endosc 2016;30:3210-5.
6. Larsen SG, Pfeffer F, Kørner H, Norwegian Colorectal Cancer Group. Norwegian moratorium on transanal total mesorectal excision. Br J Surg 2019;106:1120-1.
7. Penna M, Hompes R, Arnold S, Wynn G, Austin R, et al. Incidence and risk factors for anastomotic failure in 1594 patients treated by transanal total mesorectal excision. Ann Surg 2018;269:700-11.
8. Mege D, Hain E, Lakkis Z, Maggiori L, Prost À la Denise J, et al. Is trans-anal total mesorectal excision really safe and better than laparoscopic total mesorectal excision with a perineal approach first in patients with low rectal cancer? A learning curve with case-matched study in 68 patients. Colorectal Dis 2018;20:O143-51.
9. Perdawood SK, Thinggaard BS, Bjoern MX. Effect of transanal total mesorectal excision for rectal cancer: comparison of short-term outcomes with laparoscopic and open surgeries. Surg Endosc 2018;32:2312-21.
10. Atallah SB, DuBose AC, Burke JP, Nassif G, deBeche-Adams T, et al. Uptake of transanal total mesorectal excision in North America: initial assessment of a structured training program and the experience of delegate surgeons. Dis Colon Rectum 2017;60:1023-31.
11. Koedam TWA, Veltcamp Helbach M, van de Ven PM, Kruyt PM, van Heek NT, et al. Transanal total mesorectal excision for rectal cancer: evaluation of the learning curve. Tech Coloproctol 2018;22:279-87.
12. Cottin V, Delafosse B, Viale JP. Gas embolism during laparoscopy: a report of seven cases in patients with previous abdominal surgical history. Surg Endosc 1996;10:166-9.
13. Blaser A, Rosset P. Fatal carbon dioxide embolism as an unreported complication of retroperitoneoscopy. Surg Endosc 1999;13:713-4.
14. Ratcliffe F, Hogan AM, Hompes R. CO2 embolus: an important complication of TaTME surgery. Tech Coloproctol 2017;21:61-2.
15. Dickson EA, Penna M, Cunningham C, Ratcliffe FM, Chantler J, et al. Carbon dioxide embolism associated with total mesorectal excision surgery. Dis Colon Rectum 2019;62:794-801.
16. van der Pas MHGM, Haglind E, Cuesta MA, Fürst A, Lacy AM, et al. Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. Lancet 2013;14:210-8.
17. Guillou PJ, Quirke P, Thorpe H, Walker J, Jayne DG, et al. Short-term endpoints of conventional versus laparoscopic- assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre , randomised controlled trial. Lancet 2005;365:1718-26.
18. Detering R, Roodbeen SX, van Oostendorp SE, Dekker JT, Sietses C, et al. Three-year nationwide experience with transanal total mesorectal excision for rectal cancer in the Netherlands: a propensity score-matched comparison with conventional laparoscopic total mesorectal excision. J Am Coll Surg 2019;228:235-44.
19. Bjoern MX, Nielsen S, Perdawood SK. Quality of life after surgery for rectal cancer: a comparison of functional outcomes after transanal and laparoscopic approaches. J Gastrointest Surg 2019;23:162-30.

Durand. *Mini-invasive Surg* 2019;3:35
DOI: 10.20517/2574-1225.2019.31

Mini-invasive Surgery

Original Article

Open Access

Robotic bronchial sleeve resections: technical details and early results

Marion Durand

Thoracic Unit, Ramsay Générale de Santé, Hôpital Privé d'Antony, Antony 92160, France.

Correspondence to: Dr. Marion Durand, Thoracic Unit, Hôpital Privé d'Antony, 1 rue Velpeau, Antony 92160, France. E-mail: durandm@me.com

How to cite this article: Durand M. Robotic bronchial sleeve resections: technical details and early result. *Mini-invasive Surg* 2019;3:35. http://dx.doi.org/10.20517/2574-1225.2019.31

Received: 30 Aug 2019 **First Decision:** 18 Nov 2019 **Revised:** 18 Nov 2019 **Accepted:** 20 Nov 2019 **Published:** 29 Nov 2019

Science Editor: Valérie Lacroix **Copy Editor:** Jing-Wen Zhang **Production Editor:** Tian Zhang

Abstract

Aim: We report our four-arm robotic bronchial sleeve anatomical lung resection technique and its early results.

Methods: We retrospectively collected all the four-arm robotic sleeve anatomical lung resections we performed in our institution from February 2014 to August 2019. We reported the results as a series of cases.

Results: During that period, 582 robotic procedures were performed by a single surgeon, of which 486 were major anatomical lung resections. From this group, 10 patients (2%) underwent bronchial sleeve resections. All patients were treated on the right lung. Neither conversion nor major events occurred during surgery. The first bronchial sleeve was performed for Patient 219. The mean length of procedure was 164 (± 43) min. One patient died during hospitalization due to a non-related complication (gastric massive bleeding). Three patients had no complications. Six had minor complications (Clavien Dindo Grade 2) resulting in prolonged length of stay. The mean length of stay was 10 (± 5.7) days. No bronchial fistula occurred. All resection margins were R0.

Conclusion: Four-arm robotic bronchial sleeve is a feasible and safe procedure. Telemanipulation surgery offers excellent technical conditions to ensure a hand-sewed anastomosis and R0 resection. The technical principle and dissection are the same as those of open surgery. Patient selection and mastering of the telemanipulation device are mandatory to perform these complex and rare procedures.

Keywords: Lung carcinoma, robotic, surgery, sleeve lobectomy, sleeve segmentectomy

INTRODUCTION

Telemanipulation surgery is a significant revolution in thoracic surgery. It allows minimizing the chest trauma while preserving-or enhancing-the surgeon's skills and vision, allows bimanual surgery, provides a 3rd hand, and gives 3D magnified vision. This is of greatest interest for complex procedures that are performed to spare the patient's lung function. Two trends are noticed in this area: the merger of sub-lobar resections[1] and bronchial sleeve resections[2]. These 2 approaches require advanced skills that can be provided by the telemanipulator.

In this paper, we focus on the technical details of bronchial sleeve resections and report the early results of our experience.

METHODS

We collected retrospectively all the bronchial sleeve procedures performed in our center from the beginning of our robotic program in February 2014 to August 2019. All procedures were performed by a single surgeon. We analyzed them as a series of cases.

Surgical technique

The procedures were performed with either the Da Vinci S*i*™ system or the X*i*™ system (Intuitive Surgical California). For the S*i*™ system, a 12-mm 30° camera was used. For the X*i*™ system, an 8-mm 30° camera was used.

Patient position and port placement

The same patient position and port placement as for any robotic anatomical lung resection and node harvest were used, as described previously[3,4]. This is shown in Figure 1 and summarized below.

The patient was placed on their left side with a tissue roll below their chest to avoid the hip. The patient's body was stabilized with a vacuum cover. The right arm was placed in front of the head on the operating table. Neither central venous line nor arterial blood line was placed. A two-level paravertebral block and a serratus block were performed by the anesthesiologist with ultrasound guidance before surgical incision.

First, the design of the port placement was prepared. The shape of the scapula tip and scapula line were drawn. Then, the intercostal space (ICS) count was done from the 11th ICS from the back of the patient to the anterior side to spot the ninth for the 15-mm port access and the 8th for the camera port at the junction of the scapula line. The first port placed was the camera port to check the position of the other ports from inside the chest. After insertion of the camera, the capnothorax was started under vision control, and low pressure (5 mmHg) and medium flow (10 L/min) were applied. The other ports were placed in the following order: the right hand, the left hand, the third hand, and the port access.

The 30° camera was inserted with vision up to place the other ports. The right-hand port was placed in the 7th ICS, at the junction of the diaphragm and the end of the major fissure. The left-hand port was placed in the 9th or 10th ICS above the triangular ligament. The 3rd hand was placed in the 7th ICS, at least 2 fingers closer to the spine to avoid conflict with the left hand, and at the junction of the visible muscular part of the ICS muscle and the posterior ICS ligament. Its angle of penetration in the chest was 90°. Then, the 15-mm port access was placed in the ninth ICS at the diaphragm insertion, as low as possible to enlarge the triangle among it, the right hand, and the camera port. Then, the capnothorax insufflation was moved from camera port to port access.

Instruments and procedure steps

The instruments used for the procedures and for a right-handed surgeon were as follows:

- The right hand: permanent cautery spatula (Ref. 420184), needle holder SutureCut™ (Ref. 420296), or

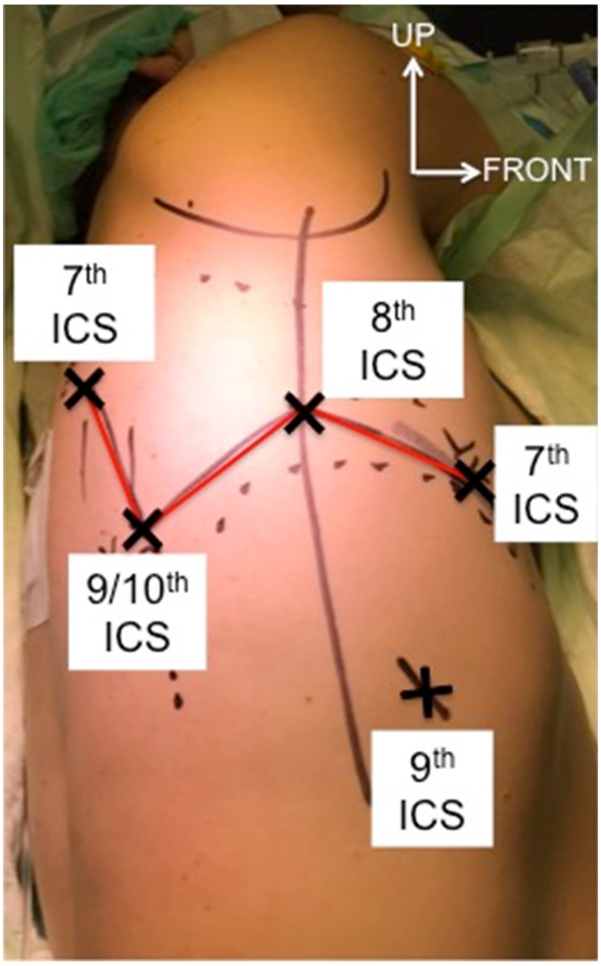


Figure 1. Port placement according to ICS. The red lines show the partial W design of the port placement; the interrupted lines show the projected major fissure (up) and diaphragm (down). ICS: inter costal space

curved scissors (Ref. 420178).
- The left hand: fenestrated bipolar forceps (Ref. 420205).
- The third hand (assistant arm): ProGrasp^{TM} forceps (Ref. 420093).

Two handmade rolled gauzes were inserted, one for each grasper, to ensure a non-direct traction or lung exposure. A fissure-first technique and sharp dissection were performed. The steps were almost the same as routine lobectomy, mainly stated as follows:
- Triangular ligament opening and zone 8/9 node harvest.
- Spot of inferior pulmonary vein.
- Zone 7 node harvest and opening the posterior interbronchial zone.
- Spot the artery in the fissure.
- Open the fissure.
- Control and section of the artery (or arteries).
- Control and section of the vein.
- Finish the remaining parenchymal section.
- Bronchus dissection at last and section in pathologic zone.
- Placement of the lobe or segment in the bag.
- Complementary section of the bronchus in healthy macroscopic margin (and then sent to frozen section).
- Bronchial anastomosis.

- Zone 2R 4R node harvest.
- Bag extraction.
- Chest tube placement and closing.

Arterial ligation was performed either by sewing 2 knots with linen 0 with the needle holder or by stapling with white 35 mm endo stappler [mainly for anterior mediastinal artery in case of right upper lobectomy (RUL)]. Venous ligation was performed either by sewing 1 knot with linen 0 doubled by a Vicryl 2/0 (22-mm needle) 10-cm suture with the needle holder or by stapling with white 35 mm endo GIA. In the case of "manual" ligation of vessels, the distal part was dissected as far as possible and the section was done by spatula burning along the forceps and then distal vessel bipolar burn. Radical hilar and mediastinal node harvest were performed during the procedure.

The assistant was holding a long suction device (Elefant® Coloplast Ltd UK) to ensure a bloodless field and to avoid smoke inside the chest. The suction device was also used to stabilize the operating field by being placed over one of the rolled gauzes. For each procedure, a frozen section analysis of the bronchus border was performed to ensure the R0 margin. The specimen was placed after resection of the bronchus in an Endobag® to prevent the chest contamination, and was extracted through the port access enlargement at the end of the procedure.

A 24 French chest drain was left in the chest through the right-hand port and minor suction was applied (minus 10 cm of water) after the patient's extubation.

Sleeve lobectomy

For the end-to-end anastomosis, V-Loc Covidien™ 3/0 180 (17-mm needle taper point, 15 cm length) sutures were used. For each anastomosis, 2 half-continuous sutures were performed.

The principle of the anastomosis technique, referring to a sleeve RUL, is as follows. A vertical axis exposure of the 2 borders was preferred. The posterior wall running suture started from outside the upper border, forehand, 3 o'clock, clockwise. After the first way out from the lower border, usually backhand, the needle was placed through the final loop of the wire to block the end of the running suture. The running suture was continued, mainly backhand, until 9 o'clock outside the lower border with the tension of the suture applied after each loop. Then, the anterior wall sewing was started with another V-Lock wire. The start of this second suture was from the lower border outside 3 o'clock, forehand. As with the previous first loop, the needle was placed through the final loop of the wire to block the end of the running suture after emerging from the upper border outside. The running suture was then conducted anti-clockwise to 9 o'clock outside the upper border, here again mainly backhand.

The airtightness was checked under water with mechanical insufflation before knotting the two wire ends, to ensure a harmonious tension of the running sutures. Then, the final knot was done and the needles were removed from the chest.

Regarding the lobe removal, exposure and gests were adapted. For a sleeve median lobectomy (ML), the bronchial section was done through a fissure exposure after pulling back the lower lobe artery with a loop (silicone 10-cm cut blue loop) to expose the intermediate bronchial trunk. The anastomosis was performed after changing the exposure for a posterior view. Then, the 2 borders were naturally placed to avoid a twist and the artery was hidden away from the sewing zone.

For inferior bilobectomy or lobectomy, the end anastomosis sleeve required a v-shaped cut of the distal part of the bronchus. Then, separate single knots were placed, using violet Vicryl 2/0 (22-mm needle, 10-cm length). Four to six wires were placed before starting to knot. A double loop was performed for the 1st knot to help tighten the knot.

For superior bilobectomy, pericardium section below the inferior pulmonary vein was achieved with the spatula to release the tension of the anastomosis. This could also be performed for RUL.

S6 sleeve segmentectomy

For sleeve segmentectomy, green light (FireFly™) was used to ensure accurate parenchymal margin resection. After section of vascular and bronchial structure, 8 mL (i.e., 15 mg of indocyanine green) were injected as an iv flush and rinsed with 10 mL of saline. About 20 s after injection, the green light was turned on to spot the margin of parenchymal resection. The margins were marked with the bipolar grasper. The grasper was previously placed in the right-hand port. Then, the specimen was placed in an Endobag®.

The complementary section of the bronchus was done with curved scissors through the fissure exposure and sent for frozen section analysis.

For better control of the bronchial section, the third arm was anteriorly tracking the basal pyramid trunk with a silicone loop (10-cm cut blue loop).

As for ML anastomosis, the posterior approach was preferred as it ensured the natural encounter of the two borders and moved the artery away during suturing. The same steps of suture were performed as RUL anastomosis.

Data analyses

Quantitative data are presented as the number of observed values, mean ± standard deviation, median, and range (min-max), while qualitative data are presented as the number of observed values. Complication severity was evaluated with Clavien Dindo classification[5].

RESULTS

During this period (February 2014 to August 2019) in our institution, 582 patients underwent robotic thoracic procedures. In this cohort, 486 anatomical lung resections were performed, which involved 351 lobectomies or bilobectomies and 135 segmentectomies. Among these patients, 10 received a bronchial sleeve, i.e., 2% of the anatomical lung resections. The first bronchial sleeve was done on Patient 219. The main characteristics of the patients and procedures are reported in Table 1 in chronological order. The first 5 procedures were performed with the Da Vinci S*i*™ system and the last five with the Da Vinci X*i*™ system.

All patient had accurate pathology diagnosis of the lesion preoperatively. All surgeries occurred on the right lung. None of the patients involved pathological nodes. All resection margins were R0. The procedure details and outcomes are reported in Table 2 in the same order as Table 1.

No major events occurred preoperatively. Surgery duration was from 121 to 243 min. No blood transfusion was required during hospital stay. No bronchial fistula occurred.

DISCUSSION

Bronchial sleeve procedures are complex and rare surgeries. The benefit of the enhanced vision and hand tool of the robotic system is significant for these surgeries. The principle of telemanipulation surgery is

Table 1. Chronological description of the characteristics of patients and procedures

Patient	Procedure	Sex	Age (years)	ASA	BMI	FEV (%)	Tumor size (mm)	Number of nodes	Pathology
1	RUL + ML	M	36	2	27	99	25	20	Carcinoid
2	ML	M	62	3	27	MD	30	15	SCC
3	ML + RIL	M	17	1	22	85	12	6	Carcinoid
4	ML	M	52	3	21	107	30	21	ADK
5	RUL	F	65	2	18	96	15	21	SCC
6	S6R	M	70	2	22	64	85	14	SCC
7	RIL	M	60	3	25	75	20	25	SCC
8	RUL	M	55	2	25	107	25	19	Carcinoid
9	ML + RIL	M	77	3	19	96	26	30	SCC
10	RUL	M	42	2	21	101	12	9	Carcinoid
	Median [Min; Max]		58 [17; 77]	2 [1; 3]	22 [18; 27]	96 [64; 10]	25 [12; 85]	19.5 [6; 30]	

ML: median lobectomy; RUL: right upper lobectomy; RIL: right inferior lobectomy; S6R: segment 6 right lung; MD, missing data; SCC: squamous cell carcinoma; ADK: adenocarcinoma

Table 2. Details of patients' procedures, outcomes, and complications

Patient	Sleeve procedure	N staplers	Surgery duration (min)	Blood loss (mL)	Chest tube (d)	LOS (d)	Complication (yes 1, no 0)	Clavien dindo	Complication type
1	RUL + ML	1	141	5	2	4	0	0	
2	ML	6	243	150	5	7	0	0	
3	ML + RIL	4	121	5	5	7	1	2	Chylothorax
4	ML	8	227	50	10	12	1	2	Air leak > 5 days
5	RUL	5	141	5	3	12	1	2	Pneumothorax
6	S6R	8	156	100	6	9	1	2	Bronchitis
7	RIL	5	125	5	4	19	1	5	Gastric hemorrhage
8	RUL	4	125	50	2	4	0	0	
9	ML + RIL	6	189	50	7	20	1	2	Air leak > 5 days
10	RUL	3	176	150	4	7	1	2	Atelectasis
	Mean (± SD)	5 (± 2.2)	164 (± 43)	57 (± 57)	4.8 (± 2.4)	10 (± 5.7)			

ML: median lobectomy; RUL: right upper lobectomy; RIL: right inferior lobectomy; S6R: segment 6 right lung; LOS: length of stay; SD: standard deviation

to allow open surgery procedures in a closed chest. This means that the procedure flow is the same as the open surgery gold standard.

In our experience, we have had no conversions. We found a longer LOS in this group rather than standard procedure or those described in[6]. First, patients requiring this procedure might have comorbidities and thus are at risk of complications, thereby requiring more hospital care. Second, the postoperative risk concerns mainly the scaring process on the bronchus, which requires a closer check of the patients and thus a longer length of stay. The aim of this surgery is not the quickest outcome but a good outcome that spares the lung. In our series, 1 patient died during hospital stay of massive gastric hemorrhage. After analyzing this case during a dedicated mortality meeting, this dramatic outcome was not found to be related to the surgical approach. The patients' comorbidities and the stress of such disease are real. This highlights the severity of the underlying pathologies and risks. We do not understate the harshness of disease and surgical risks due to miniaturization of thoracic penetration, especially for complex procedures.

Our 1st sleeve procedure was achieved for Patient 219, i.e., after significant experience with the machine. This might have given the surgeon time to be technically confident and therefore appropriate for the patient case. The learning curve for complex procedures depends on the surgeon's self-appreciation and cannot be estimated as in standard procedures at around 30 cases[7]. For complex procedures, the surgeon's mastery of the tool is the 1st step and remains based on their honest capacity assessment. The other restricting element is patient selection. As shown in our experience, these are rare indications (2%). We are aware of the patient benefit in terms of disease-free survival and do not push for technical achievement[8]. In our series of ten patients, 4 had carcinoid tumor, 5 had squamous cell carcinoma (SCC), and only 1 adenocarcinoma; none had node involvement. It makes sense, as SCC and carcinoid tumors are more proximal, endobronchial diseases than other tumors and might be more subject to such procedures.

The selection of patients is mandatory and we summarize some criteria below regarding patient status and tumor standard:
- Either poor lung function or patient's comorbidities to avoid pneumonectomy outcome[9].
- R0 achievement.
- Low degree of aggressiveness of disease (carcinoid tumors and N0 disease).

In our experience, the tumor size is not a major limit as we have removed tumors with size up to 85 mm. The distance between the tumor and the vascular structure is more limiting than the size itself. We are still waiting for appropriate tools to clamp either the pulmonary artery or the pulmonary vein to allow safe vascular sleeve resection. That might explain why we have only performed right-side bronchial sleeve, as most left-side bronchial sleeve cases require a proximal vascular control.

In our experience, it is a bloodless surgery [mean blood loss: 57 mL (± 57)]. Hemostasis during the procedure is cautiously realized as the dryness of the operating field is mandatory to assess good vision (red color decreases brightness and contrast).

The patients were placed in lateral lying position without bending the table to avoid any limitation of the venous flow of the lower body, which combined with the capnothorax might trouble the cardiac input. The partial W-shaped port position ensures a non-conflicting position of the arms and instruments either outside or inside. It can be applied for any anatomical lung resection and is the same for the left side (mirror effect). The principle is to have the camera above the hands, similar to how the head is above the shoulders, and to have an assistant on the side coming perpendicularly. This setting avoids conflict and allows a complete control of the chest target zones. The 30° vision is also important for providing an overview of the target and to avoid blind spots while twisting the camera. At the beginning of the procedure, the chest wall is viewed through 30°-up vision and the procedure is achieved through 30°-down vision. The third-hand position is also meant to avoid conflict with the left hand, inside or outside, as it enters 90° to the chest, higher and closer to the spine.

For ML bronchial anastomosis, the exposure change (from fissure view for resection of the bronchus to posterior view behind the pulmonary vein) is of great interest for presenting the 2 bronchial borders and vanishing pulmonary artery away from the suturing zone. The versatility of exposure during robotic surgery must be exploited.

The use of barbed wire secures the tension adaptation of the running suture, but it is not mandatory. Previously published small series of patients have described the use of braided waxed sutures such as Vicryl running sutures or separate sutures and the use of monofilament such as polydioxanone[6,10-14]. These papers show similar outcomes to our series but do not describe our fully-closed-chest four-arm robotic technique. The use of absorbable monofilament might be tricky as its elasticity might be difficult to handle without haptic feedback. The choice of the needle is also important, as it must be small (17 mm) and semicircular to be scaled and fit to the instruments and bronchial structures. To limit the risk of wire rupture while knotting due to excess of "manual" tension, we suggest the use of the strongest V-Loc™, i.e., 180. Even then, the surgeon must be aware of this risk and be as delicate as possible while applying distraction force on the wire. The barbed suture does not require more than four knots to be stable, which is fewer than monofilament wires. The lack of haptic feedback is balanced by enhanced vision in most situations.

The size of the wire must not be too thick to prevent the cut of the borders. Because of magnification, the surgeon might tend to take smaller border margins and quicker steps to progress than in open surgery during the running suture. It might then be useful to pay attention to the size of the instruments to keep an accurate scale evaluation of measure.

The surgeons' hard skills are conserved, indeed enhanced, by the telemanipulator and favor the precise and tremorless moves of the instruments for either forehand or backhand sutures (bimanual surgery). This technical improvement ensures manual knot and stitch of distal arteries, which are a key point of these advanced procedures. First, it is the basis of the surgeon's hard skills development and retention. Second, it helps for control and exposure of vascular structures when required. A stapleless artery is safer to manipulate and the presence of a nude arterial stump to hold can be useful to mobilize/expose the artery.

During our experience, we switched from the Da Vinci S*i*™ system to the X*i*™ system. The benefit of this upgrade is valuable for the surgeon and the operating room setting. With the S*i*™ system, we were using a 12-mm camera to ensure the best vision; with the X*i*™ system, the full high definition vision is provided through an 8-mm camera, and smaller is better for the patient's postoperative pain. The S*i*™ system needed to be placed on the axis of the scapula line, which limited the head access for the anesthesiologist during the procedure and prolonged the procedure setting. The X*i*™ system has smaller and wider motion zone moves than the S*i*™ system, as well as an autofocus camera and surgeon console control of the upside-down twist of camera, which might save time and comfort during the procedure. This might explain the decreasing trend of procedure lengths between the first half and second half of our series.

In our experience, four-arm robotic bronchial sleeve lung resection and node harvest is safe and feasible. Patient selection and surgeon's robotic expertise are mandatory to perform such rare procedures. Dedicated vascular clamping devices are awaited to enlarge indications to left side and vascular sleeve resections.

DECLARATIONS

Authors' contributions
The author contributed solely to the article.

Availability of data and materials
Not applicable.

Financial support and sponsorship
None.

Conflicts of interest
Author is an official proctor for Intuitive Surgical.

Ethical approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

REFERENCES

1. Li C, Han Y, Han D, Chen X, Chen K, et al. Robotic approach to combined anatomic pulmonary subsegmentectomy: technical aspects and early results. Ann Thorac Surg 2019;107:1480-6.
2. Shanahan B, O'Sullivan KE, Redmond KC. Robotic sleeve lobectomy-recent advances. J Thorac Dis 2019;11:1074-5.
3. Durand M, Dabboura E, Lamonerie L, Herkert A, Zarka V, et al. Four-arm robotic lung resection versus muscle-sparing mini-thoracotomy: retrospective experience. J Thorac Dis 2019;11:1433-42.
4. Durand M. Four-arm robotic sleeve right upper lobectomy. Ann Cardiothorac Surg 2019;8:286-7.
5. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-13.
6. Jiao W, Zhao Y, Qiu T, Xuan Y, Sun X, et al. Robotic bronchial sleeve lobectomy for central lung tumors: technique and outcome. Ann Thorac Surg 2019;108:211-8.
7. Song G, Sun X, Miao S, Li S, Zhao Y, et al. Learning curve for robot-assisted lobectomy of lung cancer. J Thorac Dis 2019;11:2431-7.
8. Reddy RM. Robotic sleeve lobectomy-technically possible but is it being overused? J Thorac Dis 2019;11:S1211-2.
9. Pages PB, Mordant P, Renaud S, Brouchet L, Thomas PA, et al. Sleeve lobectomy may provide better outcomes than pneumonectomy for non-small cell lung cancer. A decade in a nationwide study. J Thorac Cardiovasc Surg 2017;153:184-95. e3.
10. Cerfolio RJ. Robotic sleeve lobectomy: technical details and early results. J Thorac Dis 2016;8:S223-6.
11. Lin MW, Kuo SW, Yang SM, Lee JM. Robotic-assisted thoracoscopic sleeve lobectomy for locally advanced lung cancer. J Thorac Dis 2016;8:1747-52.
12. Pan X, Gu C, Wang R, Zhao H, Shi J, et al. Initial experience of robotic sleeve resection for lung cancer patients. Ann Thorac Surg 2016;102:1892-7.
13. Gu C, Pan X, Chen Y, Yang J, Zhao H, et al. Short-term and mid-term survival in bronchial sleeve resection by robotic system versus thoracotomy for centrally located lung cancer. Eur J Cardiothorac Surg 2018;53:648-55.
14. Li C, Zhou B, Han Y, Jin R, Xiang J, et al. Robotic sleeve resection for pulmonary disease. World J Surg Oncol 2018;16:74.

Moroni *et al. Mini-invasive Surg* 2019;3:36
DOI: 10.20517/2574-1225.2019.34

Mini-invasive Surgery

Review

Open Access

Check for updates

Minimally invasive right colectomy - from conventional laparoscopic resection to robotic-assisted surgery: a narrative review

Paolo Moroni[1], Carmen Payá-Llorente[2], Lelde Lauka[1], Elisa Reitano[1], Riccardo Memeo[3], Paschalis Gavriilidis[4], Francesco Brunetti[1], Aleix Martínez-Pérez[2]

[1]Department of Digestive and Hepatobiliary surgery, Henri-Mondor Hospital, University Paris Est-Créteil - UPEC, Créteil 94010, France.
[2]Department of General and Digestive Surgery, Hospital Universitario Doctor Peset, Valencia 46017, Spain .
[3]Department of Emergency and Organ Transplantation, University Aldo Moro of Bari, Bari 70121, Italy .
[4]Department of Hepato-Biliary-Pancreatic and Oesophago-Gastric Surgery, Imperial College Healthcare NHS Trust, Hammersmith Hospital, London W12 0HS, UK.

Correspondence to: Dr. Paolo Moroni, Department of Digestive and Hepatobiliary surgery, Henri-Mondor Hospital, University Paris Est-Créteil - UPEC, 51 Avenue du Maréchal de Lattre de Tassigny, Créteil 94010, France. E-mail: dr.pmoroni@gmail.com

How to cite this article: Moroni P, Payá-Llorente C, Lauka L, Reitano E, Memeo R, Gavriilidis P, Brunetti F, Martínez-Pérez A. Minimally invasive right colectomy - from conventional laparoscopic resection to robotic-assisted surgery: a narrative review. *Mini-invasive Surg* 2019;3:36. http://dx.doi.org/10.20517/2574-1225.2019.34

Received: 8 Sep 2019 **First Decision:** 24 Oct 2019 **Revised:** 8 Nov 2019 **Accepted:** 13 Nov 2019 **Published:** 12 Dec 2019

Science Editor: Giulio Belli **Copy Editor:** Jing-Wen Zhang **Production Editor:** Tian Zhang

Abstract
Robotic-assisted abdominal surgery was introduced with the aim of overcoming the drawbacks of the conventional laparoscopic approach. The present narrative review focuses on the comparison between laparoscopic and robotic-assisted approaches for right colectomy (RC) regarding short- and long-term outcomes, costs, and learning curve. The main technical aspects related to the use of robotic assistance for this specific procedure are further discussed. Minimally invasive RC is considered technically challenging due to the particularities of the right and middle colic vascular anatomy. Robotic RC is not yet widespread due to its high cost and longer operating time. However, its use may result in advantages regarding short-term clinical outcomes, and it facilitates the acquisition of basic surgical skills by speeding up the learning curve of minimally invasive colorectal surgery.

Keywords: Minimally-invasive right colectomy, robotic surgery, laparoscopic surgery, colon cancer, anastomosis, learning curve, costs

INTRODUCTION

Colorectal cancer (CRC) is the most common malignant disease of the gastrointestinal tract and the third most common cancer worldwide with over 1,000,000 new diagnoses and 500,000 deaths per year in the United States[1]. Approximately 40% of all CRCs are located in the right colon[2]. In recent years, several technical requirements have been established to improve the post-surgery outcomes for colon cancer. The American Joint Committee on Cancer (AJCC) has defined that, for a radical colectomy, a minimum of 12 lymph nodes must be examined to avoid understaging[3,4]. Other milestones include the introduction of the principles of complete mesocolic excision (CME)[5] and the introduction and widespread use of minimally-invasive surgery (MIS)[6]. For the resection of colon cancer, the use of conventional laparoscopy seems to reduce the length of hospital stay, postoperative pain, and the time until daily activities return to normal, as well as improve cosmetic outcomes when compared to the open approach[7-10]. Nevertheless, the adoption of laparoscopic right colectomy (LRC) might not be as widespread as expected[11-15], probably due to the high complexity of the vascular anatomy of the right and transverse colon[16].

For minimally-invasive right colectomy (RC), the debate continues regarding whether the ileo-colonic anastomosis should be performed intra- or extra-corporeally. The majority of the published series on minimally invasive RC have reported an extra-corporeal anastomosis (EA) fashioning[16]. Few studies comparing EA with intra-corporeal anastomosis (IA) have been published recently[17]. The principles of CME require a meticulous dissection, which increases the technical challenge of LRC. In this scenario, the use of robotic assistance may overcome the limitations of the straight conventional laparoscopic instruments and allow performing a safer CME with central vascular ligation (CVL), especially in obese patients[18]. The latest *da Vinci Xi*® robotic system (dVXi) presents some additional advantages for colorectal procedures when compared with previous versions (*da Vinci S*® and *Si*®), such as simpler docking, possibility to position the optical system in all of its arms, which are thinner (width 1.7' *vs.* 2.9'), easier to move, and allow multi-quadrant surgery. The present narrative review aims to describe the main technical aspects of robotic right colectomy (RRC) and compare the learning curve, the short- and long-term outcomes, and the costs between LRC and RRC. A literature search was performed in MEDLINE database (PubMed); articles published in English between 2000 and 2019 using the following terms were screened: "MIS", "RC/colon resection", "robotic surgery", AND "laparoscopic surgery" [Tables 1-3][17,19-32].

TECHNICAL ASPECTS OF RRC

Positioning

There is no consensus about the position of patient and robot in the operating room. In our center, we put the patient in a supine position tilted on the left side (10°-25°) with the arms tight to the body and legs closed. Generally, the table is positioned in Trendelenburg position (5°-10°)[33,34] and the robot is placed on the right side of the patient [Figure 1].

Docking

The pneumoperitoneum is first established. Different options to position the ports have been described, some of which are similar to the conventional laparoscopic approach[35,36]. Advances in robotic systems allow variations of the port placement. Moreover, dVXi arms are thinner and have more flexibility, thus decreasing the risk of external collisions when compared to previous robot versions.

Diagonal or oblique port placement

Four trocars are positioned drawing an oblique line from 4 cm above the pubic symphysis (Port 1) to the left mid-clavicular line crossing over the left sub-costal margin (Port 4), separated by 7.5 cm. One assistant port can be placed at the level of the umbilicus on the middle clavicular line [Figure 2, red points][37].

Table 1. Descriptive table

Author	Year	Journal	Period of recruitment	Type of paper	Number patients	Median age (range) *Mean age ± SD	Mean BMI	ASA			
								1	2	3	4
Ballantyne *et al.*[19]	2006	Surg Laparosc Endosc Percutan Tech	2003-2004	Prosp	16						
D'Annibale *et al*[20].	2004	Dis Colon Rectum	2001-2009	Retrosp	50	73.3	24 (49)	5 (10)	31 (62)	13 (26)	1 (2)
Juo *et al.*[21]	2015	Surg Endosc	2010-2013	Retrosp	31	60.3	26.6				
Trastulli *et al.*[17]	2015	Surg Endosc	2005-2014	Retrosp	102	68.8	25.6	8 (7.8)	55 (53.9)	39 (38.2)	0
Formisano *et al.*[22]	2016	Updates Surg		Retrosp	53						
Petz *et al.*[23]	2017	EJSO	2016	Prosp	20	69					
Lujan *et al.*[24]	2017	J Robot Surg	2009-2015	Retrosp	89	71	28.4				
Mégevand *et al*[25].	2019	Updates Surg	2010-2015	Retrosp	50	70.3		6 (12)	37 (74)	7 (14)	0
Blumberg[26]	2018	J Robot Surg	2003-2016	Retrosp	21	65	30	0	6 (39)	15 (71)	0
Cleary *et al.*[27]	2018	Surg Endosc	2010-2016	Retrosp	588						
Scotton *et al.*[28]	2018	J Laparoendosc Adv Surg Tech A	2001-2015	Retrosp	206	70.1	26	28 (13.7)	120 (58.8)	52 (25.5)	4 (2.0)
Johnson *et al*[29]	2018	J Robot Surg	2015-2016	Retrosp	113	66.4					
Spinoglio *et al*[30].	2018	Ann Surg Oncol	2005-2013	Prosp	101	71.2	25.1	13 (12.8)	40 (39.6)	38 (37.6)	10 (10)
Park *et al.*[31]	2019	Surg Endosc	2009-2011	Prosp	35	62.8	24.4	15 (42.9)	16 (45.7)	4 (11.4)	0
Schulte *et al.*[32]	2019	BMC Surg	2016-2018	Retrosp	31	75					

Prosp: prospective; Retrosp: restrospective

Suprapubic port placement

This approach has been increasingly used [Figure 2, blue points]. The trocars are positioned on a horizontal line 3-4 cm above the pubic symphysis, separated by 6.5-7.5 cm[23,32,38,39]. The unconventional viewpoint is a potential barrier against its widespread use. This placement allows the extraction of the specimen using trocar's incisions.

Single-Incision Robotic Colectomy

The approach is technically challenging as surgical instruments can collide and freedom of motion may be impaired. It has been recently described that this approach should not be recommended in obese patients (BMI > 30 kg/m^2)[21,40]. Further limitations for its current widespread use include the cost of multi-port access and increased incisional hernia rates[41-43].

Medial-to-lateral vs. lateral-to-medial approaches

Two main approaches are used for the right colonic mobilization in both LRC and RRC. Some authors suggest using the medial to lateral approach (MtL)[28] while others prefer the lateral to medial (LtM)[9,19,44] alternative. The MtL technique starts after identifying the inferior part of the duodenum and performing an incision in the mesocolon. Ileo-colic and right colic arteries are clipped close to the superior mesenteric axis in order to insure a CME. MtL mobilization continues with the dissection of Toldt-Gerota fascia from "bottom-to-up", ending with the division of the lateral peritoneal attachments. In the LtM approach, the ligation of vascular pedicle is performed after the mesocolic dissection and the mobilization of the lateral peritoneal attachments, as in an open

Table 2. Table for surgical approach

Author	Type Robot	Trocar's site	Approach	Mean Op. time (min)	Anastomosis					
					Stapled	Handsewn	Intracorporeal	Extracorporeal	Isoperistaltic	Anisoperistaltic
Ballantyne *et al.*[19]	S		MtL, LtM			Y		Y	Y	N
D'Annibale *et al.*[20]	S		MtL	223		Y	Y	Y	Y	N
Juo *et al.*[21]	SIRC	Umbilicus								
Trastulli *et al.*[17]	Si and Xi		MtL	287	Y	Y	Y	N	Y	N
Formisano *et al.*[22]	Xi	Diagonal/Suprapubic	MtL							
Petz *et al.*[23]	Xi	Suprapubic	MtL	249	Y		Y		Y	
Lujan *et al.*[24]	Xi		MtL		Y		Y		Y	
Mégevand *et al.*[25]	Xi		MtL	204	Y		Y		Y	
Blumberg[26]	Si		MtL	330	Y		Y		Y	
Cleary *et al.*[27]	Si and Xi		MtL-LtM		Y		Y (335)	Y (253)	Y	Y
Scotton *et al.*[28]	Xi	Diagonal	MtL	253	Y		Y		Y	
Johnson *et al*[29]	Xi			149	Y		Y			
Spinoglio *et al.*[30]	S and Si			279	Y		Y		Y	
Park *et al.*[31]	Si			195	Y		Y	Y		
Schulte *et al.*[32]	Xi	Suprapubic	MtL	285						

MtL: medial to lateral; LtM: lateral to medial; Y: yes; N: no

surgery. There is no evidence of relevant differences between the 2 approaches. MtL approach may reduce the necessary movements, therefore facilitating the use of robotic assistance[22,28]; early pedicle ligation may also prevent the tumor spreading throughout the mesentery[45].

Complete mesocolic excision

The surgical principles of total mesorectal excision (TME) for rectal cancer were applied in RC, resulting in the concept of CME with CVL, as described by Hohenberger *et al.*[5] in 2008. D3 lymphadenectomy has been performed for decades in Eastern countries when operated on colon cancer and is equivalent to CME[46]. The long-term outcomes after RC have not been improved to the same degree as those for rectal cancer after the introduction of TME[47]. Some studies showed that CME may decrease local recurrences (from 6.5% to 3.6%)[5] and improve survival rates, especially for stage III tumors[48]. The absence of data from well-powered studies, as well as the technical difficulty added by the extended dissection, has impeded the routine implementation of CME for RCC and it is nowadays far from being the "gold standard" in Western countries. Some authors suggest that robotic assistance allows overcoming the technical difficulties of CME in RCC with lower conversion rate than LRC[30].

Intra-corporeal *vs.* EA

EA has traditionally been the preferred method for intestinal reconstruction after LRC. IA may present some advantages, such as reducing the chance of twisting intestinal stumps and causing injuries by specimen traction. IA also allows choosing the location of the specimen extraction incision, reducing the possibility of incisional hernia[41,49,50]. IA application in LRC has been limited due to its technical difficulty[25,51-54], which may be mitigated by the use of

Table 3. Table post-operative

Author	Conversion (%)	Clavien-Dindo postoperative complications				Leak	Reoperation (%)	Readmission (%)
		1 (%)	2 (%)	3 (%)	4 (%)			
Ballantyne *et al.*[19]	0					0		
D'Annibale *et al.*[20]	0			1 (2)		0	1 (2)	0
Juo *et al.*[21]	1 (3.2)					0	0	0
Trastulli *et al.*[17]	4 (3.9)					3 (2.9)	7 (6.8)	0
Formisano *et al.*[22]	1 (1.8)					0	0	0
Petz *et al.*[23]	0	0	0	2 (10)	0	0	0	0
Lujan *et al.*[24]	2 (2.3)	19 (21.3)	6 (6.7)	1 (1.1)	0	1 (1.1)	1 (1.1)	2 (2.2)
Mégevand *et al.*[25]	0					2 (4)		
Blumberg[26]	0							
Cleary *et al.*[27]								
Scotton *et al.*[28]	5 (2.4)					1 (0.4)	6 (2.9)	
Johnson *et al*[29]	0						0	0
Spinoglio *et al.*[30]	0		2 (2)			1 (0.9)	2 (2)	
Park *et al.*[31]	0			1 (2.8)		1 (2.8)	1 (2.8)	0
Schulte *et al.*[32]	0	9 (29)	2 (6.4)	0	0	0		

robotic assistance[55,56]. EA may require an extensive mobilization of the transverse colon for reaching the specimen extraction incision[54,57]. Two recent meta-analyses in LRC have shown shorter time for first defecation, and oral liquid diet, and decreased length of hospital stay in the IA group[58,59]. Van Oostendorp *et al.*[59] also showed a reduction of the short-term postoperative morbidity and surgical-site infection rate in the IA group. No differences were found regarding the other short-term clinical and histopathological variables evaluated[59]. Technical advantages of robotic surgery permit performing an IA more easily. Mégevand *et al.*[25] reported a series of 100 cases comparing RRC and LRC with IA, and they observed faster intestinal recovery and fewer conversions in the RRC group. Solaini *et al.*[60], in a subgroup meta-analysis comparing only EA, found no significant differences between RRC and LRC. To date, no randomized controlled trial has been reported comparing RRC and LRC with the same type of anastomosis. Further studies are therefore needed before drawing any conclusion regarding the potential benefits of both IA and robotic assistance in decreasing the odds of anastomotic leak or improving intestinal recovery after RC.

THREE-DIMENSIONAL VERSUS TWO-DIMENSIONAL VIEW IN LRC

Since the first steps of minimally-invasive surgical procedures, technological research continues to improve its outcomes. In the field of surgical view, a notorious revolution is expected and it is still ongoing. The new laparoscopic platforms together with the new generation of optics allow exceeding the limits of the two-dimensional (2D) view. Abdelrahman *et al.*[61] reported that three-dimensional (3D) optics with ultra-high definition 4k allow a faster learning curve. This experimental evidence was confirmed by Currò *et al.*[62], who concluded that the 3D vision improves the depth of perception, which is especially useful in performing an IA, and it also produces less physical strain to the surgeon. However, further studies are needed before drawing any definitive conclusions regarding the potential benefits of 3D (with or without 4k) *versus* conventional 2D. To date, the choice between 3D and 2D systems relies only on the surgeon's preferences and the hospital's resources.

LEARNING CURVE OF MINIMALLY-INVASIVE RC

Robotic surgery, similar to all the minimally-invasive surgical procedures, requires the acquisition of specific abilities and skills. The learning curve is the number of cases required to achieve expertise with minimal procedural time and complications[63,64]. LRC requires a high degree of dexterity and technical skills which result in a learning curve of 20-30 procedures[36,65,66]; this number may increase with IA fashioning[59]. Operative time for the first cases of robotic surgery is shorter than that in laparoscopy[67].

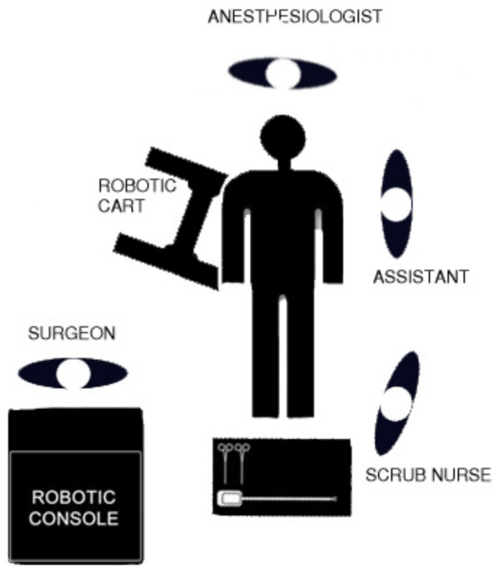


Figure 1. ROBOTIC CONSOLE: robotic platform. SURGEON: first surgeon; ROBOTIC CART: robotic arms; ANESTHESIOLOGIST: anesthesiologist; ASSISTANT: second surgeon; SCRUB NURSE: operative nurse

Additionally, RRC has been proposed as an ideal procedure for the surgeon's initial steps with robotics[68]. de'Angelis *et al.*[36] observed that RRC with EA was associated with a faster learning curve than LRC with EA. Only 16 procedures in the RRC group were needed to significantly reduce operative time versus 25 surgeries in the LLC group. This may be explained by the fact that robotic surgery improves the surgeon's dexterity and depth of perception. Parisi *et al.*[69] concluded that the learning curve for RRC is around 44 procedures. This long curve was necessary to significantly reduce operative time and conversion to open surgery rate, as well as to significantly increase the number of harvested lymph nodes. Performing RRC can be justified in different situations depending on the type of surgical unit, for example as a training procedure for robotic colorectal surgery for young surgeons in centers that are already skilled at performing RRC. Moreover, centers aiming to incorporate complex robotic procedures could start with RRC as one of the first of them.

SHORT- AND LONG-TERM OUTCOMES

Several studies have demonstrated the safety and efficacy of RRC for both short- and long-term outcomes[31,60,70,71]. Only one randomized controlled trial found no differences in lengths of hospital stay and the surgical complications rate between RRC and LRC groups[72]. The latest meta-analysis published by Ma *et al.*[73] in 2019 concluded that RRC has a longer operation time, lower estimated blood loss, shorter hospital stay, and lower postoperative complication rate than LRC. Solaini *et al.*[60] reported that conversion to open surgery was more common during LRC, with no significant differences in mortality and postoperative complication rate. Lim *et al.*[70] concluded that the time for diet, first flatus, and first defecation, and the length of hospital stay were significantly decreased for RRC. Similarly, Rondelli *et al.*[74] showed that the time for the first flatus was significantly shorter in RRC. Such differences in recovery may also be related to the less traumatic intra-peritoneal approach provided by the use of IA, rather than purely by the use of robotic assistance. When combined, they can provide a quicker bowel recovery with less need of analgesics[17,75] and fewer post-operative complications[24,74,76-78] [Tables 4 and 5][17,24,30,54,72,76-79].

In a recent retrospective study with 101 patients receiving RRC with CME from 2005 to 2015, Spinoglio *et al.*[30] showed that it is possible to perform routine RRC with CME and IA safely, with comparable long-term oncologic outcomes to laparoscopic techniques [five-year overall survival (OS) of 77% and disease-free survival (DFS) of 85%]. They also showed a non-significant improvement in DFS for AJCC/UICC stage

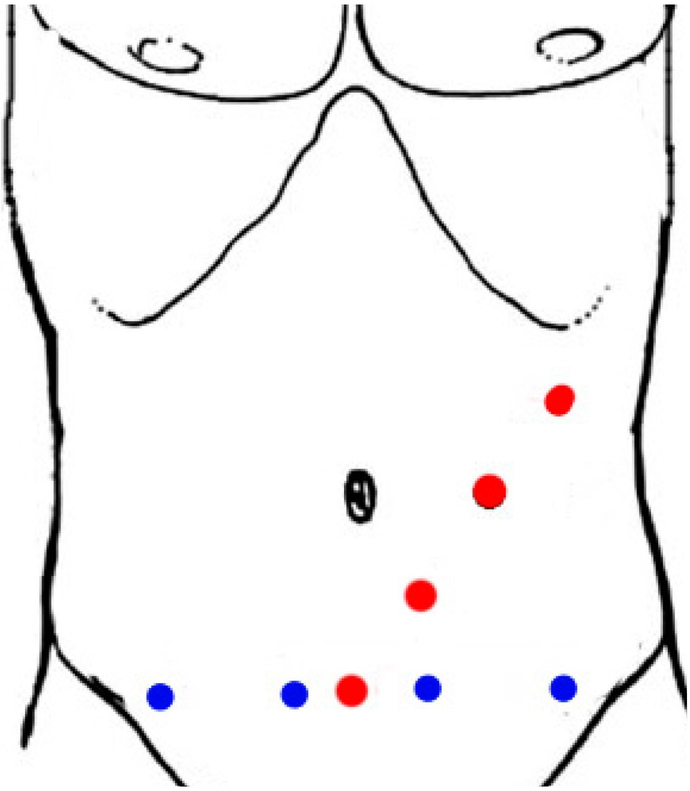


Figure 2. Robot trocar's positions. Red points: diagonal approach; blue points: suprapublic approach

III patients undergoing RRC. Park *et al.*[31] randomized 71 patients and compared robotic and LRC, and they observed that the long-term outcomes were similar between RRC and LRC with no statistically significant differences at three- and five-year DFS and OS. These findings are consistently reproduced in the contemporary literature[80] [Table 6][20,30,72,80,81].

COSTS

Cost evaluation in robotic colorectal surgery is crucial to implementing and maintaining the new technology. Nowadays, increased costs are the most important drawback of robotic-assisted surgery and could imply a non-neglectable burden on healthcare systems. Direct costs can be divided into fixed and variable types. The fixed costs include the acquisition of the robotic system, ranging $0.6-2.5 million, and the costs of further maintenance. The variable costs depends on the consumable instruments, operating room charges, and professional fees. There is a consensus that RRC is more expensive than LRC[36,60,74,82,83]. Park *et al.*[72] determined that the mean direct patient payment for a robotic colectomy was about US $3600 more expensive than for a laparoscopic procedure. Cleary *et al.*[27] reported lower rates of conversion in RRC than in LRC; they also found that RRC was more expensive than LRC, but, when converted patients were included, the difference in cost between RRC and LRC decreased substantially. The total length of hospital stay has an impact on the costs; some of the recent meta-analyses showed that RRC is associated with shorter hospital stay, which may translate to reduced costs[73]. It is clearly difficult to assign a monetary value to measured outcomes in cost-effectiveness studies. In a recent study, laparoscopic and robotic colectomy were shown to be more cost-effective than the traditional open resection, laparoscopy being the most cost-effective approach[84]. Decreasing costs of robotic platforms and devices is mandatory for its future widespread adoption. Under careful assessment of indications for the different robotic system applications, the advantages of robotic assistance, such as higher degrees of rotation, articulation, and 3D imaging, can outweigh the existing drawbacks provided by the higher costs. The expected arrival of competitive industry players could dramatically change this situation soon.

Table 4. Operative data table

Author	Year	Journal	Number patients		Mean Op. time (min)		Mean BL (mL)		Conversion (%)		Harvest Node		Anastomotic Leak (%)	
			RRC	LRC	RRC	LRC	RRC	LRC	RRC	LRC	RRC	LRC	RRC	LRC
Delaney *et al.*[77]	2003	Dis Colom Rectum	2	2	270.5	138	100	150	0	0	NR	NR	0	0
Rawlings *et al*[79]	2007	Surg Endosc	17	15	218.9	198.2	40	66.3	0	2 (1.3)	NR	NR	1 (0.6)	0
Park *et al.*[72]	2012	Br J Surg	35	35	195	130	35.8	56.8	0	0	29.9	30.8	1 (0.2)	0
Deutsch *et al.*[78]	2012	Surg Endosc	18	47	219.2	214.4	76.4	123.2	2 (1.1)	0	21.1	18.7	1 (5.5)	1 (2.1)
Morpurgo *et al.*[54]	2013	J Laparoendosc Adv Surg Tech A	48	48	266	223	NR	NR	NR	NR	26	25	0	3 (6.2)
Lujan *et al.*[24]	2013	J Robot Surg	22	25	251	149	40	50	0	0	24	15	NR	NR
Casillas *et al.*[76]	2014	Am J Surg	54	110	143	79	63	57	4 (7.4)	11 (10)	28	24	0	7 (6.4)
Trastulli *et al.*[17]	2015	Surg Endosc	102	134	287.4	207	30	40	4 (3.9)	14 (10.4)	20.3	19	3 (2.9)	2 (1.5)
Spinoglio *et al.*[30]	2018	Ann Surg Oncol	100	100	279	236	NR	NR	0	7 (7)	28.2	30.4	1 (1)	1 (1)

RRC: robotic right colectomy; LRC: laparoscopic right colectomy; BL: blood loss; NR: not reported

Table 5. Short-term outcomes comparative table

Author	Year	Journal	Number patients		First flatus (days)		Major complication*		Mean hospital stay (days)		30 days mortality [N (%)]	
			RRC	LRC	RRC	LRC	RRC	LRC	RRC	LRC	RRC	LRC
Delaney *et al.*[77]	2003	Dis Colom Rectum	2	2	NR	NR	0	0	3.5	2.5	0	0
Rawlings AL *et al*[79]	2007	Surg Endosc	17	15	NR	NR	0	2 (1.3)	5.2	5.5	0	0
Park *et al.*[72]	2012	Br J Surg	35	35	2.6	2.9	NR	NR	7.9	8.3	0	0
Deutsch *et al.*[78]	2012	Surg Endosc	18	47	3	3.6	NR	NR	4.3	6.3	0	1 (2.1)
Morpurgo *et al.*[54]	2013	J Laparoendosc Adv Surg Tech A	48	48	2.4	3.4	NR	NR	7.5	9	0	0
Lujan *et al.*[24]	2013	J Robot Surg	22	25	NR	NR	NR	NR	3	3	NR	NR
Casillas *et al.*[76]	2014	Am J Surg	54	110	NR	NR	NR	NR	6.2	5.5	0	1 (0.9)
Trastulli *et al.*[17]	2015	Surg Endosc	102	134	2	3.5	NR	NR	4	6.5	0	0
Spinoglio *et al.*[30]	2018	Ann Surg Oncol	100	100	NR	NR	4 (4)	6 (6)	7.9	7.9	1 (1)	0

*Clavien-Dindo III or IV. RRC: robotic right colectomy; LRC: laparoscopic right colectomy; NR: not reported

CONCLUSION

RRC is a safe and feasible procedure with comparable outcomes to the standard laparoscopic approach. The slight benefits regarding recovery outcomes still need to be confirmed by future prospective studies. The cornerstone of those studies should be comparing the techniques with respect to the anastomotic fashioning (EA *vs*. IA). To date, there is no difference in terms of three- and five-year DFS and OS between laparoscopic and robotic approaches, supporting RRC as a safe and feasible technique. If CME provides better oncologic results, robotic surgery may improve the ability to assess it by decreasing the technical complexity. RRC remains much more expensive than LRC. Further studies demonstrating clinically relevant benefits over the other alternatives are still needed to determine the definitive role of robotic surgery for right colonic cancer resection. Breaking the monopoly by competitive producers of robotic

Table 6. Long-term outcomes comparative table

Author	Year	Journal	Number patients		DFS 3-year		DFS 5-year		OS 3-year		OS 5-year	
			RRC	LRC	RRC	LRC	RRC	LRC	RRC	LRC	RRC	LRC
D'Annibale *et al.*[20]	2010	Ann Surg Oncol	50	0	90.0%	NR	NR	NR	92.0%	NR	NR	NR
Cho[80]	2015	Ann Surg	0	205	NR	NR	NR	82.9%	NR	NR	NR	89.8%
Spinoglio *et al.*[30]	2018	Ann Surg Oncol	100	0	NR	NR	91.4%*	NR	NR	NR	90.3%*	NR
Kang[81]	2016	Surg Lap Endosc Percutan Tech	20	43	NR	NR	89.5%	84.0%	NR	NR	73.1%	79.2%
Park *et al.*[72]	2012	Br J Surg	35	36	88.1%	91.1%	77.4%	83.6%	96.8%	94.0%	91.1%	91.0%
Spinoglio *et al.*[30]	2018	Ann Surg Oncol	101	101	NR	NR	85%	83%	NR	NR	77%	73%

*40 months follow-up. RRC: robotic right colectomy; LRC: laparoscopic right colectomy; DFS: disease free survival; OS: overall survival; NR: not reported

systems could dramatically increase accessibility and widespread use of this approach.

DECLARATIONS

Authors' contributions

Concept and design: Moroni P, Martínez-Pérez A

Manuscript writing: Moroni P, Payá-Llorente C

Provision of study materials or patients, collection and assembly of data, data analysis and interpretation, and final approval of manuscript: All authors.

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Siegel RL, Miller KD, Fedewa SA, Ahnen DJ, Meester RGS, et al. Colorectal cancer statistics, 2017. CA Cancer J Clin 2017;67:177-93.
2. Ulanja MB, Rishi M, Beutler BD, Sharma M, Patterson DR, et al. Colon cancer sidedness, presentation, and survival at different stages. J Oncol 2019;2019:4315032.
3. Compton C, Fenoglio-Preiser CM, Pettigrew N, Fielding LP. American joint committee on cancer prognostic factors consensus conference: colorectal working group. Cancer 2000;88:1739-57.
4. Yarbro JW, Page DL, Fielding LP, Partridge EE, Murphy GP. American joint committee on cancer prognostic factors consensus conference. Cancer 1999;86:2436-46.
5. Hohenberger W, Weber K, Matzel K, Papadopoulos T, Merkel S. Standardized surgery for colonic cancer: complete mesocolic excision and central ligation - technical notes and outcome. Colorectal Dis 2009;11:354-64; discussion 64-5.
6. Schwenk W, Haase O, Neudecker J, Muller JM. Short term benefits for laparoscopic colorectal resection. Cochrane Database Syst Rev 2005:Cd003145.
7. Green BL, Marshall HC, Collinson F, Quirke P, Guillou P, et al. Long-term follow-up of the Medical Research Council CLASICC trial of conventional versus laparoscopically assisted resection in colorectal cancer. Br J Surg 2013;100:75-82.
8. Buunen M, Veldkamp R, Hop WC, Kuhry E, Jeekel J, et al. Survival after laparoscopic surgery versus open surgery for colon cancer: long-term outcome of a randomised clinical trial. Lancet Oncol 2009;10:44-52.
9. Nelson H, Sargent DJ, Wieand HS, Fleshman J, Anvari M, et al. A comparison of laparoscopically assisted and open colectomy for colon cancer. N Engl J Med 2004;350:2050-9.
10. Veldkamp R, Kuhry E, Hop WC, Jeekel J, Kazemier G, et al. Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial. Lancet Oncol 2005;6:477-84.
11. Kwon S, Billingham R, Farrokhi E, Florence M, Herzig D, et al. Adoption of laparoscopy for elective colorectal resection: a report from the surgical care and outcomes assessment program. J Am Coll Surg 2012;214:909-18.e1.
12. Delaney CP, Chang E, Senagore AJ, Broder M. Clinical outcomes and resource utilization associated with laparoscopic and open colectomy using a large national database. Ann Surg 2008;247:819-24.
13. Simorov A, Shaligram A, Shostrom V, Boilesen E, Thompson J, et al. Laparoscopic colon resection trends in utilization and rate of conversion to open procedure: a national database review of academic medical centers. Ann Surg 2012;256:462-8.
14. Klugsberger B, Haas D, Oppelt P, Neuner L, Shamiyeh A. Current state of laparoscopic colonic surgery in Austria: a national survey. J Laparoendosc Adv Surg Tech A 2015;25:976-81.
15. Schootman M, Hendren S, Ratnapradipa K, Stringer L, Davidson NO. Adoption of robotic technology for treating colorectal cancer. Dis Colon Rectum 2016;59:1011-8.
16. Bailey MB, Davenport DL, Vargas HD, Evers BM, McKenzie SP. Longer operative time: deterioration of clinical outcomes of laparoscopic colectomy versus open colectomy. Dis Colon Rectum 2014;57:616-22.
17. Trastulli S, Coratti A, Guarino S, Piagnerelli R, Annecchiarico M, et al. Robotic right colectomy with intracorporeal anastomosis compared with laparoscopic right colectomy with extracorporeal and intracorporeal anastomosis: a retrospective multicentre study. Surg Endosc 2015;29:1512-21.
18. Cardinali L, Belfiori G, Ghiselli R, Ortenzi M, Guerrieri M. Robotic versus laparoscopic right colectomy for cancer: short-term outcomes and influence of body mass index on conversion rate. Minerva Chir 2016;71:217-22.
19. Ballantyne GH, Ewing D, Pigazzi A, Wasielewski A. Telerobotic-assisted laparoscopic right hemicolectomy: Lateral to medial or medial to lateral dissection? Surg Laparosc Endosc Percutaneous Tech 2006;16:406-10.
20. D'Annibale A, Morpurgo E, Fiscon V, Trevisan P, Sovernigo G, et al. Robotic and laparoscopic surgery for treatment of colorectal diseases. Dis Colon Rectum 2004;47:2162-8.
21. Juo YY, Agarwal S, Luka S, Satey S, Obias V. Single-incision robotic colectomy (SIRC) case series: initial experience at a single center. Surg Endosc 2015;29:1976-81.
22. Formisano G, Misitano P, Giuliani G, Calamati G, Salvischiani L, et al. Laparoscopic versus robotic right colectomy: technique and outcomes. Updates Surg 2016;68:63-9.
23. Petz W, Ribero D, Bertani E, Borin S, Formisano G, et al. Suprapubic approach for robotic complete mesocolic excision in right colectomy: oncologic safety and short-term outcomes of an original technique. Eur J Surg Oncol 2017;43:2060-6.
24. Lujan HJ, Maciel VH, Romero R, Plasencia G. Laparoscopic versus robotic right colectomy: a single surgeon's experience. J Robot Surg 2013;7:95-102.
25. Mégevand JL, Amboldi M, Lillo E, Lenisa L, Ganio E, et al. Right colectomy: consecutive 100 patients treated with laparoscopic and robotic technique for malignancy. Cumulative experience in a single centre. Updates Surg 2019;71:151-6.
26. Blumberg D. Robotic colectomy with intracorporeal anastomosis is feasible with no operative conversions during the learning curve for an experienced laparoscopic surgeon developing a robotics program. J Robot Surg 2019;13:545-55.
27. Cleary RK, Mullard AJ, Ferraro J, Regenbogen SE. The cost of conversion in robotic and laparoscopic colorectal surgery. Surg Endosc 2018;32:1515-24.
28. Scotton G, Contardo T, Zerbinati A, Tosato SM, Orsini C, et al. From laparoscopic right colectomy with extracorporeal anastomosis to robot-assisted intracorporeal anastomosis to totally robotic right colectomy for cancer: the evolution of robotic multiquadrant abdominal surgery. J Laparoendosc Adv Surg Tech A 2018;28:1216-22.
29. Johnson CS, Kassir A, Marx DS, Soliman MK. Performance of da Vinci Stapler during robotic-assisted right colectomy with

intracorporeal anastomosis. J Robot Surg 2019;13:115-9.
30. Spinoglio G, Bianchi PP, Marano A, Priora F, Lenti LM, et al. Robotic versus laparoscopic right colectomy with complete mesocolic excision for the treatment of colon cancer: perioperative outcomes and 5-year survival in a consecutive series of 202 patients. Ann Surg Oncol 2018;25:3580-6.
31. Park JS, Kang H, Park SY, Kim HJ, Woo IT, et al. Long-term oncologic after robotic versus laparoscopic right colectomy: a prospective randomized study. Surg Endosc 2019;33:2975-81.
32. Schulte Am Esch J, Iosivan SI, Steinfurth F, Mahdi A, Forster C, et al. A standardized suprapubic bottom-to-up approach in robotic right colectomy: technical and oncological advances for complete mesocolic excision (CME). BMC Surg 2019;19:72.
33. Rausa E, Kelly ME, Asti E, Aiolfi A, Bonitta G, et al. Right hemicolectomy: a network meta-analysis comparing open, laparoscopic-assisted, total laparoscopic, and robotic approach. Surg Endosc 2019;33:1020-32.
34. Fabozzi M, Cirillo P, Corcione F. Surgical approach to right colon cancer: from open technique to robot. State of art. World J Gastrointest Surg 2016;8:564-73.
35. Huettner F, Rawlings AL, McVay WB, Crawford DL. Robot-assisted laparoscopic colectomy: 70 cases-one surgeon. J Robot Surg 2008;2:227-34.
36. de'Angelis N, Lizzi V, Azoulay D, Brunetti F. Robotic versus laparoscopic right colectomy for colon cancer: analysis of the initial simultaneous learning curve of a surgical fellow. J Laparoendosc Adv Surg Tech A 2016;26:882-92.
37. Nicola de'Angelis, Paolo Moroni, Francesco Brunetti, Aleix Martínez-Pérez. Indocyanine green fluorescence - guided robotic right colectomy with intra-corporeal anastomosis - a video vignette. Colorectal Dis 2019; Epub ahead of print. doi: 10.1111/codi.14820
38. Lee HJ, Choi GS, Park JS, Park SY, Kim HJ, et al. A novel robotic right colectomy for colon cancer via the suprapubic approach using the da Vinci Xi system: initial clinical experience. Ann Surg Treat Res 2018;94:83-7.
39. Yeo SA, Noh GT, Han JH, Cheong C, Stein H, et al. Universal suprapubic approach for complete mesocolic excision and central vascular ligation using the da Vinci Xi® system: from cadaveric models to clinical cases. J Robot Surg 2017;11:399-407.
40. Ostrowitz MB, Eschete D, Zemon H, DeNoto G. Robotic-assisted single-incision right colectomy: early experience. Int J Med Robot 2009;5:465-70.
41. Samia H, Lawrence J, Nobel T, Stein S, Champagne BJ, et al. Extraction site location and incisional hernias after laparoscopic colorectal surgery: should we be avoiding the midline? Am J Surg 2013;205:264-7; discussion 268.
42. Lee L, Mappin-Kasirer B, Sender Liberman A, Stein B, Charlebois P, et al. High incidence of symptomatic incisional hernia after midline extraction in laparoscopic colon resection. Surg Endosc 2012;26:3180-5.
43. Singh R, Omiccioli A, Hegge S, McKinley C. Does the extraction-site location in laparoscopic colorectal surgery have an impact on incisional hernia rates? Surg Endosc 2008;22:2596-600.
44. Weeks JC, Nelson H, Gelber S, Sargent D, Schroeder G. Short-term quality-of-life outcomes following laparoscopic-assisted colectomy vs. open colectomy for colon cancer: a randomized trial. Jama 2002;287:321-8.
45. Lynch ML, Brand MI. Preoperative evaluation and oncologic principles of colon cancer surgery. Clin Colon Rectal Surg 2005;18:163-73.
46. West NP, Kobayashi H, Takahashi K, Perrakis A, Weber K, et al. Understanding optimal colonic cancer surgery: comparison of Japanese D3 resection and European complete mesocolic excision with central vascular ligation. J Clin Oncol 2012;30:1763-9.
47. Heald RJ, Ryall RD. Recurrence and survival after total mesorectal excision for rectal cancer. Lancet 1986;1:1479-82.
48. West NP, Morris EJ, Rotimi O, Cairns A, Finan PJ, et al. Pathology grading of colon cancer surgical resection and its association with survival: a retrospective observational study. Lancet Oncol 2008;9:857-65.
49. Ricci C, Casadei R, Alagna V, Zani E, Taffurelli G, et al. A critical and comprehensive systematic review and meta-analysis of studies comparing intracorporeal and extracorporeal anastomosis in laparoscopic right hemicolectomy. Langenbecks Arch Surg 2017;402:417-27.
50. Harr JN, Juo YY, Luka S, Agarwal S, Brody F, et al. Incisional and port-site hernias following robotic colorectal surgery. Surg Endosc 2016;30:3505-10.
51. Reitz ACW, Lin E, Rosen SA. A single surgeon's experience transitioning to robotic-assisted right colectomy with intracorporeal anastomosis. Surg Endosc 2018;32:3525-32.
52. Fabozzi M, Allieta R, Brachet Contul R, Grivon M, Millo P, et al. Comparison of short- and medium-term results between laparoscopically assisted and totally laparoscopic right hemicolectomy: a case-control study. Surg Endosc 2010;24:2085-91.
53. Hanna MH, Hwang GS, Phelan MJ, Bui TL, Carmichael JC, et al. Laparoscopic right hemicolectomy: short- and long-term outcomes of intracorporeal versus extracorporeal anastomosis. Surg Endosc 2016;30:3933-42.
54. Morpurgo E, Contardo T, Molaro R, Zerbinati A, Orsini C, et al. Robotic-assisted intracorporeal anastomosis versus extracorporeal anastomosis in laparoscopic right hemicolectomy for cancer: a case control study. J Laparoendosc Adv Surg Tech A 2013;23:414-7.
55. Tam MS, Kaoutzanis C, Mullard AJ, Regenbogen SE, Franz MG, et al. A population-based study comparing laparoscopic and robotic outcomes in colorectal surgery. Surg Endosc 2016;30:455-63.
56. Tou S, Duncan A, Giuratrabocchetta S, Bergamaschi R. Robotic right colectomy with intracorporeal anastomosis - a video vignette. Colorectal Dis 2015;17:1030-1.
57. Cirocchi R, Trastulli S, Farinella E, Guarino S, Desiderio J, et al. Intracorporeal versus extracorporeal anastomosis during laparoscopic right hemicolectomy - systematic review and meta-analysis. Surg Oncol 2013;22:1-13.
58. Wu Q, Jin C, Hu T, Wei M, Wang Z. Intracorporeal versus extracorporeal anastomosis in laparoscopic right colectomy: a systematic review and meta-analysis. J Laparoendosc Adv Surg Tech A 2017;27:348-57.
59. van Oostendorp S, Elfrink A, Borstlap W, Schoonmade L, Sietses C, et al. Intracorporeal versus extracorporeal anastomosis in right hemicolectomy: a systematic review and meta-analysis. Surg Endosc 2017;31:64-77.
60. Solaini L, Bazzocchi F, Cavaliere D, Avanzolini A, Cucchetti A, et al. Robotic versus laparoscopic right colectomy: an updated

systematic review and meta-analysis. Surg Endosc 2018;32:1104-10.
61. Abdelrahman M, Belramman A, Salem R, Patel B. Acquiring basic and advanced laparoscopic skills in novices using two-dimensional (2D), three-dimensional (3D) and ultra-high definition (4K) vision systems: a randomized control study. Int J Surg 2018;53:333-8.
62. Currò G, Cogliandolo A, Bartolotta M, Navarra G. Three-dimensional versus two-dimensional laparoscopic right hemicolectomy. J Laparoendosc Adv Surg Tech A 2016;26:213-7.
63. Marusch F, Gastinger I, Schneider C, Scheidbach H, Konradt J, et al. Experience as a factor influencing the indications for laparoscopic colorectal surgery and the results. Surg Endosc 2001;15:116-20.
64. Choi DH, Jeong WK, Lim SW, Chung TS, Park JI, et al. Learning curves for laparoscopic sigmoidectomy used to manage curable sigmoid colon cancer: single-institute, three-surgeon experience. Surg Endosc 2009;23:622-8.
65. Li JC, Hon SS, Ng SS, Lee JF, Yiu RY, et al. The learning curve for laparoscopic colectomy: experience of a surgical fellow in an university colorectal unit. Surg Endosc 2009;23:1603-8.
66. Dincler S, Koller MT, Steurer J, Bachmann LM, Christen D, et al. Multidimensional analysis of learning curves in laparoscopic sigmoid resection: eight-year results. Dis Colon Rectum 2003;46:1371-8; discussion 8-9.
67. Melich G, Hong YK, Kim J, Hur H, Baik SH, et al. Simultaneous development of laparoscopy and robotics provides acceptable perioperative outcomes and shows robotics to have a faster learning curve and to be overall faster in rectal cancer surgery: analysis of novice MIS surgeon learning curves. Surg Endosc 2015;29:558-68.
68. Witkiewicz W, Zawadzki M, Rząca M, Obuszko Z, Czarnecki R, et al. Robot-assisted right colectomy: surgical technique and review of the literature. Wideochir Inne Tech Maloinwazyjne 2013;8:253-7.
69. Parisi A, Scrucca L, Desiderio J, Gemini A, Guarino S, et al. Robotic right hemicolectomy: analysis of 108 consecutive procedures and multidimensional assessment of the learning curve. Surg Oncol 2017;26:28-36.
70. Lim S, Kim JH, Baek SJ, Kim SH, Lee SH. Comparison of perioperative and short-term outcomes between robotic and conventional laparoscopic surgery for colonic cancer: a systematic review and meta-analysis. Ann Surg Treat Res 2016;90:328-39.
71. deSouza AL, Prasad LM, Park JJ, Marecik SJ, Blumetti J, et al. Robotic assistance in right hemicolectomy: is there a role? Dis Colon Rectum 2010;53:1000-6.
72. Park JS, Choi GS, Park SY, Kim HJ, Ryuk JP. Randomized clinical trial of robot-assisted versus standard laparoscopic right colectomy. Br J Surg 2012;99:1219-26.
73. Ma S, Chen Y, Guo T, Yang X, Lu Y, et al. Short-term outcomes of robotic-assisted right colectomy compared with laparoscopic surgery: a systematic review and meta-analysis. Asian J Surg 2019;42:589-98.
74. Rondelli F, Balzarotti R, Villa F, Guerra A, Avenia N, et al. Is robot-assisted laparoscopic right colectomy more effective than the conventional laparoscopic procedure? a meta-analysis of short-term outcomes. Int J Surg 2015;18:75-82.
75. Xu H, Li J, Sun Y, Li Z, Zhen Y, et al. Robotic versus laparoscopic right colectomy: a meta-analysis. World J Surg Oncol 2014;12:274.
76. Casillas MA Jr, Leichtle SW, Wahl WL, Lampman RM, Welch KB, et al. Improved perioperative and short-term outcomes of robotic versus conventional laparoscopic colorectal operations. Am J Surg 2014;208:33-40.
77. Delaney CP, Lynch AC, Senagore AJ, Fazio VW. Comparison of robotically performed and traditional laparoscopic colorectal surgery. Dis Colon Rectum 2003;46:1633-9.
78. Deutsch GB, Sathyanarayana SA, Gunabushanam V, Mishra N, Rubach E, et al. Robotic vs. laparoscopic colorectal surgery: an institutional experience. Surg Endosc 2012;26:956-63.
79. Rawlings AL, Woodland JH, Vegunta RK, Crawford DL. Robotic versus laparoscopic colectomy. Surg Endosc 2007;21:1701-8.
80. Cho MS, Baek SJ, Hur H, Soh Min B, Baik SH, et al. Modified complete mesocolic excision with central vascular ligation for the treatment of right-sided colon cancer: long-term outcomes and prognostic factors. Ann Surg 2015;261:708-15.
81. Davis BR, Yoo AC, Moore M, Gunnarsson C. Robotic-assisted versus laparoscopic colectomy: cost and clinical outcomes. JSLS 2014;18:211-24.
82. Kang J, Park YA, Baik SH, Sohn SK, Lee KY. A Comparison of Open, Laparoscopic, and Robotic Surgery in the Treatment of Right-sided Colon Cancer. Surg Laparosc Endosc Percutan Tech 2016;26:497-502
83. Dolejs SC, Waters JA, Ceppa EP, Zarzaur BL. Laparoscopic versus robotic colectomy: a national surgical quality improvement project analysis. Surg Endosc 2017;31:2387-96.
84. Simianu VV, Gaertner WB, Kuntz K, Kwaan MR, Lowry AC, et al. Cost-effectiveness evaluation of laparoscopic versus robotic minimally invasive colectomy. Ann Surg 2019; Epub ahead of print doi: 10.1097/SLA.0000000000003196

Serra-Aracil *et al. Mini-invasive Surg* 2019;3:37
DOI: 10.20517/2574-1225.2019.36

Mini-invasive Surgery

Original Article

Open Access

Management of the main postoperative surgical complications after transanal endoscopic microsurgery: an observational study

Xavier Serra-Aracil, Laura Mora-López, Anna Pallisera-Lloveras, Sheila Serra-Pla, Albert Garcia-Nalda, Esther Gil-Barrionuevo, Salvador Navarro-Soto

Colorectal Surgery Unit, Department of General and Digestive Surgery, Parc Taulí University Hospital, Universitat Autònoma de Barcelona (UAB), Sabadell 08208, Barcelona, Spain.

Correspondence to: Dr. Xavier Serra-Aracil, Colorectal Surgery Unit, Department of General and Digestive Surgery, Parc Taulí University Hospital, Universitat Autònoma de Barcelona (UAB), Parc Taulí s/n, Sabadell 08208, Barcelona, Spain.
E-mail: xserraa@gmail.com

How to cite this article: Serra-Aracil X, Mora-López L, Pallisera-Lloveras A, Serra-Pla S, Garcia-Nalda A, Gil-Barrionuevo E, Navarro-Soto S. Management of the main postoperative surgical complications after transanal endoscopic microsurgery: an observational study. *Mini-invasive Surg* 2019;3:37. http://dx.doi.org/10.20517/2574-1225.2019.36

Received: 13 Sep 2019 **First Decision**: 12 Nov 2019 **Revised**: 14 Nov 2019 **Accepted**: 3 Dec 2019 **Published**: 12 Dec 2019

Science Editor: Giulio Belli **Copy Editor**: Cai-Hong Wang **Production Editor**: Jing Yu

Abstract

Aim: Rates of clinically relevant postoperative morbidity after transanal endoscopic microsurgery (TEM) are low. For this reason, there are few descriptions in the literature on the management of these complications. Because of this lack of information, their importance may be either underestimated or overestimated (in the latter case, leading to overtreatment). The present article reports the frequency of the occurrence of postoperative surgical complications after TEM and describes various approaches to their management.

Methods: An observational study was carried out with prospective data collection and retrospective analysis from June 2004 to June 2019, including all patients undergoing TEM for rectal tumors. All postoperative complications were recorded using the Clavien-Dindo classification (Cl-D), as well as preoperative, surgical, postoperative, and pathological variables.

Results: During the study period, 778 patients underwent TEM, of whom 716 met the inclusion criteria. Postoperative morbidity was 22.1% (158/716). Clinically relevant morbidity (Cl-D > II) was 5% (36/716). The most frequent complication was rectal bleeding, occurring in 115/716 (16.1%) patients; 85 of these 115 (73.9%) patients were grade I Cl-D. Urinary complications were rare (30/716, 4.2%). Similarly, infectious complications of perianal and pelvic abscesses appeared in 7/716 (1%) patients, two of whom required colostomy.

Conclusion: Clinically relevant complications after TEM are rare. For this reason, experience of these complications is limited. Here, we propose a management protocol to ensure that these complications are neither underestimated nor subjected to excessively aggressive or unnecessary treatment.

Keywords: Transanal endoscopic microsurgery, TEM, transanal endoscopic operation, minimally invasive surgery, morbidity and morbidity management

INTRODUCTION

The approach to benign or initially malignant rectal lesions through local surgery posed a considerable challenge until the advent of Transanal Endoscopic Microsurgery (TEM), introduced by Buess in the 1980s[1]. Thanks to the creation of a pneumorectum, this technique makes it possible to perform local resections even beyond the rectum-sigmoid junction.

Later technical variations on TEM include transanal endoscopic operation (TEO)[2], which uses a high definition monitor, and TAMIS[3] (TransAnal Minimally Invasive Surgery), a more recent development that incorporates a single-port system. The application of strict selection criteria and careful surgical techniques obtain good results for postoperative morbidity and mortality, function, and cure.

Overall postoperative morbidity after TEM ranges from 7.7% to 31.4%[4,5]. However, the absence of standardization in the recording and the description of the complications makes the results of different studies difficult to compare. A previous study by our group[6] reported a morbidity rate of 23.6%, grouped according to the Clavien–Dindo classification (Cl-D)[7]. More than half of these complications (Cl-D grade I) required observation alone, and clinically relevant morbidity (Cl-D ≥ II) was recorded in only 5.6% of the patients.

The most frequent complications after TEM are rectal bleeding (as in the study just mentioned)[6] or urinary morbidity, with reported rates ranging between 5.9% and 10.8%[8,9].

The management of complications after TEM has not been widely reported. Rectal bleeding, the most frequent complication, has a Cl-D classification ranging from I to IVa/b. In the remaining postoperative complications, such as urinary morbidity, infection, asymptomatic postoperative fever, and massive pneumo-retroperitoneum on computed tomography (CT) or chest radiography, it is unclear what protocol should be applied. The main aim of the present study was to describe the frequency of occurrence of postoperative surgical complications after TEM according to their Cl-D classification. The secondary aim was to describe the therapeutic management protocol in the most frequent complications.

METHODS

Study design

An observational, single-center study in consecutive patients undergoing TEM was carried out with prospective data collection and retrospective analysis. Computerized data management was carried out with the Microsoft® Access 2003 software in a protected format.

Patients and setting

All patients were operated on by surgeons at the Parc Tauli University Hospital, Coloproctology Unit from June 2004 to June 2019. All patients with indication of TEM underwent a preoperative study protocol[10] incorporating endorectal ultrasound (US) and rectal magnetic resonance imaging (MRI). These examinations classify the patients into five groups of preoperative indication: Group I with curative intention (benign tumors), which, after US and MRI, are staged US-MRI,T0-1 and US-MRI,N0; Group II, with curative intent (low grade adenocarcinomas, US-MRI,T0-1 and US-MRI,N0); Group III, consensus indication (low grade adenocarcinomas, US-MRI,T2 and US-MRI,N0) who reject radical surgery; Group IV, palliative care; and Group V, atypical indication[11].

Inclusion criteria were patients in preoperative indication Groups I-IV who were candidates for TEM surgery.

Exclusion criteria were patients in preoperative indication Group V, and those who, after intraoperative assessment of possible TEM, were assigned to abdominal surgery on technical grounds.

Preoperative preparation, surgical technique, and postoperative evolution

In our protocol[10], all patients with indication for TEM undergo anterograde mechanical preparation of the colon together with antibiotic and thromboembolic prophylaxis. General anesthetic is applied in most cases, unless the anesthesiologist decides to use spinal anesthesia due to the patient's condition. The techniques used for local rectal excision are either TEM (Richard Wolf, Knittlingen, Germany) or TEO (Karl Storz GmbH, Tüttlingen, Germany). Full wall resection is performed by ultrasound scalpel, following the superficial plane of the perirectal fat.

The lesion's defect on the rectal wall should be sutured to prevent complications due to stenosis of the rectal lumen (in large defects) and postoperative bleeding due to fecal erosions. A long-lasting 3-0 absorbable monofilament suture such as polydioxanone (PDS, MonoPlus) is used with a 20-22 gauge curved cylindrical atraumatic needle. A 10 cm length is cut to facilitate handling in the interior of the rectoscope. A Vicryl (Ethicon) clip is placed at the ends, using an instrument known as Lapra-TY for placement, as an anchor and to avoid knot tying. A curved needle holder is used, which facilitates handling the suture.

The suture should always be made in a transverse direction to avoid compromising the rectal lumen and to avoid formation of stenosis. The stitches are placed as full-thickness continuous sutures that are passed through the rectal wall, as previously described. Upon completion of suturing, irrigate once again with povidone iodine solution diluted to 1% with physiological saline solution.

The bladder catheter is removed at the end of the surgery. Oral diet and ambulation are initiated after 6 h, and patients are discharged after 24 h unless they present complications.

Main variable

The main variable was post-surgical complications in patients undergoing TEO/TEM within 30 days of the intervention.

Secondary variables

The secondary variables were epidemiological, preoperative (patient- and tumor-dependent variables), surgical, postoperative (Clavien-Dindo Classification, Table 1)[7], and pathological variables.

In addition, postoperative morbidity (postoperative complications or adverse effects), defined as an unexpected consequence or injury caused to the patient due to the treatment, not due to their underlying disease, was evaluated. Morbidity was considered clinically relevant with a Cl-D grade ≥ II requiring specific medical action.

Rectal bleeding was defined as more than 100 mL of red blood, or a bowel movement completely of blood (evaluated by nurse or surgeon). The same criteria were applied to patients consulting the emergency department.

Table 1. Clavien-Dindo classification[7]

Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications Blood transfusions and total parenteral nutrition are also included
Grade III	Requiring surgical, endoscopic or radiological intervention Intervention not under general anesthesia Intervention under general anesthesia
Grade IV	Life-threatening complication (including CNS complications)* requiring IC/ICU management
Grade IVa	Single organ dysfunction (including dialysis)
Grade IVb	Multiorgan dysfunction
Grade V	Death of a patient
Suffix "d"	If the patient suffers from a complication at the time of discharge (see examples in Table 2), the suffix "d" (for "disability") is added to the respective grade of complication. This label indicates the need for a follow-up to fully evaluate the complication

*Brain hemorrhage, ischemic stroke, subarrachnoidal bleeding, but excluding transient ischemic attacks. CNS: central nervous system; IC: intermediate care; ICU: intensive care unit

Since January 2005, morbidity has been prospectively recorded in all patients admitted to the Colorectal Unit and the Department of General and Digestive Surgery at our hospital[6]. The assessment of adverse effects is peer-reviewed. The present study was approved by the local Institutional Ethics Committee (CEIC: 2016-636) and complied with the criteria of the Declaration of Helsinki. The STROBE guidelines for observational studies were followed.

Statistical analysis

SPSS version 23 was used for statistical analysis. Prospective data collection allowed analysis of the data without the presence of missing values. The quantitative variables were described using mean values and standard deviation if normality criteria were met; otherwise, median, interquartile range (IQR), and range (R) were used. Categorical variables were described in absolute values and percentages.

RESULTS

During the study period, 788 patients underwent TEM in our Coloproctology Unit. Seventy-two patients did not meet the inclusion criteria, leaving a total of 716 patients. Figure 1 shows the patients included according to indication group.

Table 2 displays the epidemiological and preoperative variables of patients undergoing TEM. Median age was 71 years, and 430 (60%) patients were men. Median lesion size was 4 cm. Neoadjuvant treatment was administered in 44 (6.1%) patients. Median distance from the lower edge of the lesion to the anal verge was 7 cm, and from the upper edge to the anal verge was 11 cm. The most frequent location was the lateral quadrant, reported in 318 (44.4%) patients. Sessile morphology was the most common in 329 (47.1%) patients.

As regards surgical, postoperative, and pathological variables [Table 3], 655 (91.4%) patients underwent general anesthetic. The frequency of TEM and TEO use was similar (349 (48.7%) and 367 (51.3%), respectively), although in recent years TEO has been more widely used. *En bloc* resection was possible in 658 (91.9%) patients. Median surgical time was 70 min. Peritoneal cavity perforation was recorded in 51 (7.1%) cases, without major morbidity and only one case required conversion to abdominal surgery. Vaginal perforation was observed in 12 patients; despite repair, five recto-vaginal fistulas appeared (5/12, 41.7%). The overall postoperative morbidity rate was 22.1% (158/716), although 98 (13.7%) complications were Cl-D

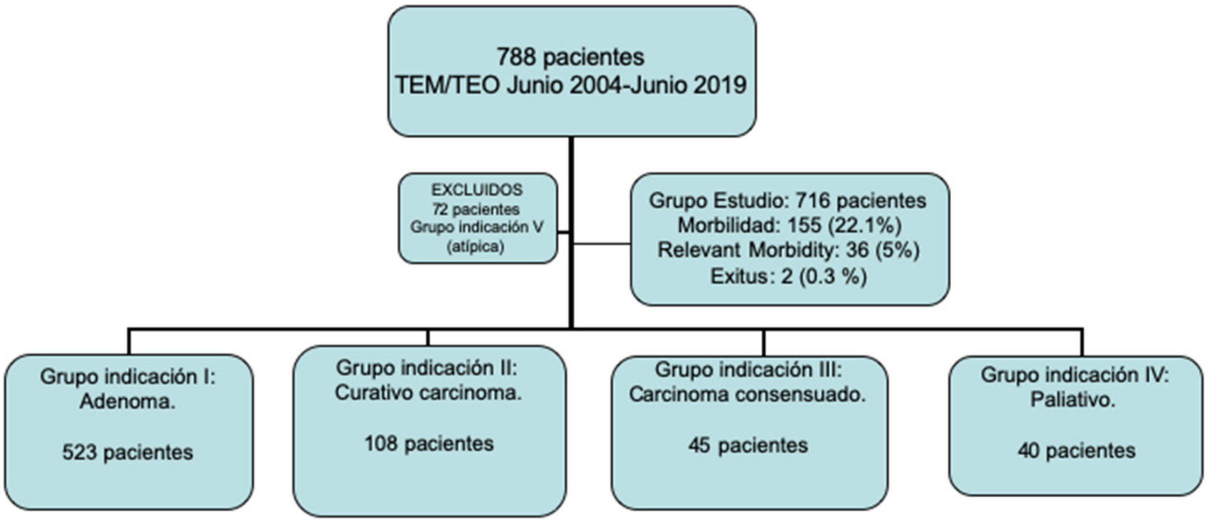


Figure 1. Flow chart of the study patients. TEM: transanal endoscopic microsurgery; TEO: transanal endoscopic operation

Table 2. Descriptive epidemiological and preoperative data of patients who underwent TEM

Variables			Overall patients *n* = 716 (%)
Epidemiology	Age (years) (median-IQR-range)		71 (IQR 16) (range 31-92)
	Sex (%)	Male	430 (60%)
		Female	286 (40%)
	Tumor size (cm) (median-IQR-range)		4 (IQR 2) (range 0.5-12)
	Preoperative chemo-radiotherapy		44 (6.1%)
	Re-TEM		24 (3.4%)
	TEM after polypectomy with positive margin resection		48 (6.8%)
	Distance from anal verge (cm) (median-IQR-range)		7 (IQR 5) (range 1-22)
	Distance from tumor proximal margin to anal verge (cm) (median-IQR-range)		11 (IQR 4.5) (range 1-26)
	Location of the tumor (%)	Anterior	185 (25.8%)
		Lateral	318 (44.4%)
		Posterior	213 (29.7%)
	Morphology of the lesion (%)	Flat	169 (23.6)
		Pedunculated	150 (21.3%)
		Sessile	329 (47.1%)
		Ulcerated	54 (7.6%)
	ASA (%)	I	23 (3.2%)
		II	381 (53.2%)
		III	254 (35.5%)
		IV	58 (8.1%)

TEM: transanal endoscopic surgery; ASA: American Society of Anesthesiology scale; IQR: Interquartile range; Re-TEM: recurrence-TEM

grade I. Clinically relevant morbidity (Cl-D ≥ II) was reported in 36 (5%) patients with a Comprehensive Complication Index (CCI)[12] of 0. Fifty-nine (8.2%) patients presented asymptomatic postoperative fever. The causes of death in the two (0.3%) patients who were exituswere reported in our previous publication[6]. The most frequent pathology was adenoma in 422 (58.9%) patients. Full wall resection was achieved in 710 (99.2%) patients and only 61 (8.6%) patients presented positive margins.

Table 4 displays the most frequent types of complications related to TEM. In 139/158 (88%) patients, the complications were surgical. The most frequent complication was rectal bleeding in 115/716 (16.1%) patients; however, the bleeding was Cl-D grade I in 85/115 (73.9%) patients. Fifteen of 115 (13%) patients required surgical treatment (a new TEM in all cases). Rectal bleeding was a clinically relevant complication (Cl-D ≥ II) in 25/716 (3.5%) patients.

Table 3. Descriptive surgical, postoperative and pathological variables

Variables			**Overall patients** *n* **= 716**
Surgical	Anesthesia type	General	655 (91.4%)
		Locoregional	61 (8.6%)
	Surgical equipment	TEM	349 (48.7%)
		TEO	367 (51.3%)
	Fragmentation of the specimen	*En bloc*	658 (91.9%)
		Piecemeal	58 (8.1%)
	Surgical time(min) (median-IQR-range)		70 (IQR 50) (range 17-265)
	Perforation into abdominal cavity		51 (7.1%)
	Vaginal perforation		12 (1.7%)
	Suture of the defect after excision	Complete	614 (85.8%)
		Incomplete	94 (13.1)
		Absent	8 (1.1%)
	Conversion to abdominal surgery		1 (0.1%)
Postoperative	Overall morbidity		158 (22.1%)
	Morbidity (Clavien-Dindo)	0	558 (77.9%)
		I	98 (13.7%)
		II	24 (3.4%)
		IIIa	11 (1.5%)
		IIIb	17 (2.4%)
		Iva	5 (0.7%)
		IVb	1 (0.1%)
		V (mortality)	2 (0.3%)
	Clinically relevant morbidity (Cl-D > II)		36 (5%)
	CCI		0 (IQR 0) (range 0-100)
	Asymptomatic fever post-TEM		59 (8.2%)
Pathology	Definitive pathology	Adenoma	422 (58.9%)
		Adenocarcinoma	239 (33.4%)
		No pathology	55 (7.7%)
	Positive margin		61 (8.6%)
	Wall excision	Full-thickness	710 (99.2%)
		Partial	6 (0.8%)

TEM: transanal endoscopic microsurgery; TEO: transanal endoscopic operation; IQR: interquartile range; Cl-D: Clavien-Dindo; CCI: comprehensive complex index

Urinary complications were relatively uncommon, being recorded in 30/716 (4.2%) patients. Nine of 716 (1.3%) patients presented urine infections and 20 (2.8%) patients presented acute urine retention (AUR).

Infectious complications were rare (14/716, 2%). Pelvic or perianal abscess occurred in seven (1%) patients and were treated by antibiotics and local debridement, except in two cases that required colostomy. All of them were associated with tumors located in the lower third of the rectum. In the cases that required colostomy, one was an immunosuppressed patient with lymphoma who developed perineal cellulitis. In the other patient, with no history of interest, a perianal abscess was observed on Postoperative Days 4-5; after local debridement, the perianal infection progressed, obliging the creation of a colostomy.

Two patients underwent exploratory laparotomy, one for severe pneumoperitoneum on chest X-ray [Figure 2], and the other due to massive neuro-retroperitoneum on abdominal CT [Figure 3]. The abdominal CT did not record any free intra-abdominal fluid or collections. In neither case was rectal perforation observed, or the presence of intestinal contents.

DISCUSSION

Postoperative surgical complications after TEM are rare and tend to be unimportant. In this study, 98/158 (62.1%) complications recorded were Cl-D grade I, and only 5% of patients presented clinically relevant

Figure 2. Chest X-ray with massive pneumoperitoneum

Table 4. Description of surgical complications related to TEM

Total number of patients with complications related to TEM			**158/716 (22.1%)**
Patients with surgical complications			139 (19.4%)
Patients with medical complications			13 (1.8%)
Patients with both medical and surgical complications			6 (0.8%)
Rectal bleeding	Overall morbidity		115/716 (16.1%)
	Morbidity (Cl-D)	I	85/115 (73.9%)
		II	5/115 (4.3%)
		IIIa	10/115 (8.7%)
		IIIb	11/115 (9.6%)
		IVa	4/115 (3.5%)
		IVb	0/115 (0%)
		V (mortality)	0/115(0%)
	Clinically relevant morbidity (Cl-D > II)		25/716 (3.5%)
Urinary complications			30/716 (4.2%)
AUR			20/716 (2.8%)
UTI			9/716 (1.3%)
Hematuria and traumatic urine catheter insertion			5/716 (0.7%)
Infectious complications			14/716 (2%)
Abscess			7/716 (1%)
Pneumoperitoneum/retropneumoperitoneum/pneumomediastinum			2/716 (0.3%)
Recto-vaginal fistula			5/716 (0.7%)

TEM: transanal endoscopic microsurgery; AUR: acute urine retention; UTI: urinary tract infection; Cl-D: Clavien-Dindo

complications (Cl-D ≥ II). We believe that the description of postoperative complications should apply the same classification to allow comparison of the results. The Clavien-Dindo classification[7] is probably the most widely used in the literature; the Comprehensive Complication Index (CCI)[12] is useful for completing the description of complications in procedures associated with high morbidity, but in TEM it is of little value[6].

As noted above, there are few references to the management of these complications in the literature. Because of the lack of information, some of these complications may be overtreated; alternatively, others may be ignored and may evolve into more complex forms. For this reason, the objective of this study was to assess the most frequent types of complication based on our experience and on the literature.

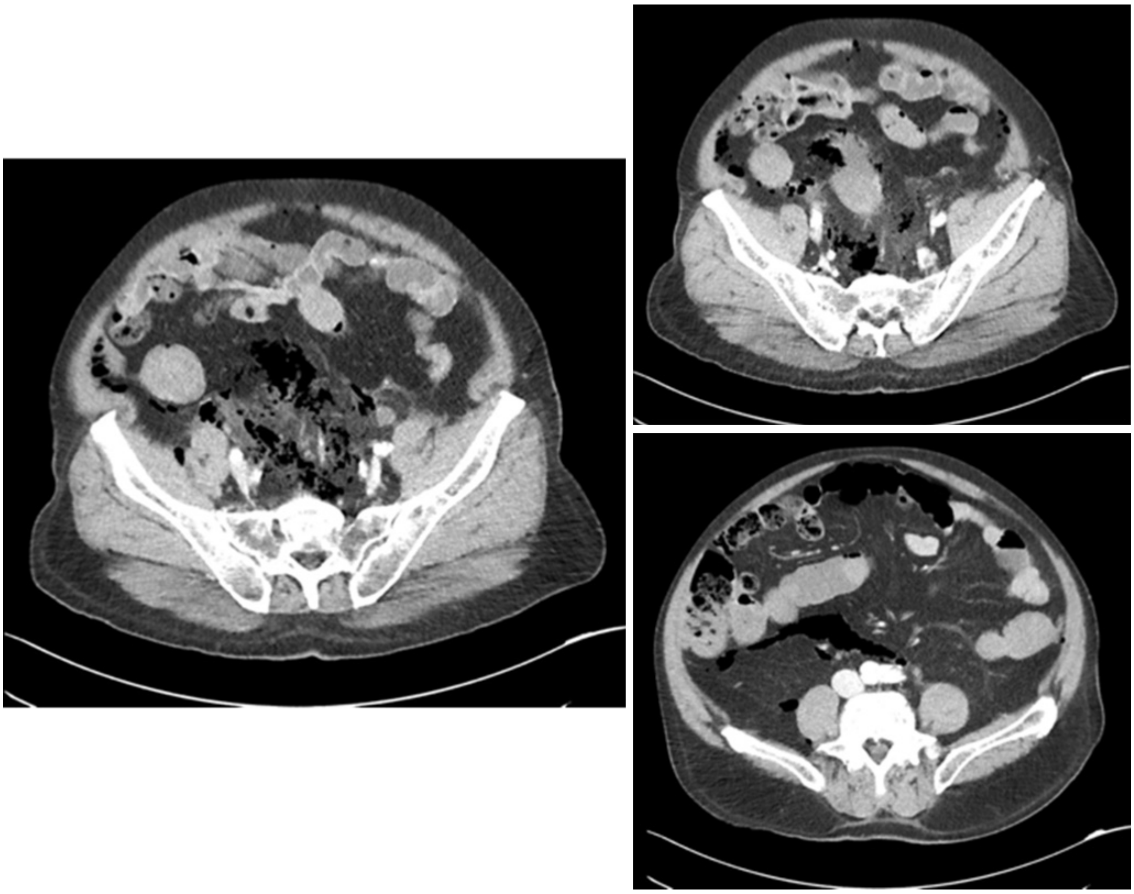


Figure 3. Abdominal computed tomography scan with pneumoretroperitoneum, without intra-abdominal free fluid or collections

Rectal bleeding

The presence of a wound inside the rectum, whether completely sutured, partially sutured, or left open, causes a minimal blood emission after contact with the feces and the internal pressure of the rectum with defecation. This is a common occurrence and is considered normal within the process. Therefore, it is important to define the concept of rectal bleeding[6].

Table 4 shows that rectal bleeding is the most frequent complication, accounting for 72.8% (115/158) of the total complications. Eighty-four of these 115 (73%) complications were Cl-D grade I. For this reason, when a patient consults our hospital's emergency department or after the immediate postoperative period, the first approach is conservative: hemodynamic control, withdrawal of anticoagulant or antiplatelet medication, and observation. If the complication persists, with a decrease in hemoglobin (> 2-3 g/dL) or hemodynamic alteration, the next step is to perform a flexible rectosigmoidoscopy under sedation in an attempt to visualize the source of bleeding and perform sclerosis or insert a hemostatic clip. In our study, this maneuver was performed in 25 patients with clinically relevant morbidity (Cl-D ≥ II) and was effective in 10 cases (40%).

The rest of the patients operated upon for rectal bleeding (15/115, 13%) were controlled with a new TEM. None underwent abdominal surgery or arteriography embolization. However, the performance of a new TEM requires a number of precautionary steps. Bleeding may be due to a deshiscence suture, or may be observed directly over the resection bed if it has not been sutured. First, as the rectal lumen is filled completely with blood clots, we will not be able to see anything inside via the rectoscope. The first step is to introduce the TEM rectoscope into the rectum without the working attachment. Then, the rectum undergoes intensive washing to remove all the blood clots from the rectal ampulla. Subsequently, the working attachment is introduced once more and the rectum is distended. In many cases, a rectal catheter is inserted via the TEM to complete the aspiration of the blood clots, since the conventional TEM aspirator is not effective. The bleeding may be as low diffuse bleeding or may start from a particular point; the amounts are small, but constant. The inflammation of the tissues means that any sutures inserted would tear. The most effective procedure is to perform coagulation with aspiration maintained over the point of bleeding and the entire surface of the resection bed. Finally, new washes are performed and the defect is left open.

Urinary complications

Some studies have reported urinary complications to be the most frequent, affecting between 5.9% and 10.8% of patients[8,9]. In our study, 30/716 (4.2%) patients presented urinary morbidity and only 20 (2.8%) patients had AUR, a complication which other studies (e.g., Kumar *et al.*[8]) have reported to be more frequent. One possible explanation is that in our protocol we remove the bladder catheter at the end of the surgery in all patients except those with a history of prostate disease; in these latter patients, the medication against benign prostatic hyperplasia is not withdrawn and the catheter is removed early the next morning. Another possible reason is the use of general anesthetic in 655/716 (91.4%) patients, which does not favor AUR (unlike spinal anesthetic).

Peritoneal cavity perforation

Peritoneal cavity perforation has been considered a cause of major morbidity in some studies[13]; others[14,15], however, have not found it to be a significant risk factor for postoperative complications. In our view, if peritoneal perforation is detected intraoperatively and is repaired by TEO/TEM, this is considered as a standard technical variant of the procedure[15].

Anterior resections with perforation in the vagina and recto-vaginal fistulas. Urethral lesions?

Special care must be taken in the resection of anterior lesions in women. The integrity of the recto-vaginal septum should be monitored, and a vaginal examination performed in case of doubt. Vaginal perforation should be considered an important complication; indeed, five of our 12 patients with vaginal perforations developed recto-vaginal fistula, due to the poor vascularization of the recto-vaginal septum and the pressure exerted on it during defecation. These fistulas constitute a rare complication (appearing in five of our 716 (0.7%) patients), but they are difficult to treat. In most cases, they require reoperation with a temporary stoma and subsequent repair of the fistula. We have registered no urethral injuries after TEM in our experience.

Postoperative pneumo-retropneumoperitoneum

As shown in Figures 2 and 3, the appearance of massive pneumo- and retroperitoneum on chest radiographs and abdominal CT is relatively common during the immediate postoperative period. Provided that the clinical and inflammatory parameters are normal, pneumo- and retroperitoneum need not be a matter for concern. As noted above, two patients with asymptomatic postoperative fever presented these features and were assigned to exploratory laparotomy, which turned out to be negative in both cases.

Asymptomatic postoperative fever

Fever is defined as asymptomatic and postoperative if it appears during the first 24-48 h, without other symptoms, hemodynamic repercussion, or any focus. Fever may be as high as 39 °C[6]; it is not associated with leukocytosis or with abdominal or pelvic pain and remits with antipyretics. In our study, 59/716 (8.2%) patients presented fever, which we considered to be a normal feature of the postoperative course. In contrast, fever associated with abdominal pain and leukocytosis is termed post-TEM syndrome[16].

The etiology of this asymptomatic fever is not known, although it is probably caused by an inflammatory reaction to the surgical aggression rather than to a self-limited infection or contamination; in all cases, it was controlled with antipyretics. We do not consider it as postoperative complication.

Severe perianal infection and the need for colostomy

The removal of lesions in the rectum, with fecal contamination of the resection area, entails a high risk of developing serious and frequent pelvic infections. Infections are very rare (in our study, only seven (1%) cases were recorded) but they can be serious. When they appear, antibiotic treatment and local debridement should be applied as quickly as possible to avoid the need for more radical treatments. Two of these patients required an end colostomy: one an immunosuppressed patient with a lymphoma, and the other without associated morbidity.

The limitations of this study are those inherent in observational studies performed at a single center. Its main strength is the unusually large sample size. All the data reported were recorded prospectively over a period of 15 years; the experience gathered over this time has allowed us to discuss and establish protocols for responding to the different complications.

In conclusion, clinically relevant complications after TEM are rare occurrences. Nonetheless, a protocol for their management needs to be established to ensure that their importance is not underestimated, and to avoid unnecessary or excessively aggressive treatments.

DECLARATIONS

Acknowledgments

We thank the rest of the members of the Coloproctology Unit for applying the study protocol. We thank Cristina Gomez Vigo for correcting the manuscript and Michael Maudsley for helping with the English.

Authors' contributions

Made substantial contributions to conception and design of the study and performed data analysis and interpretation: Serra-Aracil X, Mora-López L, Pallisera-Lloveras A, Serra-Pla S

Performed data acquisition and provided administrative, technical, and material support: Garcia-Nalda A, Gil-Barrionuevo E, Navarro-Soto S

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

The present study was approved by the Local Institutional Ethics Committee (CEIC: 2016-636), and complied with the criteria of the Declaration of Helsinki. The STROBE guidelines for observational studies were followed.

Consent for publication

Not applicable.

REFERENCES

1. Buess G, Hutterer F, Theiss J, Böbel M, Isselhard W, et al. A system for a transanal endoscopic rectum operation. Chirurg 1984;55:677-80.
2. Rocha JJ, Feres O. Transanal endoscopic operation: a new proposal. Acta Cir Bras 2008;23:93-104; Discussion 104.
3. Atallah S, Albert M, Larach S. Transanal minimally invasive surgery: a giant leap forward. Surg Endosc. 2010;24:2200-5.
4. Allaix ME, Arezzo A, Caldart M, Festa F, Morino M. Transanal endoscopic microsurgery for rectal neoplasms: experience of 300 consecutive cases. Dis Colon Rectum 2009;52:1831-6.
5. Laliberte AS, Lebrun A, Drolet S, Bouchard P, Bouchard A. Transanal endoscopic microsurgery as an outpatient procedure is feasible and safe. Surg Endosc. 2015;29:3454-9.
6. Serra-Aracil X, Labró-Ciurans M, Rebasa-Cladera P, Mora-López L, Pallisera-Lloveras A, et al. Morbidity after transanal endoscopic surgery. Risk factors for postoperative complications in a one-day surgery program. Surg Endosc 2019;33:1508-17.
7. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-13.
8. Kumar AS, Coralic J, Kelleher DC, Sidani S, Kolli K, et al. Complications of transanal endoscopic microsurgery are rare and minor: a single institution's analysis and comparison to existing data. Dis Colon Rectum 2013;56:295-300.
9. Tsai BM, Finne CO, Nordenstam JF, Christoforidis D, Madoff RD, et al. Transanal endoscopic microsurgery resection of rectal tumors: outcomes and recommendations. Dis Colon Rectum 2010;53:16-23.
10. Serra-Aracil X, Mora-Lopez L, Alcantara-Moral M, Caro-Tarrago A, Gomez-Diaz CJ, et al. Transanal endoscopic surgery in rectal cancer. World J Gastroenterol 2014;20:11538-45.
11. Serra-Aracil X, Mora-Lopez L, Alcantara-Moral M, Corredera-Cantarin C, Gomez-Diaz C, et al. Atypical indications for transanal endoscòpic microsurgery to avoid major surgery. Tech Coloproctol 2014;18:157-64.
12. Slankamenac K, Graf R, Barkun J, Puhan MA, Clavien PA. The comprehensive complication index: a novel continuous scale to measure surgical morbidity. Ann Surg 2013;258:1-7.
13. Palma P, Freudenberg S, Samel S, Post S. Transanal endoscopic microsurgery: indications and results after 100 cases. Colorectal Dis 2004;6:350-5.
14. Gavagan JA, Whiteford MH, Swanstrom LL. Full-thickness intraperitoneal excision by transanal endoscopic microsurgery does not increase short-term complications. Am J Surg 2004;187:630-4.
15. Serra-Aracil X, Pallisera-Lloveras A, Mora-Lopez L, Rebasa P, Serra-Pla S, et al. Perforation in the peritoneal cavity during transanal endoscopic microsurgery for rectal tumors: a real surgical complication with a challenging prognosis? Surg Endosc 2019;33:1870-9.
16. Brown C, Raval MJ, Phang PT, Karimuddin AA. The surgical defect after transanal endoscopic microsurgery: open versus closed management. Surg Endosc 2017;31:1078-82.

Jeong *et al. Mini-invasive Surg* 2019;3:38
DOI: 10.20517/2574-1225.2019.42

Mini-invasive Surgery

Editorial

Open Access

Transanal minimally invasive surgery: from transanal minimally invasive surgery to pure natural orifice transluminal endoscopic surgery

Won Jun Jeong[1,2], Byung Jo Choi[1,2], Sang Chul Lee[1,2]

[1]Department of Surgery, Daejeon St. Mary's Hospital, Daejeon 94349, Republic of Korea.
[2]Department of Surgery, College of Medicine, the Catholic University of Korea, Seoul 06591, Republic of Korea.

Correspondence to: Prof. Sang Chul Lee, Department of Surgery, Daejeon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 520-2 Daeheung-dong, Jung-gu, Daejeon 301-723, Republic of Korea.
E-mail: zambo9@catholic.ac.kr; zambo9@hanmail.net

How to cite this article: Jeong WJ, Choi BJ, Lee SC. Transanal minimally invasive surgery: from transanal minimally invasive surgery to pure natural orifice transluminal endoscopic surgery. *Mini-invasive Surg* 2019;3:38. http://dx.doi.org/10.20517/2574-1225.2019.42

Received: 15 Oct 2019 **Accepted:** 3 Dec 2019 **Published:** 12 Dec 2019

Science Editor: Xavier Serra-Aracil **Copy Editor:** Jing-Wen Zhang **Production Editor:** Tian Zhang

ANATOMICAL CHARACTERISTICS OF RECTUM

The rectum, the last stage of the digestive tract, inevitably crosses the pelvic cavity to the anus. The pelvic cavity is a tunnel-shaped space consisting of pelvic bones and is compactly filled with soft tissues including urogenital organs, blood vessels, nerves, and lymph nodes as well as the rectum. Rectal surgery performed in this narrow and visually adverse environment is difficult, regardless of surgical modalities in terms of firm procedures, securing margins, and nerve and blood vessel preservation. This is particularly acute in the distal rectum, because the rectum travels forward and close to the prostate and seminal vesicles in men and the vaginal wall in women.

HISTORY OF RECTAL SURGERY

The first description of rectal cancer was given by Joannes Baptista (1682-1771), and the first operation was performed by Jacques Lisfranc in 1826 in a transanal approach. The first colostomy to relieve large bowel obstruction was performed by Amussat in 1839 and the first transsacral approach to rectal cancer by Kraske in 1885. The combining of transabdominal and transperineal approaches to rectal cancer was already published by Czerny and Mayo in 1884 and 1904, respectively, but it is evaluated as a conventional surgery. The first rectal resection intended for radical treatment is generally known to have been performed by WE Miles in 1907[1].

At the same time, as distal resections including for rectal cancer, the Hartmann operation was performed by Henri A. Hartmann in 1921 and the anterior resection by Dixon in 1948. In 1967, the "No-touch isolation technique" was introduced by Rubert Turnbull Jr., and in the same year the circular stapler was first introduced by the Russian pediatric surgeon Mark Mitchell Ravitch, making it widely used for convenient and easy anastomosis. In 1982, Bill Heald introduced the concept of total mesorectal excision (TME), which led to a dramatic improvement in the local recurrence rate. Since then, the Holy plane has been the gold standard for rectal cancer surgery[2].

In 1998, Maas *et al*.[3] reported that autonomic nerves sparing could reduce the rate of postoperative urinary and sexual dysfunction.

Recently, with the development of minimally invasive surgery such as laparoscopic surgery and robotic surgery, favorable results of several studies (COST, CLASSIC, COLOR II, and COREAN trials) have been published one after another[4,5].

HISTORY OF TRANSANAL APPROACH

As mentioned above, transanal resection of rectal cancer was first performed by Jacques Lisfranc in 1826 and was accompanied by a transanal or transperineal approach as a form of combined surgery. In 1983, transanal endoscopic microsurgery (TEM) was introduced by Gerhard Buess. The system is inserted into the anus using a metallic cylinder with a beveled end (proctoscope) of 40-mm diameter and can be operated using laparoscopic instruments under a three-dimensional view after setting. In 2010, Atallah *et al*.[6] introduced TransAnal Minimally Invasive Surgery (TAMIS), a hybrid of TEM and single port laparoscopic surgery.

This type of operation is advantageous because it enters the surgical field of view at both the end lumen and the side wall of the intestinal tract, compared to the TEM, which has only the cylinder end area as the operation field and a relatively short port length. In addition, it is larger and can provide a free range of motion (ROM)[7].

Furthermore, experimental transanal total mesorectal excision (TaTME) surgeries were performed, mostly on swine or cadaver. In 2010, the first laparoscopic transanal TME was reported by Sylla *et al*.[8] after the first clinical application in 2009. They used a two-team approach, transabdominal and transanal. While the transabdominal team performed multiport laparoscopic colonic dissection and vessel ligation, the transanal team met in the middle with TaTME through the anus[8].

In 2013, Leroy *et al*.[9] and Zhang *et al*.[10] reported surgery for rectal lesions using natural orifice transluminal endoscopic surgery (NOTES) by transanal TME without transabdominal assistance. Leroy *et al*.[9] used TEO system and Zhang *et al*.[10] used soft single port.

In 2014, Chouillard *et al*.[11] reported small series of transanal "down-to-up" TME without any form of abdominal assistance, namely the pure NOTES for rectal cancer. According to their experience, among the total trial of 16 patients, operations on 10 patients could be finished by pure NOTES.

Since then, TaTME approaches to rectal cancer have been developed in various ways around the world. In addition, some trials have already been made to combine robotic surgery. Recently, the pure NOTES method for rectal cancer has been further developed. We performed transanal total proctocolectomy with IPAA for triple colorectal cancer without abdominal assistance in 2017. This may be the end point or final goal of minimally invasive surgery[12].

CONCERNS ON TRANSANAL APPROACH

TAMIS

Natural orifice specimen extraction

When the operation is performed by the transanal approach, the specimen should be discharged through the anus. In addition, transanal or transvaginal extraction is possible after conventional laparoscopy using the transabdominal approach. In the case of benign lesion or specimen by local excision, it is easy to remove, but, when the lesion itself is large or the specimen is bulky by TaTME, transanal extraction is relatively impossible due to the condition of anal sphincter (specimen-sphincter mismatch). In this case, it is necessary to switch to transabdominal extraction. In some cases, it can be safely removed by gentle and slow dilation; otherwise, excessive removal can cause sphincter injury and eventually lead to dysfunction[13,14].

While transanal extraction has the advantage that it can be applied irrespective of gender, transvaginal extraction is only possible in women and in some cases. It is also known that the rate of protective ileostomy is higher because of the relatively difficult incisions and the associated complications during the removal of the extract[15].

However, there are advantages in that relatively large extracts, for example those after RHC, can be taken out without large incisions and sphincter injury can be avoided[16].

Technical notes

Initially, a combination of surgical glove and wound protector was rolled down to create a homemade type port. Later, readymade ports were introduced, and the SILS port, OCTO port, and mini port were used, sequentially. Recently, however, a combination of Globe port and PPH's circular anal dilator has been used. This combination is easier and cheaper to install than the TEM system, and it is also superior in terms of view, as it can see the side of the view that cannot be seen in the TEM system at the same time. It is also advantageous for technical manipulation, as Atallah explained, with much more freedom and wider scope of application (ROM).

Instead of an Airseal system, a homemade reservoir system using surgical gloves can be manufactured easily and quickly. In this case, it is useful to secure a stable operative field at no additional cost [Figure 1].

TAMIS is a single port laparoscopic surgery format. Therefore, an inevitable jam is caused because the narrow space must be shared with the camera assistant. This is inconvenient for both the operator and the assistant. The answer to this inconvenience is solo surgery. The camera holder can be secured to the bed rail and the procedure can be performed without an assistant according to operator's own control and fixed focus [Figure 2].

The level of lesion available with this type of surgery (TAMIS) is commonly considered as mid or low rectal lesion. In practice, however, techniques such as access and excision are possible for lesions that exist at higher heights. The peritoneal reflection is usually regarded as a height equivalent to the second Houston valve level with some variation. Proximal lesions at higher heights are more likely to be perforated when resected into the whole layer, and infiltration of air into the abdominal cavity may cause difficulty in securing a stable field of vision and maintaining a stable surgical field. There is also a possibility of contamination.

Given the structure of the peritoneal reflex, the probability of perforation is relatively high, especially in lesions present in the anterior aspect.

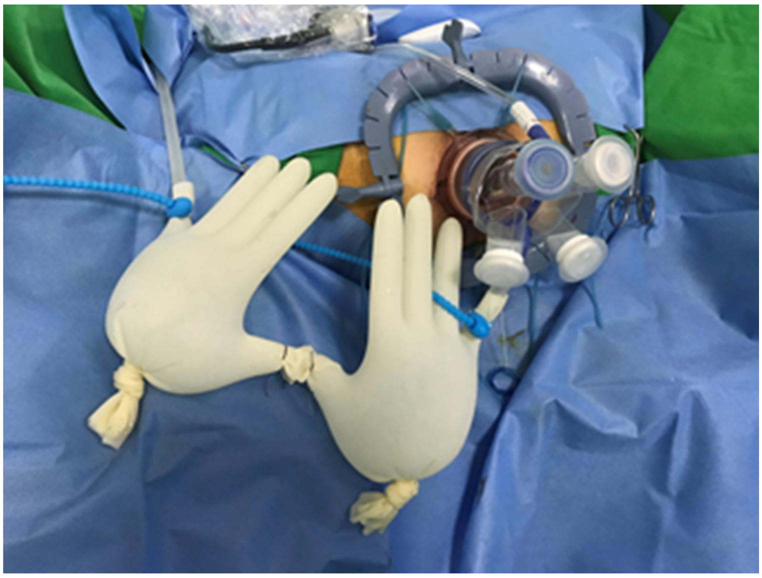


Figure 1. Surgical gloves as a reservoir. Powder free surgical glove can be used as a reservoir instead of Airseal system. Using a pair of gloves is good enough and provides stable pneumo-rectum/pelvis during transanal procedures

Figure 2. Solo surgery using a camera holder. Inevitable jam during single port laparoscopic surgery can be solved by applying the solo surgery. With the help of a camera holder fixed to rail of bed, the operator can use the space freely for stable procedures

Once perforation occurs, suture is possible even under TAMIS conditions, so it can be repaired by transanal manipulation. However, if the injury is large or there is already contamination of the abdominal cavity by the intestinal contents, repair and lavage may be necessary by the transabdominal approach. In this case, a single port laparoscopic procedure is usually preferred. Once the transabdominal approach is added, the length of stay is usually longer.

Patient position is also important in TAMIS surgery. In general, it is true that positioning the lesion at the bottom is convenient and advantageous for surgery. However, it is not necessary to vary the position of the patient to place the lesion at 6 o'clock as in TEM conditions, or to adjust the system to center the field of vision during surgery.

Wherever the lesion is located under the lithotomy position, it is relatively easy to access, but some authors still mention that the prone position is helpful for anterior proximal lesions[17].

Albert *et al.*[18] first suggested that the lesions be placed below when introducing the TAMIS, but a recent publication stated that lithotomy position could resolve all lesions.

Even in malignant lesions, local recurrence rate is low in lesions within T1, but local recurrence rate is significantly increased in T2 lesions.

NCCN guidelines for rectal cancer: local excision

Current guidelines for local excision of rectal cancer, e.g., the criteria for including the use of TAMIS, are based on long-term survival and outcome data. National guidelines recommend transanal local excision of only those T1N0 rectal cancers that meet the following criteria: < 30% circumference of bowel, < 3 cm in size, > 3-mm margins, mobile, nonfixed, within 8 cm of anal verge, endoscopically removed polyp with cancer or indeterminate pathology, no negative pathologic features such as lymphovascular or perineural invasion, no evidence of lymphadenopathy on pretreatment imaging, and tumors that are well to moderately differentiated. Furthermore, they recommend that local excision of more proximal lesions would be technically feasible using transanal microscopic surgery or TAMIS[19].

FUTURE AND THE FINAL GOAL OF TRANSANAL MINIMALLY INVASIVE SURGERY

NOTES for rectal cancer

When the pelvic delamination is complete through TaTME, this space can serve as a common path for access into the abdominal cavity. Under these conditions, various organs and intestines can be accessed from the abdominal cavity and surgical procedures can be performed. This is NOTES if the resulting extract is removed through the anus[20].

This procedure consists of three steps: anal, intraperitoneal, and second anal stage. In the first stage, TaTME takes place. In the second stage, vascular and mesenteric dissection is performed simultaneously with colonic mobilization. If necessary, splenic flexure mobilization is also performed. Finally, in the third stage, specimen pull through, transection, and anastomosis occur [Figure 3].

However, to approach the intraperitoneal through the transanal approach, there are some challenges that must be considered as well as some difficulties to overcome in the technical aspect. First, the condition of the anal sphincter should be compared with the characteristics of the lesion. The anus should be sufficiently intact and allow for safe passage of the extract, including the lesion. The second is the prominence of pelvic promontory. Usually, the transanal approach to inferior mesenteric artery (IMA) and inferior mesenteric vein (IMV) is possible without major difficulties. However, in some older patients, there are severe bends and protrusions of the pelvic promontory. This acts as a major obstruction to accessing the abdominal cavity and, in severe cases (in cases where it is impossible to attempt a straightening of the spine by changing the patient's position), a transabdominal approach should be added. Third, long shafted devices should be prepared for possible splenic flexure mobilization, as well as smooth manipulation of IMA and IMV. Commercially available laparoscopic instruments can reach up to 46 cm. If further distances are predicted from the patient's radiology data, surgery by NOTES should be considered difficult [Figure 4].

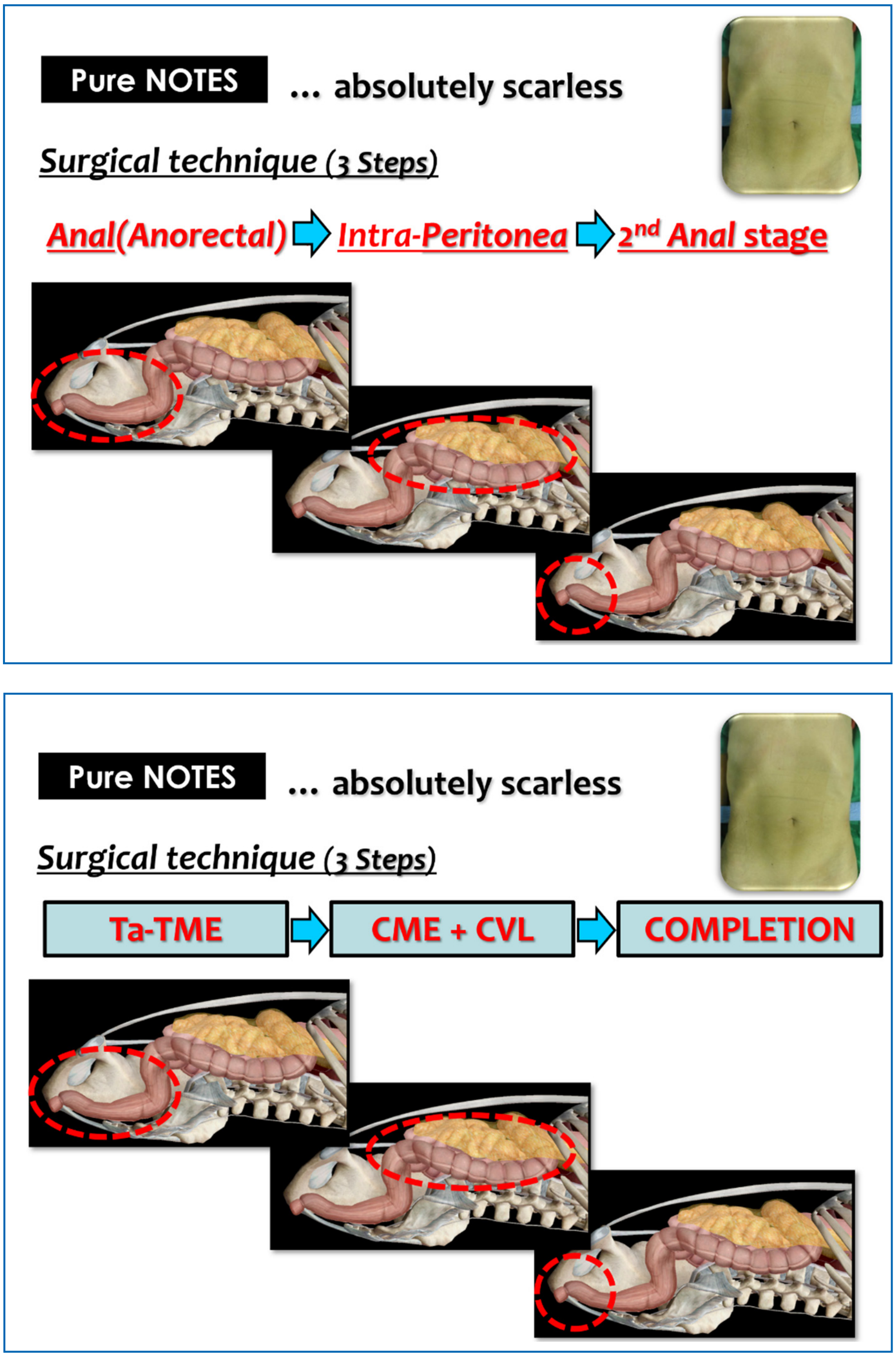


Figure 3. Three steps of pure NOTES. Pure NOTES consist of three steps: anal (anorectal), intracorporeal, and second anal step. According to each step, TaTME, CME + CVL, and anal completion are performed, respectively. Anal completion can be done by finishing of pull through, transection of specimen, and anastomosis. NOTES: natural orifice transluminal endoscopic surgery; TaTME: transanal total mesorectal excision; CME: complete mesocolic excision; CVL: central vascular ligation

In addition, NOTES-style surgery may be difficult under conditions such as redundancy of the colon length, anatomical variation, and surgical history including urological gynecology, and it is difficult to predict the future, such as severe natural adhesion of the colon to the left low quadrant (LLQ) area or excessive extension. Care should be taken to prevent or reduce the possibility of soiling or spillage. The author's method is to use a Lap-bag (Endo-catch bag). With sufficient TME in the pelvic cavity, entry into the abdominal cavity is necessary for further dissection and progression. At this time, an incision is made in the anterior peritoneal reflexion through the abdominal cavity and pushed into the abdominal cavity

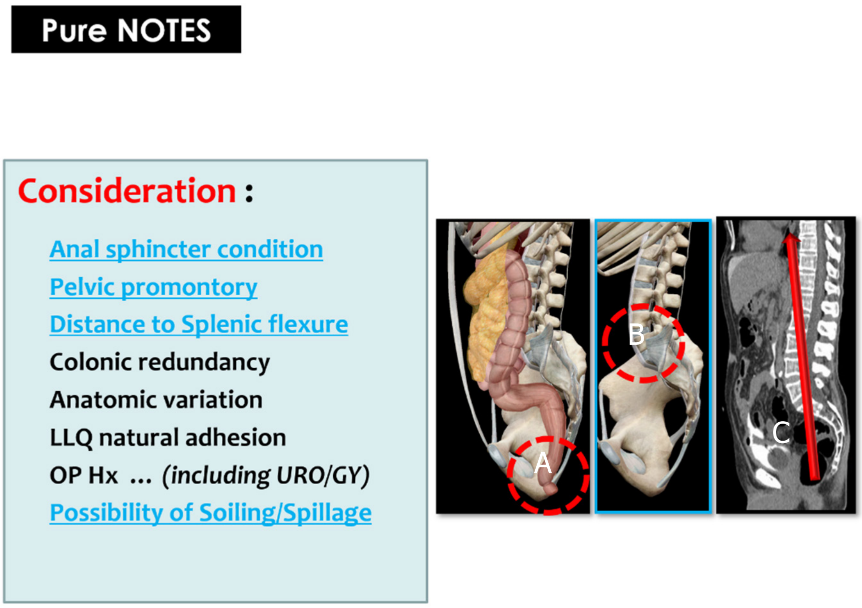


Figure 4. Considerations in pure NOTES. Preoperative considerations are anal sphincter condition (A), pelvic promontory (B), distance to splenic flexure (C), operative history, etc. NOTES: natural orifice transluminal endoscopic surgery; LLQ: left low quadrant

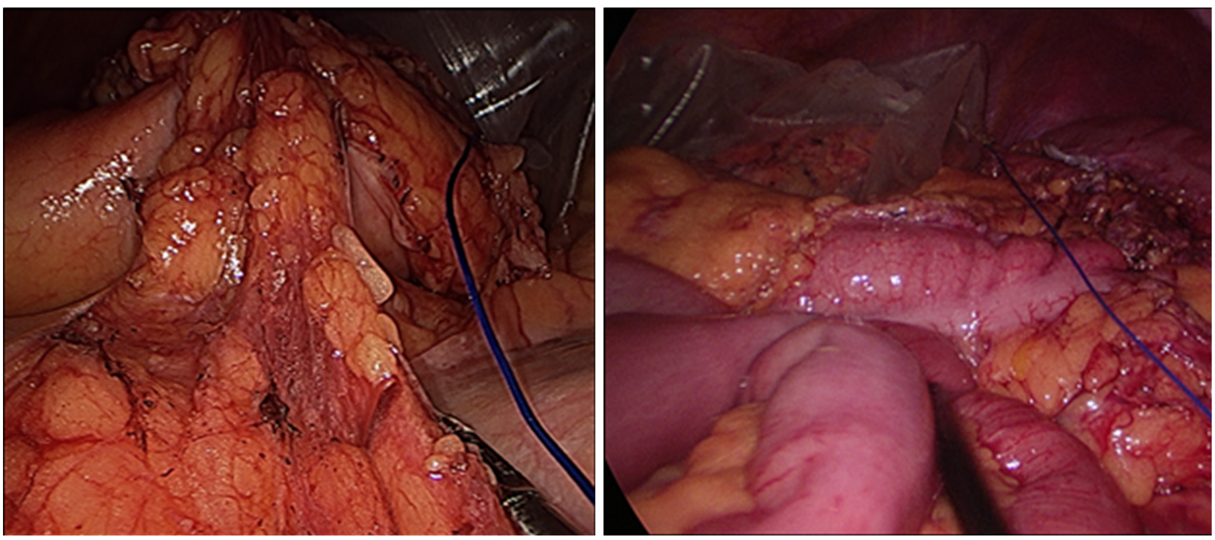


Figure 5. Lap-bag application. Especially Lap-bag should be considered for prevention from soiling and spillage during intraperitoneal step

with a rectal stump in the Lap-bag. This prevents soiling or spillage and at the same time improves the field of view because the rectal stump, including the lesion, is out of the center of the field of view [Figure 5].

In general, Hemo-loc or clip is usually used for ligation of IMA or IMV in laparoscopic surgery. However, when implementing transanal NOTES, a series of operations such as loading, entering, and firing must be performed several times in succession, and the moving range is relatively long. In this process, there is the possibility of damaging surrounding organs or tissues by blindly reciprocating a fairly long section. In contrast, when an energy device with a good sealing effect is used, the procedures can be carried out continuously by using "Overlapping sealing technique" in the field without repeating the work carried out during use of Hemo-loc or clips. Sealing power and security are also firm and safe enough. This can be said

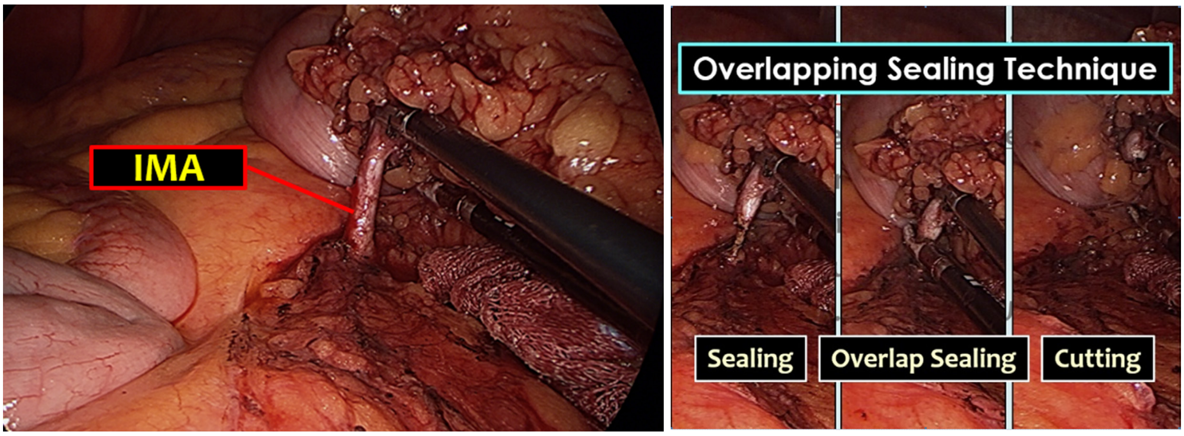


Figure 6. Overlapping sealing technique. Using of energy device instead of Hemo-loc or clip is beneficial to save time and reduce possible complications related with Hemo-loc or clip. "Overlapping sealing technique" may increase security. IMA: inferior mesenteric artery

Figure 7. Specimen and post-OP abdominal view. Even though a large-scale operation produces a bulky specimen, there is absolutely no visible operative incision or wound. Circles indicate Ascending colon cancer (A), Sigmoid colon ca (B), and Rectal cancer lesions respectively (C)

to be a reasonable advantage as it not only saves time but also reduces complications that can occur during entry and exit [Figure 6].

Reported case: transanal total proctocolectomy with IPAA

In February 2017, we performed transanal total proctocolectomy with IPAA without abdominal assistance in patients with triple colorectal cancers (ascending, sigmoid colon, and rectum) using pure NOTES[12] [Figure 7].

Case summary

A 70-year-old male patient without specific medical history was diagnosed with synchronous triple colorectal cancers (ascending colon, rectosigmoid colon, and rectum). We performed transanal total

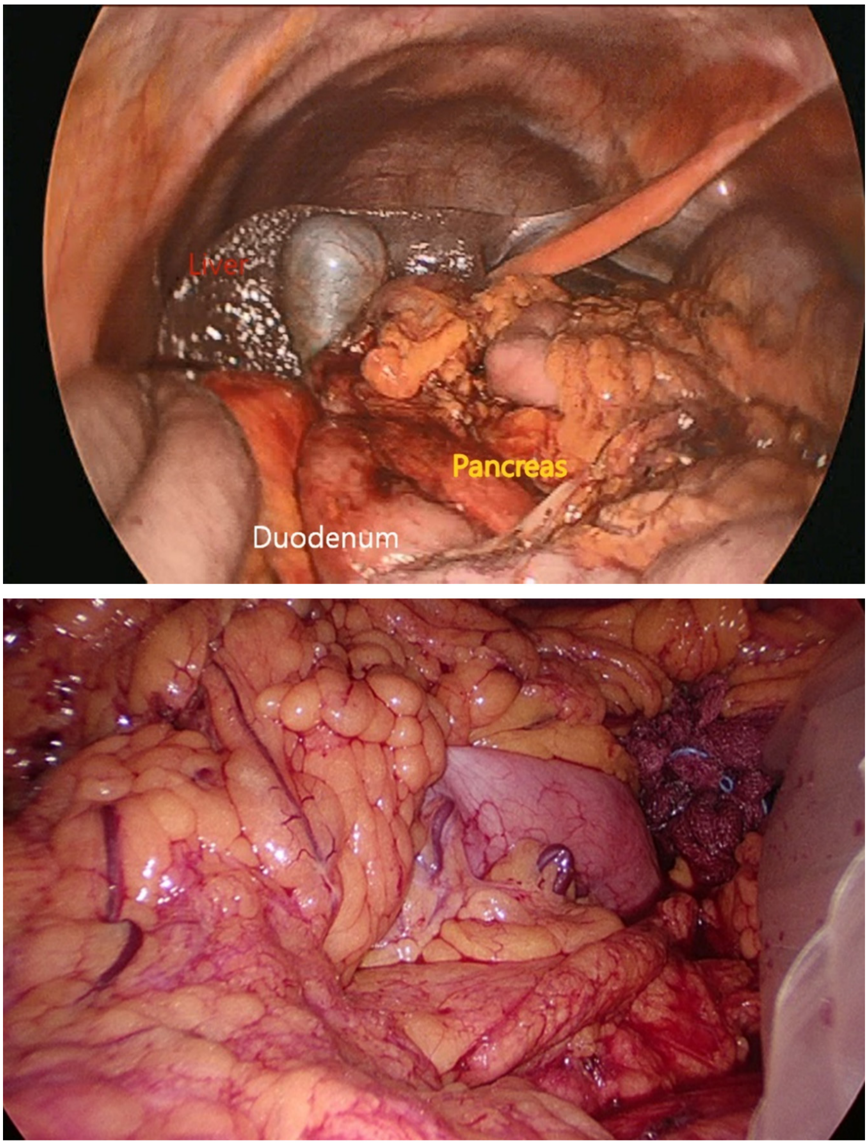


Figure 8. Transanal hepatic and splenic flexure mobilization. These are somewhat unique afterviews of transanal hepatic and splenic flexure mobilization

proctocolectomy with ileal pouch-anal anastomosis. On preoperative MRI, there was no pelvic lateral lymph node, thus we did not need to perform chemoradiation therapy. After transanal dissection of the mesorectum, rectum was flipped into the intraperitoneal space for further dissection. In our setting, we used conventional laparoscopic instruments for most procedures and long-shafted instruments helped during mobilization of the splenic and hepatic flexures [Figure 8].

The entire specimen was extracted transanally. The ileal pouch was constructed intracorporeally using two cartridges of linear staplers and ileal pouch-anal anastomosis was performed using a 25-mm circular stapler. We did not create a defunctioning stoma. Total operating time was 328 min and blood loss was < 50 mL. These were based on anesthesiologist records. We harvested 61 lymph nodes, and one regional lymph node metastasis was found. The patient experienced temporary paralytic ileus, was discharged on Postoperative Day 10, and had no major complications. The patient received antidiarrheal drug but had no incontinence. The patient refused adjuvant chemotherapy. During the 32-month follow-up period, there were no recurrences or metastases during five colonoscopies and CT scans. This operation was performed in February 2017 and this pure NOTES transanal total colectomy has been the first case and is a unique case thus far.

NOTES for intraperitoneal organs

NOTES methods for accessing the abdominal cavity may include transanal and transvaginal routes, and, especially in patients with stoma, the stoma may be recognized as one of the natural openings. For the transanal approach, matching between the specimen size including the mass and the accommodation of the sphincter is important, and, for the transvaginal approach, virginity or parity can be an important consideration. The transvaginal approach is advantageous for the extraction of quite large specimens, especially specimens made with en-bloc resection. It also has an advantageous approach in terms of angle with the abdominal cavity. Postoperative sutures may also be easier than intestinal anastomosis performed by transanal access surgery, and relatively less burden on leakage. In patients with stoma, the stoma can be recognized as one of the natural openings in a broad sense. The abdominal cavity can be accessed by taking down the stoma or partial splitting the margin of the stoma without inflicting any other wound. This is done by performing a single laparoscopy and finishing again with stoma to maintain the same condition as before.

In other surgical areas, various NOTES-type surgeries are newly introduced and performed. Surgery for various organs and intestines in the abdominal cavity is ultimately developing as absolutely scarless surgery. Some of them are already making significant progress, and, in cancer surgery, homework remains a matter of approach and adherence to oncological laws as in any surgery.

DECLARATIONS

Authors' contributions

Performed surgeries and contributed to conception and design of the study: Lee SC
Performed data acquisition and analysis, as well as provided technical support: Choi BJ
Wrote the thesis: Jeong WJ

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Copyright

REFERENCES

1. Lange MM, Rutten HJ, van de Velde CJ. One hundred years of curative surgery for rectal cancer: 1908-2008. Eur J Surg Oncol 2009;35:456-63.
2. Lirici MM, Hüscher CG. Techniques and technology evolution of rectal cancer surgery: a history of more than a hundred years. Minim

Invasive Ther Allied Technol 2016;25:226-33.
3. Maas CP, Moriya Y, Steup WH, Kiebert GM, Kranenbarg WM, et al. Radical and nerve-preserving surgery for rectal cancer in The Netherlands: a prospective study on morbidity and functional outcome. Br J Surg 1998;85:92-7.
4. Van der Pas MH, Haglind E, Cuesta MA, Fürst A, Lacy AM, et al. Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. Lancet Oncol 2013;14:210-8.
5. Jeong SY, Park JW, Nam BH, Kim S, Kang SB, et al. Open versus laparoscopic surgery for mid-rectal or low-rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): survival outcomes of an open-label, non-inferiority, randomised controlled trial. Lancet Oncol 2014;15:767-74.
6. Atallah S, Albert M, Larach S. Transanal minimally invasive surgery: a giant leap forward. Surg Endosc 2010;24:2200-5.
7. Atallah S, Albert M, Monson JR. Critical concepts and important anatomic landmarks encountered during transanal total mesorectal excision (taTME): toward the mastery of a new operation for rectal cancer surgery. Tech Coloproctol 2016;20:483-94.
8. Sylla P, Rattner DW, Delgado S, Lacy AM. NOTES transanal rectal cancer resection using transanal endoscopic microsurgery and laparoscopic assistance. Surg Endosc 2010;24:1205-10.
9. Leroy J, Barry BD, Melani A, Mutter D, Marescaux J. No-scar transanal total mesorectal excision: the last step to pure NOTES for colorectal surgery. JAMA Surg 2013;148:226-30; discussion 231.
10. Zhang H, Zhang YS, Jin XW, Li MZ, Fan JS, et al. Transanal single-port laparoscopic total mesorectal excision in the treatment of rectal cancer. Tech Coloproctol 2013;17:117-23.
11. Chouillard E, Chahine E, Khoury G, Vinson-Bonnet B, Gumbs A, et al. NOTES total mesorectal excision (TME) for patients with rectal neoplasia: a preliminary experience. Surg Endosc 2014;28:3150-7.
12. Jeong WJ, Choi BJ, Lee SC. Transanal total proctocolectomy with ileal pouch-anal anastomosis for synchronous triple colorectal cancer. J Laparoendosc Adv Surg Tech Videoscopy 2019; Epub ahead of print. Available from: http://doi.org/10.1089/ vor.2018.0566 [Last accessed on 9 Dec 2019]
13. Kim SJ, Choi BJ, Lee SC. A novel single-port laparoscopic operation for colorectal cancer with transanal specimen extraction: a comparative study. BMC Surg 2015;15:10.
14. Choi BJ, Lee SC, Kang WK. Single-port laparoscopic total mesorectal excision with transanal resection (transabdominal transanal resection) for low rectal cancer: initial experience with 22 cases. Int J Surg 2013;11:858-63.
15. Franklin ME Jr, Liang S, Russek K. Natural orifice specimen extraction in laparoscopic colorectal surgery: transanal and transvaginal approaches. Tech Coloproctol 2013;17 (Suppl 1):S63-7.
16. Park JS, Choi GS, Kim HJ, Park SY, Jun SH. Natural orifice specimen extraction versus conventional laparoscopically assisted right hemicolectomy. Br J Surg 2011;98:710-5.
17. Keller DS, Haas EM. Transanal minimally invasive surgery: state of the art. J Gastrointest Surg 2016;20:463-9.
18. Albert MR, Atallah SB, deBeche-Adams TC, Izfar S, Larach SW. Transanal minimally invasive surgery (TAMIS) for local excision of benign neoplasms and early-stage rectal cancer: efficacy and outcomes in the first 50 patients. Dis Colon Rectum 2013;56:301-7.
19. NCCN guidelines version 3.2019 rectal cancer. NCCN Clinical Practice Guidelines in Oncology. Available from: https://www.nccn.org/professionals/physician_gls/default.aspx [Last accessed on 9 Dec 2019]
20. Jeong WJ, Choi BJ, Lee SC. Pure natural orifice transluminal endoscopic surgery for rectal cancer: Ta-TME and CME without abdominal assistance. J Asian J Surg 2019;42:450-7.

Abdalla *et al*. *Mini-invasive Surg* 2019;3:39
DOI: 10.20517/2574-1225.2019.38

Mini-invasive Surgery

Original Article

Open Access

Robotic-assisted abdominoperineal resection: technique, feasibility, and short-term outcomes

Solafah Abdalla[1], Alain Valverde[1], Jean-François Fléjou[2], Nicolas Goasguen[1], Olivier Oberlin[1], Renato Micelli Lupinacci[1]

[1]Service de Chirurgie Digestive, Groupe Hospitalier Diaconesses Croix Saint-Simon, Paris 75020, France.
[2]Service d'Anatomie Pathologique, Hôpital Saint Antoine, Paris 75012, France.

Correspondence to: Dr. Renato Micelli Lupinacci, Service de Chirurgie Digestive, Groupe Hospitalier Diaconesses Croix Saint-Simon, 125, rue d'Avron, Paris 75020, France. E-mail: rmlupinacci@gmail.com

How to cite this article: Abdalla S, Valverde A, Fléjou JF, Goasguen N, Oberlin O, Lupinacci RM. Robotic-assisted abdominoperineal resection: technique, feasibility, and short-term outcomes. *Mini-invasive Surg* 2019;3:39. http://dx.doi.org/10.20517/2574-1225.2019.38

Received: 27 Sep 2019 **First Decision**: 12 Nov 2019 **Revised**: 29 Nov 2019 **Accepted**: 12 Dec 2019 **Published**: 26 Dec 2019

Science Editor: Nicola de'Angelis **Copy Editor**: Cai-Hong Wang **Production Editor**: Jing Yu

Abstract

Aim: The use of robotic-assisted laparoscopy seems fully adapted to pelvic surgery. However, few studies focus on robotic-assisted abdominoperineal resection (RAAPR). The aim of this study was to assess the feasibility, short-term postoperative outcomes, and pathological results of RAAPR. In addition, we provide a detailed description of the operative procedure and a brief review of the current literature.

Methods: Between January 2013 and April 2018, we performed a total of 428 robotic surgeries, including 294 colorectal resections (68.7%). Data were prospectively collected and included demographics, intraoperative findings, postoperative outcomes, and pathological data. For this study, we included the first 20 consecutive RAAPRs performed with the four-arm da Vinci Si surgical system (Intuitive Surgical Inc., Sunnyvale, CA, USA).

Results: Twenty patients (nine men) with a mean age of 68 years and a mean BMI of 24.5 ± 5.0 kg/m^2 underwent RAAPR for low rectal adenocarcinoma (80%) or squamous cell carcinoma of the anal canal. Sixteen (80%) patients underwent preoperative pelvic radiotherapy and eight (40%) had a history of previous abdominal surgery. Mean operative duration was 218 ± 52 min. There was no conversion to open surgery. Mortality, reoperation, and morbidity rate were 5%, 25%, and 60%, respectively. Three (15%) patients presented perineal complications. Mean length of hospital stay was 20 days. Three (15%) patients had pT4 tumor. Mesorectal excision was considered complete in 90%. On average, 16.5 ± 7.2 lymph nodes were retrieved.

Conclusion: RAAPR is feasible, with acceptable pathologic and short-term outcomes. The current literature does not demonstrate significant differences between robotic and laparoscopic APR. Indeed, we cannot justify its use in routine on the basis on the available evidence.

Keywords: Abdominoperineal resection, total mesorectal excision, robotic surgery, feasibility, rectal cancer, anal cancer

INTRODUCTION

The frequency with which abdominoperineal resection (APR) is performed has dramatically decreased over the last decade, mostly due to technical advances, the need for shorter distal margins, and oncological therapeutic progress[1,2]. Despite this, APR remains the appropriate approach for rectal cancers with involvement of the sphincter complex or that cannot be removed with sufficient distal resection margins, and for elderly with poor baseline functional status[2]. Finally, APR remains the standard treatment for persistent or recurrent squamous cell carcinoma of the anal canal after chemoradiotherapy[3].

Minimally invasive rectal surgery (MIRS) is a challenge[4]. The reported high conversion rates and the risks of positive circumferential resection margin (CRM) are thought to reflect the high level of difficulty associated with MIRS[5]. The fulcrum effect is one of the factors incriminated in the difficulty of MIRS, as it results in reduced motion ranges, especially inside the pelvis[6]. A robotic-assisted approach could potentially overcome some of the limitations of conventional laparoscopic rectal surgery[7]. However, few studies focus on robotic-assisted APR (RAAPR), and most are retrospective. Thus, the aim of this study was to provide a detailed description on the operative procedure, and to assess the feasibility, pathological, and short-term outcomes of the first 20 RAAPR in a high-volume center.

METHODS

Patients' selection and preoperative management

All consecutive patients undergoing RAAPR in our department from January 2013 to April 2018 were prospectively included. Patients with distant metastases were not excluded. Preoperative tumor staging assessment included colonoscopy; pelvic MRI; endorectal ultrasound when indicated; and thoracic, abdominal, and pelvic injected CT scan. Neoadjuvant treatment was planned according to the French guidelines[8] after multidisciplinary staff discussion.

Postoperative care and follow-up

Histopathological mesorectal grade was classified according to Quirke *et al.*[9]. All patients were started on clear liquids at postoperative day 1, and then a soft diet on passage of gas in the stoma bag. Particular attention was made to the perineal wound healing. Patients were discharged once their pain was controlled on oral analgesics and when the healing of the perineal wound was considered satisfactory. No patient was included in any "Enhanced Recovery After Surgery" protocol. Surgical complications were evaluated during the 30-day postoperative period and were graded according to Dindo and Clavien[10].

Statistical analysis

Demographic data, operative parameters, and pathologic outcomes were recorded in a prospectively collected database. Quantitative variables were expressed as means (± standard deviation) and qualitative variables as frequencies (percentages). Statistical analyses were performed using SPSS (IBM SPSS Statistics, Version 23 for Macintosh; IBM Corp., Armonk, NY, USA).

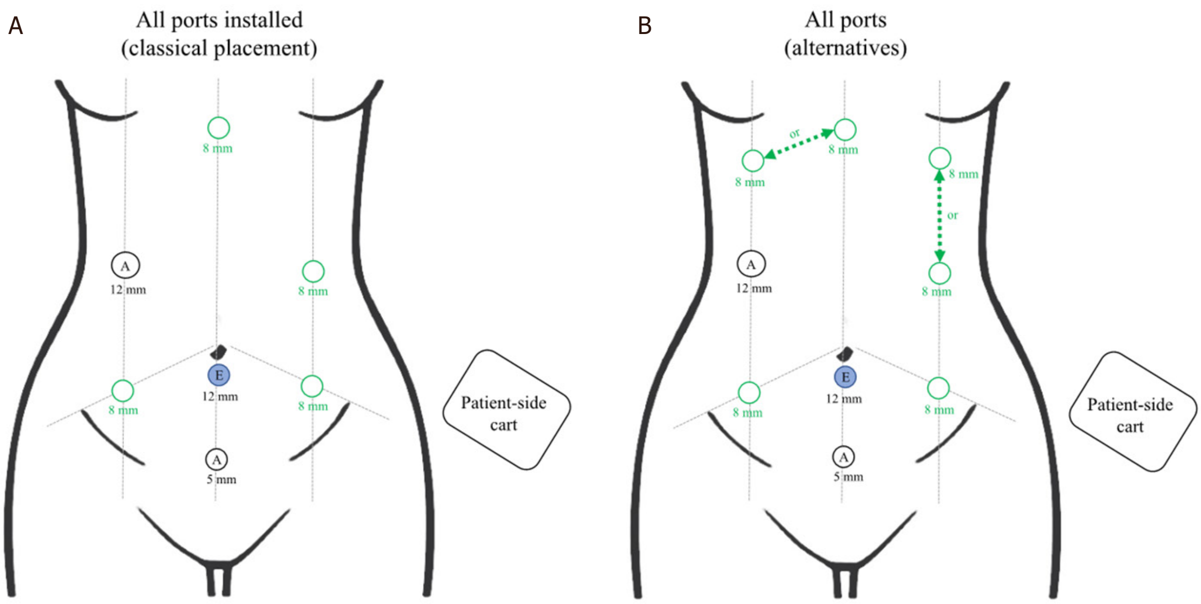


Figure 1. Port placement for robot-assisted abdominoperineal resection: operative view with all ports installed (A); and alternative placements of the ports (B). A: assistant port; E: endoscope port

Robotic-assisted abdominoperineal resection technique

The technique described below used a totally robotic colorectal mobilization and consisted of an up-to-down approach (abdominopelvic, pelvic and perineal procedures), with cylindrical extralevator APR, using the four-arm da Vinci® Si surgical system (Intuitive Surgical Inc., Sunnyvale, CA, USA). The patient was placed in the lithotomy position, and the legs were placed in stirrups, in a 20° tilted Trendelenburg and right-roll position. Transurethral or suprapubic catheter was placed.

Port placement

Seven ports were usually used, including one 12-mm endoscope port, four 8-mm robotic operative ports, and one 12-mm and one 5-mm laparoscopic ports for the assistant, with the cart placed obliquely at the left antero-superior iliac spine [Figure 1A]. The 12-mm endoscope port was introduced through an infra-umbilical incision; a 30° endoscope was used for the abdominopelvic procedure, and then switched for a 0° endoscope for the pelvic dissection. One 8-mm robotic port was placed at the level of the xyphoid process (Arm 2, abdominopelvic phase), another one in the right iliac fossa (Arm 1, abdominopelvic and pelvic phases), another in the left iliac fossa (Arm 3, abdominopelvic and pelvic phases), and the last in the left flank (Arm 2, abdominopelvic phase) [Figure 2]. A 5-mm laparoscopic port for the assistant was placed above the pubis and a 12-mm laparoscopic assistant port was placed in the right flank [Figures 1 and 2]. The xyphoidian 8-mm port could be shifted in the right hypochondrium and the left flank 8-mm port could be placed in the left hypochondrium [Figure 1B].

Exploration and robot docking

The peritoneal cavity was explored to evaluate the presence of distant metastases (liver and peritoneal carcinomatosis). Adhesiolysis was performed laparoscopically if needed. The omentum was retracted to the supramesocolic compartment and the small bowel was retracted in the right side of inferior mesenteric vein axis in order to visualize the Treitz angle. The 30° camera was placed in the 12-mm port in the infra-umbilical region, and robotic Arms 1-3 were placed in the right lower quadrant port, in the subxiphoid port, and in the left iliac fossa port, respectively.

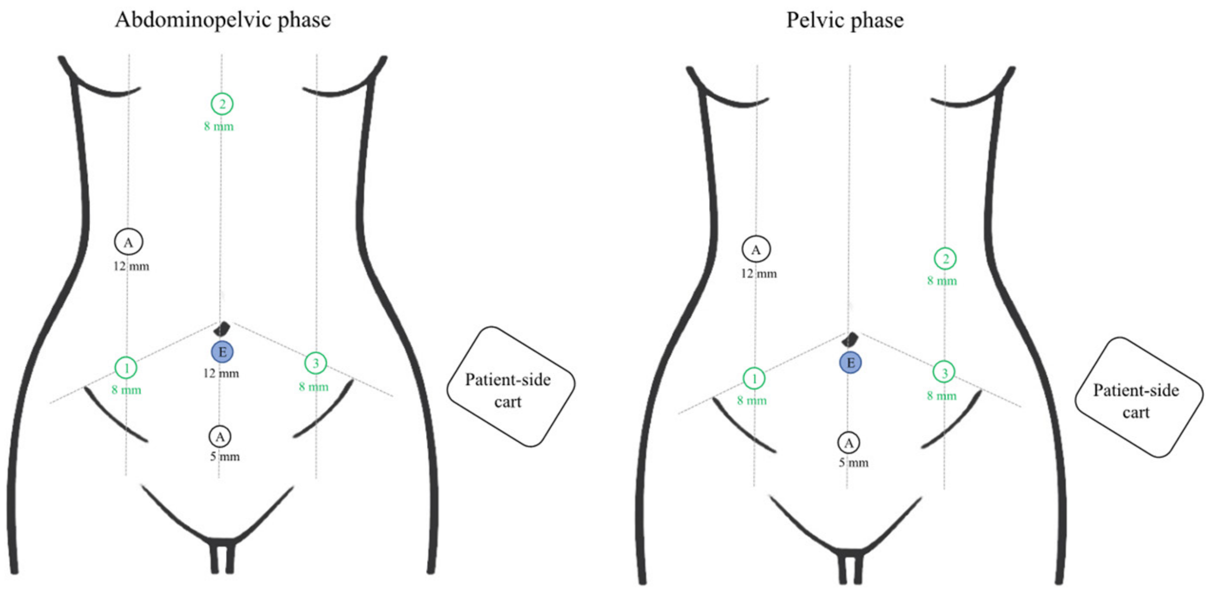


Figure 2. Port placement for robot-assisted abdominoperineal resection, in the abdominopelvic phase and in the pelvic phase. A: assistant port; E: endoscope port

Abdominopelvic procedure

The APR started with a medial to lateral approach. The mobilization of the splenic flexure and the ligation of the inferior mesenteric vein at its origin were usually not necessary. The peritoneum was incised at the level of the sacral promontory. The avascular presacral plane was entered, and this plane was developed identifying the origin of the inferior mesenteric artery and the left ureter. During this phase, dissection was performed using monopolar curved scissors (Arm 1), with tissues held by a Cadiere forceps (Arm 3), while the mesocolon was retracted using a fenestrated bipolar forceps (Arm 2). The superior rectal artery was ligated at its origin from the inferior mesenteric artery using a laparoscopic clip applier and cut. The mesenteric dissection was continued to the pelvic cavity along the prehypogastric fascia, preserving the pelvic autonomic nerves. The lateral approach was then performed with the incision of the Toldt's line, allowing complete sigmoid colon mobilization. The dissection was continued to the level of Gerota's fascia or the gastrocolic ligament, depending on the length of the sigmoid colon, and caudally to the level of the left peritoneal reflection. If the omentum was consistent, omentoplasty could be prepared by cutting right gastroepiploic vessels and mobilizing the omentum up to the left gastroepiploic pedicle.

Pelvic procedure

The pelvic procedure continued with TME. At this point, the switch of ports was required to carry on the procedure: Arm 2 was retrieved from the subxiphoid port and placed on the left iliac fossa port [Figure 2]. The pelvic dissection proceeded posteriorly first with the opening of the avascular presacral plane, then laterally, and finally anteriorly. Arm 3 was used for retraction, and Arms 1 and 2 were used to develop a plane of dissection between the presacral plane and the mesorectum until the Waldeyer fascia at the level of the anorectal junction. The rectal proper fascia was identified and preserved, and dissection was performed using robotic monopolar scissors. Then, lateral mesorectal dissection was performed. Particular attention was made to preserve hypogastric nerves. After the incision of the peritoneal reflection, lateral pelvic attachments were divided distally, until the levator ani. Lastly, the anterior mesorectal dissection was performed. The lateral peritoneal incisions were connected anteriorly at the recto-uterine pouch in women and rectovesical recess in men. Using Cadiere forceps to retract the urinary bladder and seminal vesicles, dissection was made to separate the rectum from the seminal vesicles and prostate or vagina through the Denonvillier's fascia, followed by separation of the levator muscles. When pelvic floor was reached

Table 1. Preoperative characteristics

	Overall (*n* = 20)
Male (%)	9 (45)
Age in years (mean ± SD)	68.5 ± 14.1
Age ≥ 75 years (%)	7 (35)
BMI in kg/m^2 (mean ± SD)	24.5 ± 5.0
BMI > 30 kg/m^2 (%)	2 (10)
BMI < 18 kg/m^2 (%)	1 (5)
ASA score ≥ 2 (%)	17 (85)
History of prior abdominal surgery (%)	8 (40)
Indication of APR	
Low rectum adenocarcinoma (%)	18 (90)
Epidermoid carcinoma of the anal canal (%)	2 (10)
Pretreatment T4 tumor (%)	5 (25)
Neoadjuvant treatment	17 (85)
Chemotherapy (%)	1 (5)
Radiotherapy (%)	4 (20)
Radio-chemotherapy (%)	12 (60)

BMI: body mass index; APR: abdominoperineal resection

circumferentially around the rectum, the pelvic portion of the dissection was completed. The proximal portion of the colon was stapled and cut with an endostapler. A standard incision through the abdominal wall was then created at the intended colostomy site; the distal colon was brought through this incision; and the end colostomy was fashioned.

Perineal procedure

The perineal procedure was performed as previously described for open approach, in the lithotomy position (except for one patient, for whom it was performed in prone position because of hip dysplasia)[11]: an elliptical incision was made around the anus outside the sphincter muscles. The ischiorectal fat was dissected until the levators plane was identified and cut. The section of the anococcygeal ligament gave access to the presacral space and the abdominal cavity. The specimen was extracted through the pelvic incision. Omentoplasty could be placed in the pelvic cavity at this point. The drains were positioned, and the perineal wound was closed.

RESULTS

Patients' characteristics

From January 2013 to April 2018, we performed a total of 428 robotic procedures, among which 294 colorectal resections (68.7%), including 20 consecutive RAAPR. We included nine men (45%). Mean age was 68.5 ± 14.1 years and mean BMI was 24.5 ± 5.0 kg/m^2. Eight (40%) patients had prior abdominal surgery (appendectomy in four patients, cholecystectomy in three patients, and suture repair of a perforated duodenal peptic ulcer in one patient). The majority of patients underwent APR for low rectum adenocarcinoma and 17 (85%) patients received preoperative treatment. Demographic data are summarized in Table 1.

Operative characteristics

All patients underwent robotic-assisted rectal resection with TME and cylindrical extralevator APR with total excision of the levator muscle. The mean total operating duration was 218.1 ± 52.5 min. Mean operative console time was 96.2 ± 48.0 min and perineal approach duration was 50 ± 30.0 min. Four robotic arms were used in 80% of the cases. Six ports were used in 70% of the patients. Fifteen (75%) procedures required robotic arm realignment. Six (30%) patients with fatty mesocolon required left colonic mobilization with section of the inferior mesenteric vein at its ending at the bottom edge of the pancreas,

Table 2. Intraoperative characteristics

	Overall (*n* = 20)
Total operative duration in minutes (mean ± SD)	218.1 ± 52.5
Operative console time in minutes (mean ± SD)	96.2 ± 38.3
Proctectomy duration in minutes (mean ± SD)	96.2 ± 48.0
Perineal approach duration in minutes (mean ± SD)	50 ± 30
Number of robotic arms	
3 arms (%)	4 (20)
4 arms (%)	16 (80)
Number of ports	
4 ports (%)	3 (15)
5 ports (%)	2 (10)
6 ports (%)	14 (70)
7 ports (%)	1 (5)
Necessity of robotic arm realignment (%)	15 (75)
Number of robotic arm realignment	
1 robotic arm realignment (%)	3 (15)
2 robotic arm realignments (%)	12 (60)
Splenic flexure mobilization (%)	3 (15)
Section of the inferior mesenteric vein (%)	6 (30)
Section of the inferior mesenteric artery (%)	11 (55)
Total mesorectal excision (%)	20 (100)
Specimen retrieval site	
Perineal incision (%)	19 (95)
Supra-pubic incision (%)	1 (5)
Omental pedicle flap placement (%)	5 (25)
Associated procedures (%)	6 (30)
Pelvic drainage (%)	20 (100)
Conversion to open (%)	0
Intraoperative complications (%)	2 (10)
Bleeding (%)	1 (5)
Tumor effraction (%)	1 (5)
Intraoperative bleeding in mL (mean ± SD)	297.5 ± 420.0

and splenic flexure mobilization for three (15%) of them. Specimen retrieval was conducted through the perineal incision in 95% of the patients and all had terminal colostomy. Associated omentoplasty was performed in five (25%) patients. The following associated procedures were performed in six (30%) patients: incisional hernia repair (*n* = 1), resection of an ovarian cyst (*n* = 1), partial resection of the posterior wall of the vagina (*n* = 1), partial prostatectomy (*n* = 1), partial resection of the posterior wall of the prostatic urethra and urethroplasty (*n* = 1), and partial sacrectomy (*n* = 1). No conversion to open surgery was required in this series. Macroscopic intraoperative tumor effraction occurred in one patient (5%). Mean intraoperative blood loss was 297 mL. Intraoperative variables and outcomes are summarized in Table 2.

Postoperative outcomes

One patient (5%) died at Postoperative Day 14 because of respiratory failure in the context of septic shock secondary to a *Clostridium difficile* colitis. Morbidity rate was 60%, with seven (35%) medical complications and nine (45%) surgical complications. Six patients (30%) presented a severe complication (Dindo-Clavien ≥ 3), which required reoperation in five (25%). Perineal wound complication occurred in three (15%) patients who presented complete disunion of the perineal wound and required iterative vacuum therapy until complete healing. These three patients had undergone preoperative 45 Gy pelvic irradiation and two of them had omental pedicle flap placement. The duration of hospital stay for these three patients was 29, 65, and 66 days, respectively. Four (20%) patients presented pelvic abscesses, which were treated conservatively by antibiotherapy. Two patients (10%) had ureteral fistula (one patient required reoperation and ureteral reimplantation, and the other was conservatively treated by ureteral catheter placement). The mean hospital length of stay was 20.4 days. Postoperative outcomes are summarized in Table 3.

Table 3. Postoperative outcomes

	Overall (*n* = 20)
Mortality (%)	1 (5)
Morbidity (%)	8 (40)
Medical complications (%)*	7 (35)
Urinary tract infection (%)	5 (25)
Acute urinary retention (%)	2 (10)
Malnutrition (%)	2 (10)
Pulmonary infection (%)	1 (5)
Septic shock (%)	1 (5)
Clostridium colitis (%)	1 (5)
Ileus (%)	1 (5)
Surgical complications (%)*	9 (45)
Pelvic abscess (%)	4 (20)
Perineal wound disunion (%)	3 (15)
Ureteral fistula (%)	1 (5)
Incisional abscess (%)	2 (10)
Clavien-Dindo > 2 (%)	6 (30)
Complications requiring reoperation (%)	5 (25)
Hospital length of stay in days (mean ± SD)	20.4 ± 17.1
Hospital length of stay > 7 days (%)	17 (85)

*Several patients presented more than one complication

Pathologic outcomes

Pathological results are presented in Table 4. A complete pathologic response was observed in one patient (5%). Three patients (15%) presented a pT4 tumor on final pathological report. On average, 16.5 lymph nodes were retrieved. The mean tumor size was 4.6 cm. Mesorectum was complete in 18 patients (90%).

DISCUSSION

Our study showed that RAAPR is feasible, with satisfying pathological results and acceptable postoperative outcomes.

During the last decade, the use of the robotic system has progressed[12]. Proctectomy can be technically hazardous with the straight instruments and limited retraction provided by laparoscopy. Robotic-assisted pelvic dissection can be potentially associated with better autonomic nerve preservation, lower conversion rate, and less blood loss[13]. Despite its theoretical advantages, the benefits of the mini-invasive approach compared to open surgery in rectal surgery are still under debate, and it is even more questionable for the robotic approach[14]. Indeed, the only existing randomized clinical trial (ROLARR) comparing the robotic-assisted *vs*. conventional laparoscopic surgery for rectal cancer showed that the robotic approach did not significantly reduce the conversion rate[15]. There were also no differences between the two groups in terms of intraoperative complications, postoperative mortality and morbidity, and positive CRM. The interest of robotic assistance in APR is even more challenging to demonstrate since very few studies in the literature focus on RAAPR [Table 5]. We found only four studies that included more than 20 patients: three studies compared RAAPR to open APR[16,17] or to open APR and laparoscopic APR[18], and one non-comparative study[19] focused on RAAPR. The ROLARR trial, for its part, did not analyze the outcomes in its specific sub-population of 52 RAAPR.

Compared to the conventional laparoscopic approach, the benefits of the robotic upgraded handling on the patient outcomes are difficult to bring to light. Indeed, up to now, robotic assistance seems to remain equivalent to laparoscopy. In the current study, the operative duration was 218.1 ± 52.5, which is in line with the data in the literature [Table 5] and longer than laparoscopic APR[18]. No conversion was required

Table 4. Pathologic outcomes

	Overall (n = 20)
Tumor regression grade (n = 15)	
No response (%)	3 (25)
Minimal (%)	7 (35)
Moderate (%)	3 (25)
Near total (%)	1 (5)
Complete (%)	1 (5)
Tumor histology	
Adenocarcinoma (%)	18 (80)
Epidermoid carcinoma (%)	2 (10)
pAJCC stage	
Stade 0 (%)	1 (5)
Stade I (%)	1 (5)
Stade II (%)	6 (30)
Stade III (%)	10 (50)
Stade IV (%)	2 (10)
pT-category	
pT0 (%)	2 (10)
pT1 (%)	0
pT2 (%)	2 (10)
pT3 (%)	13 (65)
pT4 (%)	3 (15)
pN-category	
pN0 (%)	10 (50)
pN1 (%)	4 (20)
pN2 (%)	6 (30)
pM-category	
pM0 (%)	18 (90)
pM1 (%)	2 (10)
Number of retrieved lymph nodes (mean ± SD)	16.5 ± 7.2
Number of metastatic lymph nodes (mean ± SD)	1.9 ± 2.9
CRM positive, ≤ 1 mm (%)	4 (20)
CRM depth in mm (mean ± SD)	2.3 ± 1.9
Tumor perforation (%)	2 (10)
Mesorectal grade	
Incomplete (%)	1 (5)
Nearly complete (%)	1 (5)
Complete (%)	18 (90)
Distal margin in cm (mean ± SD)	3.2 ± 1.9
Tumor size in cm (mean ± SD)	4.6 × 3.9 ± 0.3

in our study and Moghadamyeghaneh *et al.*[18] showed a significantly decreased conversion rate for RAAPR compared to laparoscopic APR (5.7 *vs*. 13.4%).

The robotic approach presents technical drawbacks, mostly associated with the loss of haptic feedback. Actually, despite the massive help of the immersive 3D overview, vibration, pressure, or shearing forces are not always apparent[13]. A recent analysis of 509,029 patients who underwent elective colectomy in the United States from 2009 to 2012 showed that the rate of iatrogenic complications was increased for robotic surgery[20].

Noteworthy, the results presented here are worse than our previously published results for sphincter-saving procedures[21]. The morbidity rate was 60%, with mainly perineal wound disunions and urinary complications. The mean length of hospital stay was three weeks, which is longer than in other studies in the literature [Table 5]. In this series, no patient was included in any "Enhanced Recovery After Surgery" program, and perineal wound complications were associated with longer hospital stay. Indeed, three

Table 5. Summary of the relevant literature about robotic-assisted abdominoperineal resection

First author, study period, type of study	Number of RAAPR	BMI > 30 kg/m^2 *n* (%)	History of prior abdominal surgery *n* (%)	Preoperative treatment *n* (%)	Conversion to open *n* (%)	Mean operative time (min)	TME time (min)	Intraoperative bleeding (mL)	Intraoperative tumor perforation *n* (%)	30-day mortality *n* (%)	30-day morbidity *n* (%)	LOS (days)	pT4 tumors *n* (%)	Positive CRM *n* (%)
Present study 2013-2018 Retrospective	20	2 (10)	8 (40)	17 (85)	0	218.1 ± 52.5	96.2 ± 48	297.5 ± 420.0	1 (5)	1 (5)	8 (40)	20.1 ± 17.1	3 (15)	4 (20)
Kim *et al.*[17] 2011-2013 Prospective RAAPR *vs*. OAPR	21	-	4 (19)	19 (91)	0	197 ± 29	-	-	0	0	4 (19)	7.6 ± 1.6	1 (4.8)	0
Kim *et al.*[16] 2010-2016 Retrospective RAAPR *vs*. OAPR	40	-	6 (15)	37 (93)	0	215 ± 56	-	> 400 mL: 5 (13)	2 (5)	0	-	8 ± 2.8	1 (3)	1 (3)
Moghadamyeghaneh *et al.*[18] 2009-2012 Retrospective OAPR *vs*. LAPR *vs*. RAAPR	872	59 (6.8)	-	-	50 (5.7)	-	-	-	-	Too small to report	235 (26.9)	8 ± 6	-	-
Eftaiha *et al.*[19] 2007-2012 Prospective	22	8 (36.4)	10 (45.5)	20 (90.9)	1 (4.5)	380 ± 91	114 ± 37	259 ± 75	1 (4.5)	1 (4.5)	16 (72.7)	6 (3-36)	-	3 (13.6)

APR: Abdominoperineal resection; BMI: body mass index; LAPR: laparoscopic abdominoperineal resection; LOS: length of hospital stay; OAPR: open abdominoperineal resection; RAAPR: robotic-assisted abdominoperineal resection

patients had complete perineal wound disunion, which required iterative vacuum therapy under general anesthesia. Two of these three patients presenting perineal wound complication had an omentoplasty, which created an interface between the bowel and the aspirative foam and helped to avoid bowel injuries. In addition, recent series showed that the usefulness of omentoplasty was limited when compared to primary perineal closure[22-24]. Noteworthy, in a recent publication, omentoplasty was not associated with a lower rate of perineal wound dehiscence[23] or a lower rate of non-healing perineal wound[22], while it was associated with organ space infection[24] after APR.

Oncological benefits could be expected from improved dissection techniques in the pelvis, and better-quality APR allowed by the theoretical advantages of the robotic approach. Indeed, open and laparoscopic APR are still associated with high local recurrence, because of higher positive CRM and tumor perforation[25]. In the literature, RAAPR did not show superiority to the open approach or the laparoscopic approach in terms of histopathological quality of the rectal resection[15-17,26] and initial oncological outcome[15,16,26].

In our study, all procedures were performed by senior surgeons trained in robotic surgery and complete resection of the mesorectum was obtained in 90%. These senior surgeons also had more than 15 years of experience in laparoscopic and open surgery for rectal cancer. CRM was positive in four patients (20%), among whom two patients had a pT4 tumor. In our study, postoperative positive CRM was not suspected in the preoperative oncologic assessment for these patients. However, this high rate of positive CRM raises the issue of preoperative patients' selection. Upfront open APR could be chosen over RAAPR according to parameters that take into account the specificities of the robotic approach.

Any proposal for the routine utilization of robotic assistance in surgery requires a proof of clinical benefit, while considering the associated full set of costs. Indeed, even if MIRS has been shown to be associated with lower morbidity rate, reduced pain, and early return to work, there are not enough data to state that oncological results are equivalent[14]. Added to the difficulty in proving its clinical benefits, the use of robotic approach in APR outside clinical studies remains questionable.

DECLARATIONS

Authors' contributions

Data acquisition, data analysis, manuscript drafting, manuscript revision: Abdalla S
Data acquisition, manuscript revision: Valverde A, Fléjou JF, Goasguen N, Oberlin O
Study design, data analysis, manuscript drafting, manuscript revision, final approval: Lupinacci RM

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

This study was conducted according to the ethical standards of the local institutional committee on human experimentation and the consent form of all patients was obtained.

Consent for publication

Not applicable.

Copyright

REFERENCES

1. Bordeianou L, Maguire LH, Alavi K, Sudan R, Wise PE, et al. Sphincter-sparing surgery in patients with low-lying rectal cancer: techniques, oncologic outcomes, and functional results. J Gastrointest Surg 2014;18:1358-72.
2. Hawkins AT, Albutt K, Wise PE, Alavi K, Sudan R, et al. Abdominoperineal resection for rectal cancer in the twenty-first century: indications, techniques, and outcomes. J Gastrointest Surg 2018;22:1477-87.
3. Pesi B, Scaringi S, Di Martino C, Batignani G, Giudici F, et al. Results of surgical salvage treatment for anal canal cancer: a retrospective analysis with overview of the literature. Dig Surg 2017;34:380-6.
4. Jamali FR, Soweid AM, Dimassi H, Bailey C, Leroy J, et al. Evaluating the degree of difficulty of laparoscopic colorectal surgery. Arch Surg 2008;143:762-7.
5. Guillou PJ, Quirke P, Thorpe H, Walker J, Jayne DG, et al. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. Lancet 2005;365:1718-26.
6. Nisky I, Huang F, Milstein A, Pugh CM, Mussa-Ivaldi FA, et al. Perception of stiffness in laparoscopy - the fulcrum effect. Stud Health Technol Inform 2012;173:313-9.
7. Lanfranco AR, Castellanos AE, Desai JP, Meyers WC. Robotic surgery: a current perspective. Ann Surg 2004;239:14-21.
8. Cotte E, Artru P, Christou N, et al. (2019) "Cancer du rectum". Thésaurus National de Cancérologie Digestive. Available from https://

www.snfge.org/sites/default/files/SNFGE/TNCD/tncd_chap-05-cancer-rectum_2019-03-20_vf.pdf [Last accessed on 24 Dec 2019]
9. Quirke P, Dixon MF. The prediction of local recurrence in rectal adenocarcinoma by histopathological examination. Int J Colorectal Dis 1988;3:127-31.
10. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-13.
11. Perry WB, Connaughton JC. Abdominoperineal resection: how is it done and what are the results? Clin Colon Rectal Surg 2007;20:213-20.
12. Shah J, Vyas A, Vyas D. The history of robotics in surgical specialties. Am J Robot Surg 2014;1:12-20.
13. Sivathondan PC, Jayne DG. The role of robotics in colorectal surgery. Ann R Coll Surg Engl 2018;100:42-53.
14. Cleary RK, Morris AM, Chang GJ, Halverson AL. Controversies in surgical oncology: does the minimally invasive approach for rectal cancer provide equivalent oncologic outcomes compared with the open approach? Ann Surg Oncol 2018;25:3587-95.
15. Jayne D, Pigazzi A, Marshall H, Croft J, Corrigan N, et al. Effect of robotic-assisted vs conventional laparoscopic surgery on risk of conversion to open laparotomy among patients undergoing resection for rectal cancer: the ROLARR randomized clinical trial. JAMA 2017;318:1569-80.
16. Kim JC, Lee JL, Kim CW. Comparative analysis of robot-assisted vs. open abdominoperineal resection in terms of operative and initial oncological outcomes. Ann Surg Treat Res 2018;95:37-44.
17. Kim JC, Kwak JY, Yoon YS, Park IJ, Kim CW. A comparison of the technical and oncologic validity between robot-assisted and conventional open abdominoperineal resection. Int J Colorectal Dis 2014;29:961-9.
18. Moghadamyeghaneh Z, Hanna MH, Carmichael JC, Pigazzi A, Stamos MJ, et al. Comparison of open, laparoscopic, and robotic approaches for total abdominal colectomy. Surg Endosc 2016;30:2792-8.
19. Eftaiha SM, Pai A, Sulo S, Park JJ, Prasad LM, et al. Robot-assisted abdominoperineal resection: clinical, pathologic, and oncologic outcomes. Dis Colon Rectum 2016;59:607-14.
20. Yeo HL, Isaacs AJ, Abelson JS, Milsom JW, Sedrakyan A. Comparison of open, laparoscopic, and robotic colectomies using a large national database: outcomes and trends related to surgery center volume. Dis Colon Rectum 2016;59:535-42.
21. Valverde A, Goasguen N, Oberlin O, Svrcek M, Fléjou JF, et al. Robotic versus laparoscopic rectal resection for sphincter-saving surgery: pathological and short-term outcomes in a single-center analysis of 130 consecutive patients. Surg Endosc 2017;31:4085-91.
22. Blok RD, Musters GD, Borstlap WAA, Buskens CJ, Bemelman WA, et al. Snapshot study on the value of omentoplasty in abdominoperineal resection with primary perineal closure for rectal cancer. Ann Surg Oncol 2018;25:729-36.
23. Rencuzogullari A, Gorgun E, Binboga S, Ozuner G, Kessler H, et al. Predictors of wound dehiscence and its impact on mortality after abdominoperineal resection: data from the national surgical quality improvement program. Tech Coloproctol 2016;20:475-82.
24. Welten VM, Fields AC, Lu P, Goldberg JE, Irani J, et al. Omental flaps in patients undergoing abdominoperineal resection for rectal cancer. Int J Colorectal Dis 2019;34:1227-32.
25. Marr R, Birbeck K, Garvican J, Macklin CP, Tiffin NJ, et al. The modern abdominoperineal excision: the next challenge after total mesorectal excision. Ann Surg 2005;242:74-82.
26. Wang YW, Huang LY, Song CL, Zhuo CH1, Shi DB, et al. Laparoscopic vs open abdominoperineal resection in the multimodality management of low rectal cancers. World J Gastroenterol 2015;21:10174-83.

Mini-invasive Surgery

Technical Note

Open Access

Check for updates

Single-port three-dimensional endoscopic subcutaneous mastectomy for gynaecomastia: an aesthetically superior and novel approach

Chi Wei Mok[1,2], Jun Xian Jeffrey Hing[1,2], Su-Ming Tan[1,2]

[1]Division of Breast Surgery, Department of Surgery, Changi General Hospital, Singapore 529889, Singapore.
[2]Singhealth Duke-NUS Breast Centre, , Singapore 529889, Singapore.

Correspondence to: Dr. Chi Wei Mok, Division of Breast Surgery, Department of Surgery, Changi General Hospital, 2 Simei Street 3, Singapore 529889, Singapore. E-mail: mok.chi.wei@singhealth.com.sg

How to cite this article: Mok CW, Hing JXJ, Tan SM. Single-port three-dimensional endoscopic subcutaneous mastectomy for gynaecomastia: an aesthetically superior and novel approach. *Mini-invasive Surg* 2019;3:40. http://dx.doi.org/10.20517/2574-1225.2019.39

Received: 2 Oct 2019 **First Decision**: 25 Nov 2019 **Revised**: 27 Nov 2019 **Accepted**: 17 Dec 2019 **Published**: 26 Dec 2019

Science Editor: Giulio Belli **Copy Editor**: Jing-Wen Zhang **Production Editor**: Jing Yu

Abstract

Gynaecomastia is a benign clinical condition that can occur in men of all ages, attributed by the proliferation of glandular tissue. Most patients are asymptomatic while symptoms ranging from mild discomfort to severe pain can present in patients with gynaecomastia. In addition to these, this condition may affect the psychological well-being of patients leading to a need for further treatment. Medical treatment of primary gynaecomastia in the form of anti-oestrogen therapy has not been proven to be effective and there is no consensus regarding the drug of choice or optimal duration of treatment. Surgical treatment is usually the standard treatment in primary gynaecomastia. There have been various techniques described in the literature with the aim of restoring a pleasant chest shape with limited scar on incision. Most of the techniques however involve the use of a peri-areolar or a Wise pattern incision, which can be obvious, especially in patients with a tendency to scar badly. The authors describe a novel approach, whereby a single-port endoscopic subcutaneous mastectomy using the three-dimensional endoscopic system with incision placed along the anterior axillary line was performed for a patient with gynaecomastia and thereby conferring excellent aesthetic outcomes.

Keywords: Gynaecomastia, subcutaneous mastectomy, endoscopic, endoscopic-assisted, three-dimensional, single port, insufflation

INTRODUCTION

Surgical techniques in gynaecomastia treatment have evolved over the years towards less invasive approaches such as liposuction[1]. However, in patients with larger amount of tissue or ptotic breast, subcutaneous mastectomy is still more effective in removing excess glandular tissue[2]. The downside to subcutaneous mastectomy are the resulting large, long and often unsightly scars[3]. Endoscopic subcutaneous mastectomy has been described in the literature[4,5] where it is commonly performed via three incisions along the mid-axillary line or a single incision in the axilla and the specimen will be morcellated and suctioned out thereafter. Single-port nipple-sparing mastectomy using three-dimensional (3D) endoscopic system in the management of breast cancer was recently reported[6] and the authors describe the advantage of enhanced 3D visualisation in the conduct of the operation, allowing precise plane recognition and dissection. In this article, the authors describe the use of single-port 3D endoscopic-assisted subcutaneous mastectomy in the management of gynaecomastia.

TECHNIQUE

Preoperative markings and positioning

Preoperative markings were performed with the patient in standing and sitting position [Figures 1 and 2]. Extent of dissection was determined with comparison to the contralateral (non-gynaecomastia) side. Under general anaesthesia, patient was then placed in a supine position with ipsilateral arm abducted at 90° [Figure 3]. The ipsilateral shoulder was then elevated to 30° to facilitate access for the operation.

Tumescent injection

Methylene blue gel was used to mark the extent of dissection to aid in identification during subsequent endoscopic dissection. A saline solution containing lignocaine 0.05% and epinephrine 1:1,000,000 was injected subcutaneously into the whole breast to minimise bleeding.

Skin flap dissection

Following that, a 3-cm incision was made over the extra-mammary region near the anterior axillary line at the level of nipple areolar complex (NAC). A working space of 4-5 cm was created by dissecting the subcutaneous flap under direct vision to allow subsequent placement of the single port. After creation of working space, subcutaneous tunnelling/blunt dissection of the anterior skin flap with Metzenbaum scissors was performed to aid in subsequent skin flap dissection. Following that, posterior dissection of breast parenchyma off pectoralis major fascia was performed under endoscopic guidance with endoscopic vein harvester [Figure 4]. Thereafter, the single port was placed with CO_2 insufflation kept at a pressure of 8 mmHg. A 30° 10-mm diameter camera TIPCAM 1 S- 3D VIDEO Endoscope (KARL STORZ, Germany), 5-mm laparoscopic Metzenbaum scissors, curved (Applied Medical, USA) and 5-mm laparoscopic grasping forceps were used to conduct the operation [Figure 5].

Endoscopic subcutaneous mastectomy

Endoscopic dissection commenced from superficial skin flaps in all quadrants with the septa between skin flap and parenchyma dissected using laparoscopic Metzenbaum scissors [Figures 6 and 7]. During skin flap dissection, a 30° upward facing 3D endoscope with reverse imaging was used to produce a clear 3D image. The angle and field of vision could be adjusted with upward, downward or reverse motion of the image by the 3D endoscope when deemed necessary. Tissue beneath the NAC were intentionally left thicker to prevent nipple retraction as well as preserve the blood supply to NAC, thereby reducing the risk of NAC necrosis [Figure 8]. With 3D visualisation, blood vessels could be clearly visualised and hence preserved [Figure 9]. After completion of superficial skin flap dissection, peripheral dissection was carried

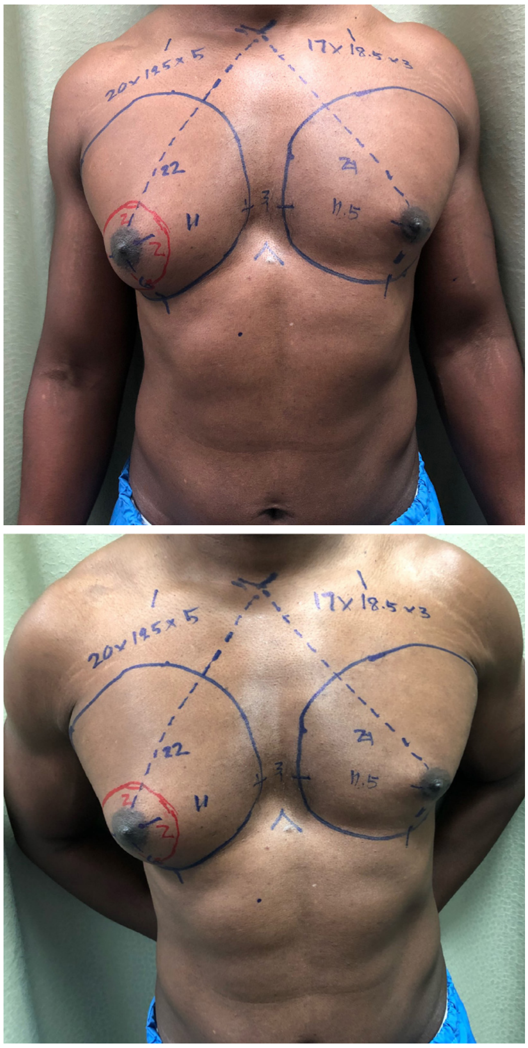


Figure 1. Preoperative front views showing preoperative markings and right gynaecomastia. Extent of planned dissection was marked out (as shown by red markings)

out by retracting breast tissue to create sufficient working space and extent of dissection was based on preoperative markings and intraoperative blue dye gel [Figure 10]. After the completion of dissection, the entire breast specimen was removed intact through the incision and haemostasis secured. A three-point fixation of the NAC to underlying pectoralis major fascia was then performed with absorbable stitches. A closed suction drain was placed.

Postoperative outcomes

Patient was discharged the next day and drain subsequently removed on Postoperative Day 5. Following the surgery, the patient was seen a month after surgery with excellent aesthetic outcomes [Figures 11-13].

CONCLUSION

Single-port 3D endoscopic subcutaneous mastectomy is a novel and aesthetically superior approach for the treatment of gynaecomastia if compared to conventional methods.

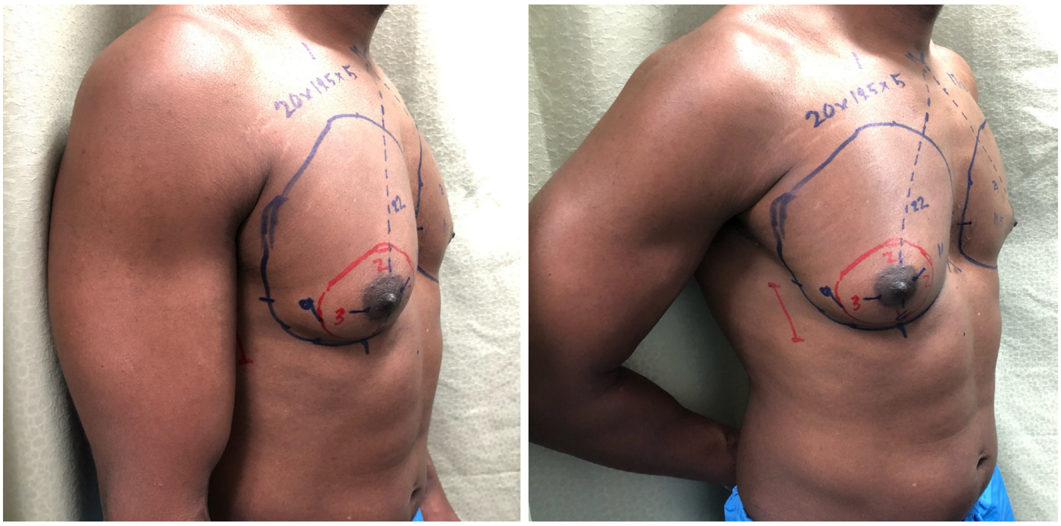


Figure 2. Preoperative lateral views showing preoperative markings and right gynaecomastia. Extent of planned dissection was marked out (as shown by red markings)

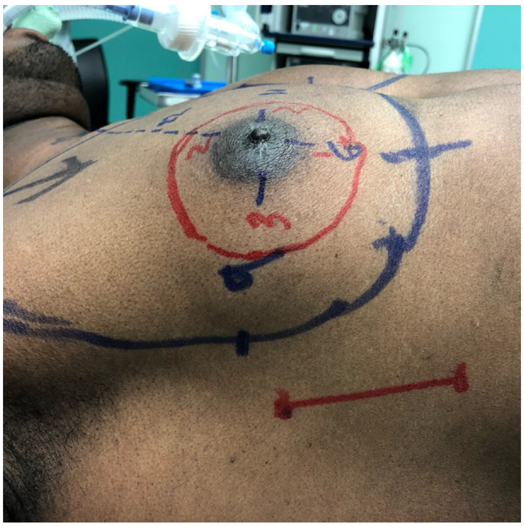


Figure 3. On-table view showing the planned incision

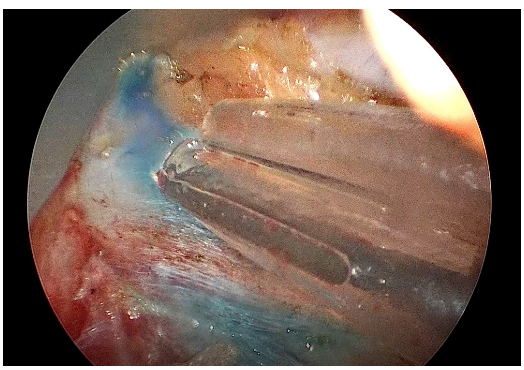


Figure 4. Endoscopic view showing the dissection of breast parenchyma off pectoralis major fascia

Figure 5. On-table view demonstrating placement of single port and instruments before commencement of endoscopic subcutaneous mastectomy

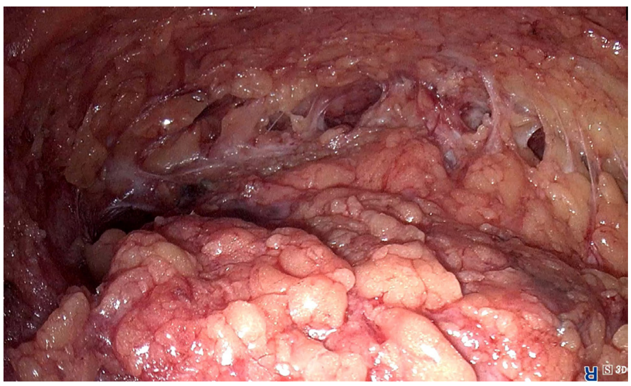


Figure 6. Endoscopic view after CO_2 insufflation demonstrating fibrous septa between skin flap and breast parenchyma

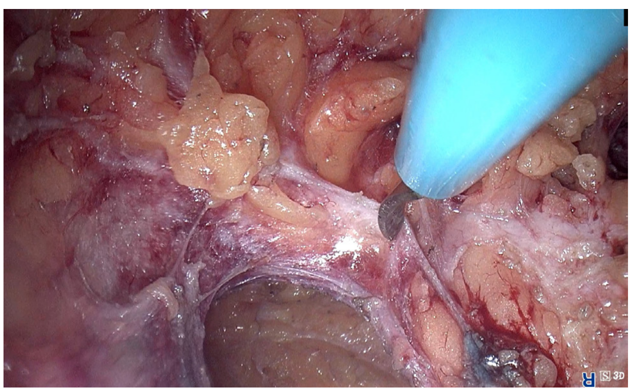


Figure 7. Skin flap dissection with fibrous septa taken down using laparoscopic curved scissors

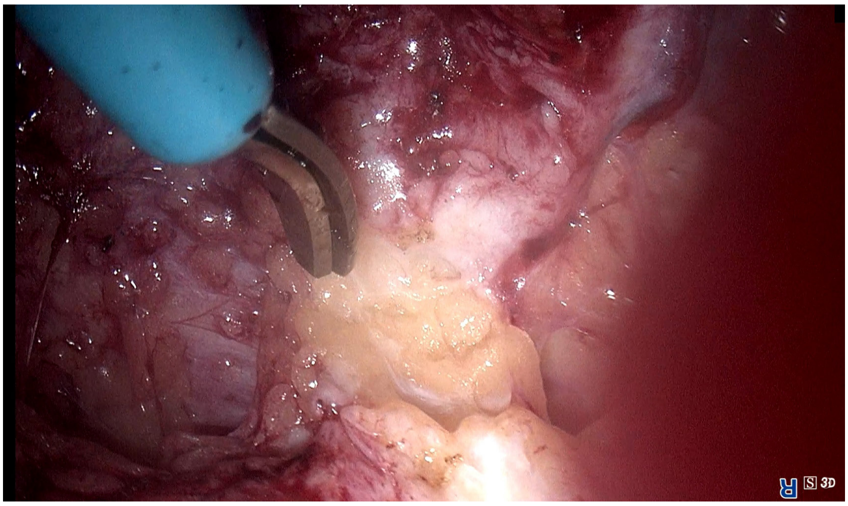


Figure 8. Thicker tissue beneath nipple areolar complex preserved to avoid nipple retraction and nipple areolar complex necrosis

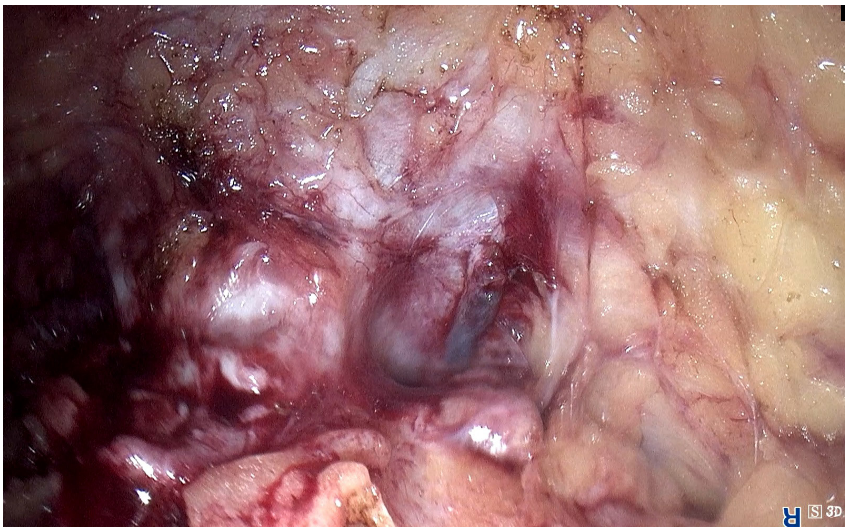


Figure 9. Blood vessel supplying nipple areolar complex can be clearly seen under three-dimensional view

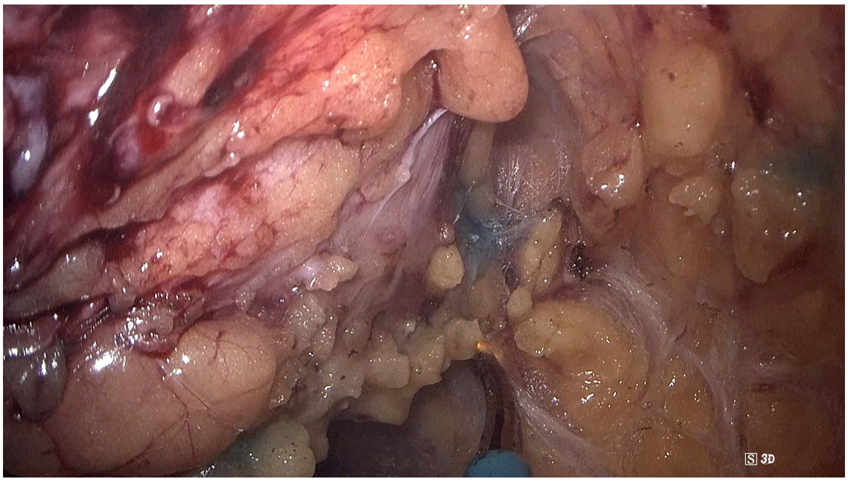


Figure 10. Extent of peripheral dissection guided by blue dye gel

Figures 11. One-month postoperative front views showing excellent symmetry and aesthetic outcomes

Figure 12. One-month postoperative lateral view showing hidden incision

Figures 13. One-month postoperative front and lateral views (dressed) showing excellent symmetry and aesthetic outcomes

DECLARATIONS

Authors' contributions

Conception and design of the study: Mok CW, Hing JXJ
Drafting of manuscript: Mok CW
Revision and final manuscript: Mok CW, Hing JXJ, Tan SM

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication
Written informed consent for publication was obtained as appropriate.

Copyright

REFERENCES
1. Wong KY, Malata CM. Conventional versus ultrasound-assisted liposuction in gynaecomastia surgery: a 13-year review. J Plast Reconstr Aesthetic Surg 2014;67:921-6.
2. Tashkandi M, Al-Qattan MM, Hassanain JM, Hawary MB, Sultan M. The surgical management of high-grade gynecomastia. Ann Plast Surg 2004;53:17-20.
3. Fischer S, Hirsch T, Hirche C, Kiefer J, Kueckelhaus M, et al. Surgical treatment of primary gynecomastia in children and adolescents. Pediatr Surg Int 2014;30:641-7.
4. Kim DH, Byun IH, Lee WJ, Rah DK, Kim JY, et al. Surgical management of gynecomastia: subcutaneous mastectomy and liposuction. Aesthetic Plast Surg 2016;40:877-84.
5. Zhu J, Huang J. Surgical management of gynecomastia under endoscope. J Laparoendosc Adv Surg Tech A 2008;18:433-7.
6. Lai HW, Chen ST, Mok CW, Lin SL, Tai CM, et al. Single port three-dimensional (3D) videoscope-assisted endoscopic nipple sparing mastectomy in the management of breast cancer. Plast Reconstr Surg Glob Open 2019;7:e2367.

AUTHOR INSTRUCTIONS

1. Submission Overview

Before you decide to publish with us, please read the following items carefully and make sure that you are well aware of Editorial Policies and the following requirements.

1.1 Topic Suitability

The topic of the manuscript must fit the scope of the journal. Please refer to Aims and Scope for more information.

1.2 Open Access and Copyright

The journal adopts Gold Open Access publishing model and distributes content under the Creative Commons Attribution 4.0 International License. Please make sure that you are well aware of these policies.

1.3 Publication Fees

There are no fees for submission, processing, and publication.

1.4 Language Editing

All submissions are required to be presented clearly and cohesively in good English. Authors whose first language is not English are advised to have their manuscripts checked or edited by a native English speaker before submission to ensure the high quality of expression. A well-organized manuscript in good English would make the peer review even the whole editorial handling more smooth and efficient.
If needed, authors are recommended to consider the language editing services provided by Charlesworth to ensure that the manuscript is written in correct scientific English before submission. Authors who publish with OAE journals enjoy a special discount for the services of Charlesworth via the following two ways.
Submit your manuscripts directly at http://www.charlesworthauthorservices.com/~OAE;
Open the link http://www.charlesworthauthorservices.com/, and enter Promotion Code "OAE" when you submit.

1.5 Work Funded by the National Institutes of Health

If an accepted manuscript was funded by National Institutes of Health (NIH), the author may inform editors of the NIH funding number. The editors are able to deposit the paper to the NIH Manuscript Submission System on behalf of the author.

2. Submission Preparation

2.1 Cover Letter

A cover letter is required to be submitted accompanying each manuscript. It should be concise and explain why the study is significant, why it fits the scope of the journal, and why it would be attractive to readers, *etc*.
Here is a guideline of a cover letter for authors' consideration:
In the first paragraph: include the title and type (e.g., Original Article, Review, Case Report, *etc*.) of the manuscript, a brief on the background of the study, the question the author sought out to answer and why;
In the second paragraph: concisely explain what was done, the main findings and why they are significant;
In the third paragraph: indicate why the manuscript fits the Aims and Scope of the journal, and why it would be attractive to readers;
In the fourth paragraph: confirm that the manuscript has not been published elsewhere and not under consideration of any other journal. All authors have approved the manuscript and agreed on its submission to the journal. Journal's specific requirements have been met if any.
If the manuscript is contributed to a special issue, please also mention it in the cover letter.
If the manuscript was presented partly or entirely in a conference, the author should clearly state the background information of the event, including the conference name, time and place in the cover letter.

2.2 Types of Manuscripts

There is no restriction on the length of manuscripts, number of figures, tables and references, provided that the manuscript is concise and comprehensive. The journal publishes Original Article, Review, Meta-Analysis, Case Report, Commentary, *etc*. For more details about paper type, please refer to the following table.

Manuscript Type	**Definition**	**Abstract**	**Keywords**	**Main Text Structure**
Original Article	An Original Article describes detailed results from novel research. All findings are extensively discussed.	Structured abstract including Aim, Methods, Results and Conclusion. No more than 250 words.	3-8 keywords	The main content should include four sections: Introduction, Methods, Results and Discussion.
Review	A Review paper summarizes the literature on previous studies. It usually does not present any new information on a subject.	Unstructured abstract. No more than 250 words.	3-8 keywords	The main text may consist of several sections with unfixed section titles. We suggest that the author includes an "Introduction" section at the beginning, several sections with unfixed titles in the middle part, and a "Conclusion" section in the end.
Case Report	A Case Report details symptoms, signs, diagnosis, treatment, and follows up an individual patient. The goal of a Case Report is to make other researchers aware of the possibility that a specific phenomenon might occur.	Unstructured abstract. No more than 150 words.	3-8 keywords	The main text consists of three sections with fixed section titles: Introduction, Case Report, and Discussion.
Meta-Analysis	A Meta-Analysis is a statistical analysis combining the results of multiple scientific studies. It is often an overview of clinical trials.	Structured abstract including Aim, Methods, Results and Conclusion. No more than 250 words.	3-8 keywords	The main content should include four sections: Introduction, Methods, Results and Discussion.
Systematic Review	A Systematic Review collects and critically analyzes multiple research studies, using methods selected before one or more research questions are formulated, and then finding and analyzing related studies and answering those questions in a structured methodology.	Structured abstract including Aim, Methods, Results and Conclusion. No more than 250 words.	3-8 keywords	The main content should include four sections: Introduction, Methods, Results and Discussion.
Technical Note	A Technical Note is a short article giving a brief description of a specific development, technique or procedure, or it may describe a modification of an existing technique, procedure or device applied in research.	Unstructured abstract. No more than 250 words.	3-8 keywords	/
Commentary	A Commentary is to provide comments on a newly published article or an alternative viewpoint on a certain topic.	Unstructured abstract. No more than 250 words.	3-8 keywords	/
Editorial	An Editorial is a short article describing news about the journal or opinions of senior editors or the publisher.	None required	None required	/
Letter to Editor	A Letter to Editor is usually an open post-publication review of a paper from its readers, often critical of some aspect of a published paper. Controversial papers often attract numerous Letters to Editor	Unstructured abstract (optional). No more than 250 words.	3-8 keywords (optional)	/
Opinion	An Opinion usually presents personal thoughts, beliefs, or feelings on a topic.	Unstructured abstract (optional). No more than 250 words.	3-8 keywords	/
Perspective	A Perspective provides personal points of view on the state-of-the-art of a specific area of knowledge and its future prospects. Links to areas of intense current research focus can also be made. The emphasis should be on a personal assessment rather than a comprehensive, critical review. However, comments should be put into the context of existing literature. Perspectives are usually invited by the Editors.	Unstructured abstract. No more than 150 words.	3-8 keywords	/

2.3 Manuscript Structure

2.3.1 Front Matter

2.3.1.1 Title

The title of the manuscript should be concise, specific and relevant, with no more than 16 words if possible. When gene or protein names are included, the abbreviated name rather than full name should be used.

2.3.1.2 Authors and Affiliations

Authors' full names should be listed. The initials of middle names can be provided. Institutional addresses and email addresses for all authors should be listed. At least one author should be designated as corresponding author. In addition, corresponding authors are suggested to provide their Open Researcher and Contributor ID upon submission. Please note that any change to authorship is not allowed after manuscript acceptance.

2.3.1.3 Abstract

The abstract should be a single paragraph with word limitation and specific structure requirements (for more details please refer to Types of Manuscripts). It usually describes the main objective(s) of the study, explains how the study was done, including any model organisms used, without methodological detail, and summarizes the most important results and their significance. The abstract must be an objective representation of the study: it is not allowed to contain results which are not presented and substantiated in the manuscript, or exaggerate the main conclusions. Citations should not be included in the abstract.

2.3.1.4 Keywords

Three to eight keywords should be provided, which are specific to the article, yet reasonably common within the subject discipline.

2.3.2 Main Text

Manuscripts of different types are structured with different sections of content. Please refer to Types of Manuscripts to make sure which sections should be included in the manuscripts.

2.3.2.1 Introduction

The introduction should contain background that puts the manuscript into context, allow readers to understand why the study is important, include a brief review of key literature, and conclude with a brief statement of the overall aim of the work and a comment about whether that aim was achieved. Relevant controversies or disagreements in the field should be introduced as well.

2.3.2.2 Methods

Methods should contain sufficient details to allow others to fully replicate the study. New methods and protocols should be described in detail while well-established methods can be briefly described or appropriately cited. Experimental participants selected, the drugs and chemicals used, the statistical methods taken, and the computer software used should be identified precisely. Statistical terms, abbreviations, and all symbols used should be defined clearly. Protocol documents for clinical trials, observational studies, and other non-laboratory investigations may be uploaded as supplementary materials.

2.3.2.3 Results

This section contains the findings of the study. Results of statistical analysis should also be included either as text or as tables or figures if appropriate. Authors should emphasize and summarize only the most important observations. Data on all primary and secondary outcomes identified in the section Methods should also be provided. Extra or supplementary materials and technical details can be placed in supplementary documents.

2.3.2.4 Discussion

This section should discuss the implications of the findings in context of existing research and highlight limitations of the study. Future research directions may also be mentioned.

2.3.2.5 Conclusion

It should state clearly the main conclusions and include the explanation of their relevance or importance to the field.

2.3.3 Back Matter

2.3.3.1 Acknowledgments

Anyone who contributed towards the article but does not meet the criteria for authorship, including those who provided professional writing services or materials, should be acknowledged. Authors should obtain permission to acknowledge from all those mentioned in the Acknowledgments section. This section is not added if the author does not have anyone to acknowledge.

2.3.3.2 Authors' Contributions

Each author is expected to have made substantial contributions to the conception or design of the work, or the acquisition, analysis, or interpretation of data, or the creation of new software used in the work, or have drafted the work or substantively revised it.

Please use Surname and Initial of Forename to refer to an author's contribution. For example: made substantial contributions to conception and design of the study and performed data analysis and interpretation: Salas H, Castaneda WV; performed data acquisition, as well as provided administrative, technical, and material support: Castillo N, Young V.

If an article is single-authored, please include "The author contributed solely to the article." in this section.

2.3.3.3 Availability of Data and Materials

In order to maintain the integrity, transparency and reproducibility of research records, authors should include this section in their manuscripts, detailing where the data supporting their findings can be found. Data can be deposited into data repositories or published as supplementary information in the journal. Authors who cannot share their data should state that the data will not be shared and explain it. If a manuscript does not involve such issue, please state "Not applicable." in this section.

2.3.3.4 Financial Support and Sponsorship

All sources of funding for the study reported should be declared. The role of the funding body in the experiment design, collection, analysis and interpretation of data, and writing of the manuscript should be declared. Any relevant grant numbers and the link of funder's website should be provided if any. If the study is not involved with this issue, state "None." in this section.

2.3.3.5 Conflicts of Interest

Authors must declare any potential conflicts of interest that may be perceived as inappropriately influencing the representation or interpretation of reported research results. If there are no conflicts of interest, please state "All authors declared that there are no conflicts of interest." in this section. Some authors may be bound by confidentiality agreements. In such cases, in place of itemized disclosures, we will require authors to state "All authors declare that they are bound by confidentiality agreements that prevent them from disclosing their conflicts of interest in this work.". If authors are unsure whether conflicts of interest exist, please refer to the "Conflicts of Interest" of OAE Editorial Policies for a full explanation.

2.3.3.6 Ethical Approval and Consent to Participate

Research involving human subjects, human material or human data must be performed in accordance with the Declaration of Helsinki and approved by an appropriate ethics committee. An informed consent to participate in the study should also be obtained from participants, or their parents or legal guardians for children under 16. A statement detailing the name of the ethics committee (including the reference number where appropriate) and the informed consent obtained must appear in the manuscripts reporting such research.

Studies involving animals and cell lines must include a statement on ethical approval. More information is available at Editorial Policies.

If the manuscript does not involve such issue, please state "Not applicable." in this section.

2.3.3.7 Consent for Publication

Manuscripts containing individual details, images or videos, must obtain consent for publication from that person, or in the case of children, their parents or legal guardians. If the person has died, consent for publication must be obtained from the next of kin of the participant. Manuscripts must include a statement that a written informed consent for publication was obtained. Authors do not have to submit such content accompanying the manuscript. However, these documents must be available if requested. If the manuscript does not involve this issue, state "Not applicable." in this section.

2.3.3.8 Copyright

Authors retain copyright of their works through a Creative Commons Attribution 4.0 International License that clearly states how readers can copy, distribute, and use their attributed research, free of charge. A declaration "© The Author(s) 2019." will be added to each article. Authors are required to sign License to Publish before formal publication.

2.3.3.9 References

References should be numbered in order of appearance at the end of manuscripts. In the text, reference numbers should be placed in square brackets and the corresponding references are cited thereafter. Only the first five authors' names are required to be listed in the references, other authors' names should be omitted and replaced with "et al.". Abbreviations of the journals should be provided on the basis of Index Medicus. Information from manuscripts accepted but not published should be cited in the text as "Unpublished material" with written permission from the source.

References should be described as follows, depending on the types of works:

Types	Examples
Journal articles by individual authors	Weaver DL, Ashikaga T, Krag DN, Skelly JM, Anderson SJ, et al. Effect of occult metastases on survival in node-negative breast cancer. N Engl J Med 2011;364:412-21. [PMID: 21247310 DOI: 10.1056/NEJMoa1008108]
Organization as author	Diabetes Prevention Program Research Group. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. Hypertension 2002;40:679-86. [PMID: 12411462]
Both personal authors and organization as author	Vallancien G, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1,274 European men suffering from lower urinary tract symptoms. J Urol 2003;169:2257-61. [PMID: 12771764 DOI: 10.1097/01.ju.0000067940.76090.73]
Journal articles not in English	Zhang X, Xiong H, Ji TY, Zhang YH, Wang Y. Case report of anti-N-methyl-D-aspartate receptor encephalitis in child. J Appl Clin Pediatr 2012;27:1903-7. (in Chinese)
Journal articles ahead of print	Odibo AO. Falling stillbirth and neonatal mortality rates in twin gestation: not a reason for complacency. BJOG 2018; Epub ahead of print [PMID: 30461178 DOI: 10.1111/1471-0528.15541]
Books	Sherlock S, Dooley J. Diseases of the liver and billiary system. 9th ed. Oxford: Blackwell Sci Pub; 1993. pp. 258-96.
Book chapters	Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. pp. 93-113.
Online resource	FDA News Release. FDA approval brings first gene therapy to the United States. Available from: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm574058.htm. [Last accessed on 30 Oct 2017]
Conference proceedings	Harnden P, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ Cell Tumour Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer; 2002.
Conference paper	Christensen S, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer; 2002. pp. 182-91.
Unpublished material	Tian D, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. Proc Natl Acad Sci U S A. Forthcoming 2002.

For other types of references, please refer to U.S. National Library of Medicine.
The journal also recommends that authors prepare references with a bibliography software package, such as EndNote to avoid typing mistakes and duplicated references.

2.3.3.10 Supplementary Materials

Additional data and information can be uploaded as Supplementary Material to accompany the manuscripts. The supplementary materials will also be available to the referees as part of the peer-review process. Any file format is acceptable, such as data sheet (word, excel, csv, cdx, fasta, pdf or zip files), presentation (powerpoint, pdf or zip files), image (cdx, eps, jpeg, pdf, png or tiff), table (word, excel, csv or pdf), audio (mp3, wav or wma) or video (avi, divx, flv, mov, mp4, mpeg, mpg or wmv). All information should be clearly presented. Supplementary materials should be cited in the main text in numeric order (e.g., Supplementary Figure 1, Supplementary Figure 2, Supplementary Table 1, Supplementary Table 2, *etc*.). The style of supplementary figures or tables complies with the same requirements on figures or tables in main text. Videos and audios should be prepared in English, and limited to a size of 500 MB or a duration of 3 minutes.

2.4 Manuscript Format

2.4.1 File Format

Manuscript files can be in DOC and DOCX formats and should not be locked or protected.

2.4.2 Length

There are no restrictions on paper length, number of figures, or amount of supporting documents. Authors are encouraged to present and discuss their findings concisely.

2.4.3 Language

Manuscripts must be written in English.

2.4.4 Multimedia Files

The journal supports manuscripts with multimedia files. The requirements are listed as follows:
Videos or audio files are only acceptable in English. The presentation and introduction should be easy to understand. The frames should be clear, and the speech speed should be moderate.
A brief overview of the video or audio files should be given in the manuscript text.
The video or audio files should be limited to a duration of 3 min and a size of up to 500 MB.

Please use professional software to produce high-quality video files, to facilitate acceptance and publication along with the submitted article. Upload the videos in mp4, wmv, or rm format (preferably mp4) and audio files in mp3 or wav format.

2.4.5 Figures

Figures should be cited in numeric order (e.g., Figure 1, Figure 2) and placed after the paragraph where it is first cited;
Figures can be submitted in format of tiff, psd, AI or jpeg, with resolution of 300-600 dpi;
Figure caption is placed under the Figure;
Diagrams with describing words (including, flow chart, coordinate diagram, bar chart, line chart, and scatter diagram, *etc*.) should be editable in word, excel or powerpoint format. Non-English information should be avoided;
Labels, numbers, letters, arrows, and symbols in figure should be clear, of uniform size, and contrast with the background;
Symbols, arrows, numbers, or letters used to identify parts of the illustrations must be identified and explained in the legend;
Internal scale (magnification) should be explained and the staining method in photomicrographs should be identified;
All non-standard abbreviations should be explained in the legend;
Permission for use of copyrighted materials from other sources, including re-published, adapted, modified, or partial figures and images from the internet, must be obtained. It is authors' responsibility to acquire the licenses, to follow any citation instruction requested by third-party rights holders, and cover any supplementary charges.

2.4.6 Tables

Tables should be cited in numeric order and placed after the paragraph where it is first cited;
The table caption should be placed above the table and labeled sequentially (e.g., Table 1, Table 2);
Tables should be provided in editable form like DOC or DOCX format (picture is not allowed);
Abbreviations and symbols used in table should be explained in footnote;
Explanatory matter should also be placed in footnotes;
Permission for use of copyrighted materials from other sources, including re-published, adapted, modified, or partial tables from the internet, must be obtained. It is authors' responsibility to acquire the licenses, to follow any citation instruction requested by third-party rights holders, and cover any supplementary charges.

2.4.7 Abbreviations

Abbreviations should be defined upon first appearance in the abstract, main text, and in figure or table captions and used consistently thereafter. Non-standard abbreviations are not allowed unless they appear at least three times in the text. Commonly-used abbreviations, such as DNA, RNA, ATP, *etc*., can be used directly without definition. Abbreviations in titles and keywords should be avoided, except for the ones which are widely used.

2.4.8 Italics

General italic words like *vs*., *et al., etc*., *in vivo*, *in vitro*; *t* test, *F* test, *U* test; related coefficient as *r*, sample number as *n*, and probability as *P*; names of genes; names of bacteria and biology species in Latin.

2.4.9 Units

SI Units should be used. Imperial, US customary and other units should be converted to SI units whenever possible. There is a space between the number and the unit (i.e., 23 mL). Hour, minute, second should be written as h, min, s.

2.4.10 Numbers

Numbers appearing at the beginning of sentences should be expressed in English. When there are two or more numbers in a paragraph, they should be expressed as Arabic numerals; when there is only one number in a paragraph, number < 10 should be expressed in English and number > 10 should be expressed as Arabic numerals. 12345678 should be written as 12,345,678.

2.4.11 Equations

Equations should be editable and not appear in a picture format. Authors are advised to use either the Microsoft Equation Editor or the MathType for display and inline equations.

2.5 Submission Link

Submit an article via https://www.oaemesas.com/mis.

OAE Publishing Inc.
www.oaepublish.com

Mini-invasive Surgery
(MIS)
Los Angeles Office
245 E Main Street ste122, Alhambra,
CA 91801, USA
Tel: +1 323 9987086
E-mail: editorialoffice@misjournal.net
Website: www.misjournal.net