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

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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 (TMIL).

Methods: Patients with cancer of the distal esophagus and esophagogastric junction were included into (HIL) and (TMIL) 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 TMIL and HIL groups, which contained 13 and 14 patients, respectively. Median intervention duration was 360 min (range: 240-420) for TMIL and 330 min (range: 240-400) for HIL ($P = 0.0647$). Median blood losses were similar for TMIL 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 TMIL and HIL, respectively.

Conclusion: Our experience suggests that TMIL 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



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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 esophagogastric junction 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 (TMIL) 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 TMIL 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 TMIL, 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 TMIL and HIL between January 2017 and July 2018 were retrospectively analyzed. Data were collected in a prospective database.

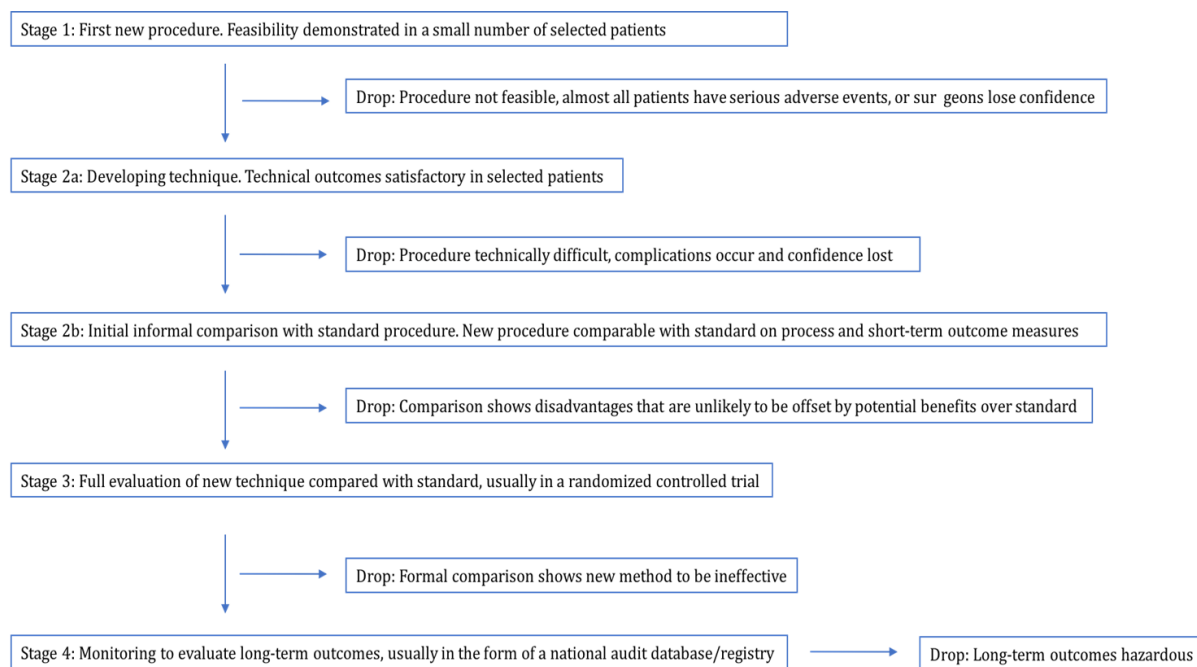


Figure 1. IDEAL recommendations framework

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 gastrolisis

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 thorotomy 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 pharyngolaryngo-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 TMIL and HIL

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

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

Table 2. Intraoperative variables

Characteristics	TMIL (<i>n</i> = 13)	HIL (<i>n</i> = 14)	<i>P</i> value
Duration of intervention median (min) (range)	360 (240-420)	330 (240-400)	0.0647
Laparoscopy converted to open surgery, <i>n</i> (%)	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; TMIL: 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 TMIL 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 TMIL 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 TMIL 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
Length 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
Lymph 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 TMIL 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 TMIL 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 TMIL.

The longer duration for TMIL 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 TMIL 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 TMIL 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 neoadjuvant treatment than in the TMIL 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 TMIL. As reported in Table 4, Tapias and Wang obtained a significant reduction of respiratory complications after TMIL; 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 TMIL and OIL, and it is widely demonstrated that laparoscopic gastrectomy 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 TMIL 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 <i>et al.</i> ^[15]	Retro	TMIL* 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 <i>et al.</i> ^[16]	Prosp	TMIL** 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 <i>et al.</i> ^[17]	Retro	TMIL* 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 <i>et al.</i> ^[18]	Retro	TMIL* 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 <i>et al.</i> ^[19]	Retro	TMIL ^{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 <i>et al.</i> ^[20]	Retro	TMIL* 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 <i>et al.</i> ^[21]	Retro	TMIL* 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 <i>et al.</i> ^[22]	Retro	TMIL	282	333 ± 98	242 ± 228	12 (9-24)	13.1	15.2	2.1
Qi <i>et al.</i> ^[23]	Retro	TMIL*/***	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(TM)]; ***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 TMIL 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 TMIL 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, TMIL seems feasible and safe in skilled hands although it represents a challenging procedure also for surgeons dedicated to esophageal 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 TMIL 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.

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