

Review

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Laparoscopic resection of liver tumors

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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



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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 <i>et al.</i> ^[28] (2007)	Meta-analysis 8 studies	LLR < OLR	No significant difference	No significant difference	LLR < OLR	No significant difference	No significant difference
Zhou <i>et al.</i> ^[29] (2011)	Meta-analysis 21 studies	LLR < OLR	LLR < OLR	No significant difference	LLR < OLR	LLR < OLR	No significant difference
Rao <i>et al.</i> ^[30] (2012)	Systematic review 10 studies	LLR < OLR	LLR < OLR	No significant difference	LLR < OLR	LLR < OLR	No significant difference
Fancellu <i>et al.</i> ^[31] (2011)	Meta-analysis 9 studies	LLR < OLR	LLR < OLR	No significant difference	LLR < OLR	LLR < OLR	No significant difference
Li <i>et al.</i> ^[32] (2012)	Meta-analysis 10 studies	LLR < OLR	LLR < OLR	No significant difference	LLR < OLR	LLR < OLR	No significant difference
Xiong <i>et al.</i> ^[33] (2012)	Meta-analysis 16 studies	LLR < OLR	LLR < OLR	No significant difference	LLR < OLR	LLR < OLR	No significant difference
Yin <i>et al.</i> ^[34] (2013)	Meta-analysis 15 studies	LLR < OLR	LLR < OLR	No significant difference	LLR < OLR	LLR < OLR	No significant difference
Fretland <i>et al.</i> ^[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 <i>et al.</i> ^[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 <i>et al.</i> ^[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 <i>et al.</i> ^[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 <i>et al.</i> ^[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 hepatobiliary 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

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All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

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