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ORIGINAL ARTICLE

Ultrasound liver map technique for laparoscopic liver resections: perioperative outcomes are not impaired by technical complexity

Alessandro Ferrero[1] · Nadia Russolillo[1] · Serena Langella[1] · Fabio Forchino[1] · Matteo Stasi[1] · Federico Fazio[1] · Roberto Lo Tesoriere[1]

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Abstract

Intraoperative liver ultrasound has a crucial role to guide open liver surgery. A 4-step ultrasound liver map technique for laparoscopic liver resection (LLR) has been standardized in our center. The aim of this study was to evaluate outcomes of our technique according to the hepatectomy technical complexity. A difficulty scale (DS) ranging from 1 to 10 was applied to each LLR. A cumulative sum control-chart analysis identified 3 periods of gradually increasing DS. Perioperative outcomes of the 3 periods were compared. 300 LLRs performed between 2006 and 2018 were analyzed. Median DS was 3 for first 100 cases (P1), 5 for cases 101–200 (P2) and 6 for cases 201–300 (P3). A significantly greater percentage of postero-superior segments resections (P1 11%, P2 36%, P3 46%, $p < 0.001$) were performed in P3. P3 LLRs had a significantly longer transection time ($p < 0.001$) and wider cut surface area ($p < 0.001$), but median blood losses were similar among the 3 periods (P1 100 cc, P2 100 cc, P3 140 cc). There were no differences among periods in overall morbidity (P1 12%, P2 17%, P3 17%), major morbidity (P1 1%, P2 2%, P3 3%) and length of hospital stay (5 days in all the three groups). Despite the increasing surgical complexity of LLR, ultrasound liver map technique allows good perioperative outcomes.

Keywords Intraoperative liver ultrasound · Laparoscopic liver resection · Technical difficulty

Introduction

Laparoscopic liver resection (LLR) has gained widespread acceptance in recent years [1–3] and has been reported to be a safe procedure that has potential advantages over open surgery in terms of morbidity, blood loss, and postoperative hospital stay [4–6]. These data have recently been confirmed by the first randomized study comparing open and laparoscopic parenchyma-sparing liver surgery [7]. The recent creation of national registries confirms the increasing interest on LLR. In particular, in Italy since 2014 started the Italian Group of Minimally Invasive Liver Surgery (I Go Mils) registry that already enrolled more than 3000 patients [5]. However, LLR has not been adopted worldwide because of inherent limitations of the technique, such as the surgeon's inability to palpate as well as difficult depth perception and loss of spatial orientation [4].

The use of laparoscopic ultrasound (LUS) was first reported in 1981 by Fukuda et al. [8]. Restricted trocar movement makes the identification of vascular structures less intuitive with LUS than with open intraoperative ultrasound (IOUS). Nevertheless, adequate training in LUS can result in performance similar to that of open IOUS [9]. As in other centers, our LLR program started with simple minor resections in anterolateral segments. However, with development of the program, there was a clear trend toward employing LLR more often for major and complex resections. This study was designed to evaluate the perioperative outcomes of ultrasound-guided laparoscopic liver resection (LLR) according to the technical complexity

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✉ Alessandro Ferrero
aferrero@mauriziano.it

[1] Department of General and Oncological surgery, Mauriziano Hospital, "Umberto I" Largo Turati, 62, 10128 Turin, Italy

Materials and methods

The study population included all consecutive patients treated with LLR between 01/2006 and 12/2018 at our center. Laparoscopic cyst fenestrations and ablation procedures were excluded. All resections were performed with a totally laparoscopic approach. The selection of the laparoscopic approach was considered each time and was based on the number and position of the liver lesions and the possibility of obtaining a parenchyma-sparing resection when indicated. The procedures were ordered chronologically from the earliest to the latest date of surgery. A difficulty scale (DS) score ranging from 1 to 10, with 1 being the least difficult and 10 being the most difficult LLR [10] was applied to each procedure. In patients who received multiple liver resections, the higher DS was chosen. Cumulative sum control-chart (CUSUM) analysis was then applied to the DS. The CUSUM of the DS of the first case was the difference between its DS and the mean DS of the entire series. The second case was calculated using the same method and added [11].

Ultrasound liver map technique

Because LUS is more complex than IOUS, we further schematized our standard technique for ultrasound guidance for resection as a 4-step method, which we named the Ultrasound Liver Map Technique. Using the mnemonic 4 C's, the 4 steps are: (1) **C**ompose the 3-dimensional (3-D) mind map, (2) **C**reate the sketch, 93) **C**heck the way, and 4) **C**orrect the direction.

1. *Compose the 3-D mind map* The first step is to perform an in-depth ultrasound study of the relationships between the lesion and the surrounding contiguous or adjacent vessels that are to be correctly identified in order to create a 3-D anatomic mind map.
2. *Create the sketch* The underlying anatomic structures are sketched on the liver surface with cautery, as previously described (9), the goal being to help the surgeon to hold in mind the map of the liver anatomy relative to the lesion. Lines of transection are drawn according to the sketch, thus planning which vessel will be ligated and cut and which will be preserved and exposed on the cut surface.
3. *Check the way* The map sketch shows only the glissonian projection of deeper structures, so it is necessary to check the section plane while proceeding with the transection. The resection line is easily visualized as an inhomogeneous hyperechoic linear artifact in the parenchyma, so the surgeon can check the resection plane, with respect to the relationships with hepatic veins, portal pedicles, and surgical margin, at any time.
4. *Correct the direction* The direction of the section plane is not always initially correct. The right angle of incidence at which to start the resection may not be obvious; often the direction has to be adjusted to stay clear of the lesion, to reach a pedicle at the correct distance from its origin, or to reach a structure that will be spared and followed.

Surgical procedure

LUS was performed using a ProSound Alpha 7 ultrasound system with a UST-5536-7.5 probe (Hitachi-Aloka Medical, Ltd., Tokyo, Japan) with 2-way and 4-way linear-array laparoscopic transducers or B-K Medical Pro Focus 2202 ultrasound with 4-way flexible probe (BK Medical, ApS,. Denmark). Before 2010, parenchymal transection was performed most often with a radiofrequency sealer-divider (LigaSure™; Covidien, Mansfield, MA, USA) and bipolar coagulation. For the last 8 years, however, an ultrasonic dissector (SonaStar® Laparoscopic Probe [MXA-L002]; Misonix, Inc., Farmingdale, NY, USA) combined with a radiofrequency sealer-divider (LigaSure™, Covidien) has routinely been used.

Definitions

Major hepatectomy was defined as the resection of > 3 of Couinaud's segments [12]. Morbidity included all postoperative complications and was graded according to Clavien–Dindo classification [13]. Complications of grade III or higher were defined as major morbidity. Cumulative postoperative morbidity was assessed using the comprehensive complication index (CCI®) [14], which measures overall morbidity on a scale from 0 (uneventful) to 100 (death). Technical complexity of LLR was defined according to the DS score [10].

Statistical analysis

All statistical analysis was performed using IBM SPSS Statistics for Windows, Version 20.0 Italian. Nonparametric analyses were used for age, body mass index, DS, intraoperative blood loss, cut surface area, transection time, CCI, and length of hospital stay, as assessed by Kolmogorov–Smirnov distribution testing ($p < 0.001$).

The differences between continuous variables were assessed with the Kruskal–Wallis test. Pairwise comparisons were performed using Dunn's (1964) procedure with a Bonferroni correction for multiple comparisons in cases

of significant differences observed among the 3 groups. Adjusted *P* values are presented. The differences between categorical variables were assessed using the Chi-square test of homogeneity (2 × c). Post hoc analysis involved pairwise comparisons using multiple Fisher's exact tests (2 × 2) with a Bonferroni correction. Statistical significance was accepted at $p < 0.016667$. DS was analyzed via CUSUM. Receiver operating characteristic curves were plotted to identify the value of cut surface area in predicting overall morbidity with a high sensitivity and specificity. The study was approved by the local ethical committee.

Results

Patient characteristics

A total of 300 LLRs were performed during the study period. Conversion to open technique was required in 13 patients (4.3%). Conversions were the result of IOUS findings in 7 cases, intraoperative bleeding in 4 cases and dense adhesions in 2 cases. 178 (59.3%) male with a median age of 67.5 (27–88) years underwent LLR. The indications for LLR included malignant tumors in 250 patients (83.4%); specifically, 143 colorectal liver metastases (57.2%), 70 hepatocellular carcinomas (28%), 21 non-colorectal liver metastases (8.4%), 11 intrahepatic cholangiocarcinomas (4.4%) and 5 gallbladder cancers (2%). Types of LLR performed are listed in Table 1. Median DS was 4 (range 1–10). 21 (7%) patients received previous live resection. 52 (17.3%) patients received multiple concurrent liver resections. Intestinal resection was associated with LLR in 23 cases (7.7%). Pedicle clamping during parenchymal liver transection was used in 138 cases (46%). Median intraoperative blood loss was 100 ± 160 mL. Overall and major morbidity rates were 15.3% and 2%, respectively. Mean CCI was 3.7 ± 10. Mortality was 0.7%. Eight patients (2.7%) required postoperative blood transfusion. Median length of hospital stay was 5 ± 3.3 days.

Stepwise difficulty comparison

CUSUM analysis of the DS (Fig. 1) identified three distinct periods with gradually increasing DS ($p < 0.001$): P1 (first 100 cases, median DS = 3), P2 (cases 101–200, median DS = 5), and P3 (cases 201–300, median DS = 6). Perioperative outcomes of the 3 periods were compared and are summarized in Table 2. No differences in sex and diagnosis were found among the three groups. P3 and P2 had a higher percentage of postero-superior segment resection (P1 11%, P2 36%, P3 46; $p < 0.001$) and associated digestive surgery (P1 9%, P2 25%, P3 25%; $p = 0.006$) than P1. P1 had the smaller number of hepatic vein exposure on the cut surface (P1 12%, P2 35%, P3 36%; $p = 0$ 0.003). Pedicle clamping was used progressively more frequently (P1 14%, P2 51%, P3 73%, $P < 0.001$). Cut surface area (P1 35 ± 23.2 cm^2, P2 42 ± 38 cm^2, P3 57 ± 40.9 cm^2, $p = 0.003$) increased significantly among the 3 groups, while the median intraoperative blood loss during transection was similar (P1 100 mL, P2 100 mL, P3 140 mL; $p = 0.115$). No patient had more than 1 L of blood loss. Postoperative outcomes of the three periods were compared and are summarized in Table 3. Two patients died postoperatively (1 due to respiratory failure complicating kidney failure and 1 due to multiple organ failure). There were no differences among the three groups in overall morbidity (P1 12%, P2 17%, P3 17%; $p = 0.526$) and major morbidity (P1 1%, P2 2%, P3 3%; $p = 0.600$). In addition, CCI was similar among the three groups (P1 2.8 ± 8.1, P2 4.4 ± 11.5, P3 4.8 ± 15.3; $p = 0.591$). The median length of hospital stay was 5 days in all the three groups.

Univariate and multivariate analyses of predictors of postoperative morbidity

Univariate analysis revealed overall morbidity to be significantly correlated with age higher than 70 years (20.3%

Table 1 Types of laparoscopic liver resection according to difficulty scale

Type of resection	Difficulty scale (DS)	Number of LLR (%)
Wedge S3, S4b	1	22 (7.3%)
Left lateral sectionectomy	2	32 (10.7%)
Wedge S2, S5, S6	3	57 (19%)
Mono (sub) segmentectomy S2-3-4b-5-6	4	54 (18%)
Left hepatectomy	5	13 (4.3%)
Wedge S4a-7-8; caudectomy	6	64 (21.3%)
Bisegmentectomy (excl Sg2-3)	7	20 (6.7%)
Segmentectomy S4a, 7–8	8	21 (7%)
Right hepatectomy, right trisectionectomy	9	16 (9%)
Mesohepatectomy, left trisectionectomy	10	1 (0.3%)

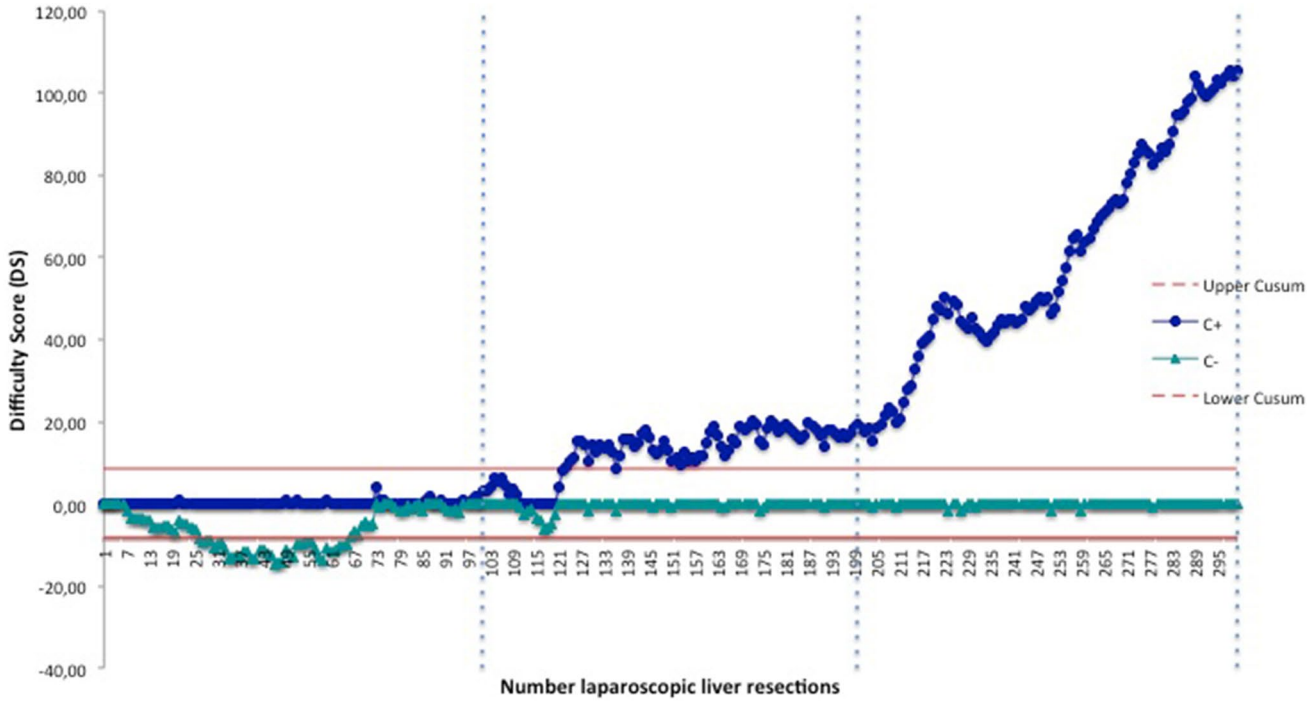

Fig. 1 CUSUM analysis of difficulty grade scale (DS) identified 3 periods of gradually increasing difficulty. P1—first 100 cases, median DS = 3, P2—cases 101–200, median DS = 5; and P3—cases 201–300, median DS = 6. *CUSUM* cumulative sum control chart, *DS* difficulty scale

vs. 11.4%, $p = 0.033$), associated digestive surgery (24.1% vs. 13.2%, $p = 0.038$) and cut surface area (71 ± 48 cm^2 vs. 40 ± 32 cm^2, $P < 0$ *0*.001). Neither the period during which LLR was performed nor DS affected postoperative course. Cut surface area (≥ 50 cm^2, $p < 0.001$, AUC 0.698) was placed into two groups according to ROC analysis. A binomial regression was run to predict overall morbidity. Age ≥ 70 years (OR 1.978, CI 95% 1.027–3.813, $p = 0.042$) and cut surface area ≥ 50 cm^2 (OR 3.138, CI 95% 1.597–6.163, $p = 0.001$) were significantly associated with an increased likelihood of postoperative morbidity.

Discussion

Intraoperative liver ultrasound is considered an indispensable tool during open liver surgery. Due to greater technical difficulties, laparoscopic ultrasound is less widespread [15] and its role during LLR is less investigated. The first International Position on Laparoscopic Liver Surgery held in Louisville [1] did not report any recommendation on intraoperative ultrasound. More recently, Morioka [2] and Southampton consensus [16] recommended the use of intraoperative ultrasound either for accuracy of clear margins and to avoid injuries of major pedicles during anatomic resection. The present study analyzed the outcomes of ultrasound-guided LLR according to hepatectomy technical complexity. In the last years, many tools to predict technical complexity of LLR were proposed but no one proved to be superior to others because all are limited by methodological flaws [17]. We chose the DS [10] for two reasons; first because it did not include radiological data such as proximity of lesion to vessels (not available in our prospective database) and second because a 10-level difficulty index increased sensitivity of the CUSUM analysis in detecting a change in technical difficulty. Using CUSUM analysis of LLRs by DS, 3 periods were identified, each including almost 100 LLRs with progressively increased value of difficulty score. The last 100 LLRs were more technically complex than those performed earlier, as shown by median DS and as evidenced by longer transection time and wider cut surface area. Despite this, intraoperative bleeding was low and postoperative outcomes good for patients treated during all 3 periods covered by the study. For example, overall morbidity was less than 17% in all 3 periods. In contrast with our data, many studies related to the pioneering phase of LLR reported improved outcomes (i.e., operative duration, conversion rate and blood loss) commensurate with increased experience [18–20]. Our data are related to the second phase of innovation of laparoscopic liver surgery i.e., exploration [2, 21], in which standardization and codification have taken place [22] and some laparoscopic procedures, such as left lateral bisegmentectomy, have become standards of care. Familiarity with the use and pitfalls of energy devices, staplers, and hemostatic strategies

Table 2 Comparison of preoperative characteristics and intraoperative data

Parameters	P1 ($n=100$) n (%)	P2 ($n=100$) n (%)	P3 ($n=100$) n (%)	p	Post hoc Adj. p
Male	56 (56)	63 (63)	59 (59)	0.600	
Age (median, range, years)	61.5 (27–86)	70.5 (31–88)	68.5 (33–85)	0.002	P1 vs. P2 $p=0.004$ P1 vs. P3 $p=0.001$
Diagnosis					
Malignant lesions	82 (82)	79 (79)	88 (88)	0.226	
Colorectal metastases	44 (44)	49 (49)	50 (50)	0.661	
Hepatocellular carcinoma	22 (22)	23 (23)	24 (24)	0.945	
Intrahepatic cholangiocarcinoma	4 (4)	5 (5)	2 (2)	0.517	
BMI	24.1 (15.3–37.2)	25.7 (17.3–37)	25.2 (19–34.8)	0.005	P1 vs. P2 $p=0.004$ P1 vs. P3 $P=0.005$
ASA 3–4	34 (34)	47 (47)	35 (35)	0.60	
Redo-resection	11 (11)	7 (7)	3 (3)	0.086	
Major hepatectomy	5 (5)	15 (15)	9 (9)	0.055	
Minor anatomic liver resection	36 (36)	50 (50)	50 (50)	0.072	
Resection of postero–superior segments[a]	11 (11)	36 (36)	46 (46)	<0.001	P1 vs. P2 $p<0.001$
Difficulty grade scale (median ± DS)	3 ± 1.4	5 ± 2.1	6 ± 2.0	<0.001	P1 vs. P2 $p<0.001$ P1 vs. P3 $P<0.001$ P2 vs. P3 $p=0.004$
Multiple liver resections	11 (11)	18 (18)	23 (23)	0.079	
Associated digestive resections	9 (9)	25 (25)	24 (24)	0.006	P1 vs P2 $p=0.003$ P1 vs P3 P = 0.004
Pedicle clamping	14 (14)	51 (51)	73 (73)	<0.001	P1 vs. P2 p < 0.001 P1 vs P3 p < 0.001 P2 vs. P3 $p=0.001$
Hepatic vein exposition on cut surface	12 (12)	35 (35)	36 (36)	0.003	P1 vs. P2 $p=0.002$ P1 vs P3 $p=0.001$
Intraoperative blood loss(cc, median, range)	100 (0-970)	100 (0-800)	140 (0-800)	0.116	
Cut surface area (cm^2, median, DS)	35 ± 23.2	42 ± 38	57 ± 40.9	<0.001	P1 vs. P2 p = 0.023 P1 vs P3 p = 0.001 P2 vs P3 p = 0.020
Transection time (minutes, median, DS)	70 ± 48.3	102 ± 50.2	99 ± 66.3	<0.001	P1 vs P2 p = 0.001 P1 vs. P3 P < 0.001

BMI body mass index, *ASA* American Society of Anesthesiologists score

[a]Segments S7, S8, S4a

Table 3 Comparison of postoperative outcomes

Parameters	P1 ($n=100$) n (%)	P2 ($n=100$) n (%)	P3 ($n=100$) n (%)	p
90-days mortality	0	0	2 (2)	0.134
Overall morbidity	12 (12)	17 (17)	17 (17)	0.526
Major morbidity (dindo 3–4)	1 (1)	2 (2)	3 (3)	0.600
CCI (mean, DS)	2.8 ± 8.1	4.4 ± 11.5	4.8 ± 15.3	0.591
Liver failure	0	2 (2)	2 (2)	0.363
Bile leakage	3 (3)	1 (1)	2 (2)	0.600
Ascites	1 (1)	4 (4)	2 (2)	0.359
Abdominal collection	0	1 (1)	1 (1)	0.604
Sepsis	1 (1)	2 (2)	3 (3)	0.600
Abdominal bleeding	0	1 (1)	0	0.367
Lung infection	3 (3)	4 (4)	3 (3)	0.856
Blood transfusion	0	3 (3)	5 (5)	0.087
Length of hospital stay (days, median, DS)	5 ± 2.3	5 ± 9.6	5 ± 4.7	0.082

CCI Comprehensive Complication Index

may partially explain the good results achieved since the beginning of our experience.

Tommasini et al. [10] used CUSUM analysis of DS to identify 3 different periods. The second period was characterized by the highest DS (5.3), which decreased to an intermediate value (4.7) in the third period. In addition, morbidity was higher, and operative duration longer, in the second period than in the other two periods. On the contrary, in our series, the highest DS occurred in P3 (6), but intraoperative and postoperative outcomes remained similar to the previous two periods.

Many reasons could justify these differences. In our center, the technical difficulty of LLR was increased in a stepwise fashion. In this way, knowledge and expertise of surgeons and surgical staff was always adequate to the difficulty to be faced. At the same time, the experience in open liver surgery and advanced laparoscopic surgery previously gained in our center allowed us to achieve good, stable results, even with more complex and non-standardized procedures such as anatomic resection of posterior segments and wedge resection of deep lesions. In particular, all liver resections, both open and laparoscopic, were performed under constant ultrasound guidance according to the 4Cs rules.

The main difficulties of laparoscopic liver surgery concern the ability to control bleeding [23, 24] and the difficult identification of the anatomic landmarks and surgical transection plane.

Intraoperative ultrasound guidance can help surgeons to deal with both these aspects.

Difficulties to reach an adequate hemostasis affect the risk of conversion [3, 25] and often discourage surgeons from performing more complex procedures. Thanks to the real-time ultrasound guidance the planes where the main vascular structures run are marked on the liver surface and major vascular injuries can be avoided. The small amount of intraoperative blood loss, the absence of major bleeding (> 1 L) and the extremely low rate of emergency conversion for bleeding characterize our series and confirm the efficacy of the technique.

Thanks to intraoperative ultrasound, a liver map that is at the base of the planned resection can be drawn. Moreover, the adequacy of the surgical plan can be checked and corrected as often as necessary. These reassurances, along with the confidence and expertise gained, allowed us to push our limits and undertake more challenging procedures.

Multivariate analysis demonstrated increasing age and cut surface area to be associated with an increased likelihood of postoperative morbidity. Studies [26–28] focusing on open liver surgery have shown a higher risk of complications in elderly patients. Adam et al. [29] confirmed the negative effect of age on postoperative outcomes in a large series of patients. In particular, the elderly are at a higher risk of non-liver-related complications, which comprise most of the comorbidities in this population. Our data are consistent with these results, and the two deaths of the third period were not related to liver complication. However, the risk in the elderly remains low, and older age is not an absolute contraindication to laparoscopic liver surgery. In fact, although surgery has in recent years become more complex, the average age of patients has increased. The second factor significantly correlated with postoperative morbidity was cut surface area. This result was expected because major hepatectomy and right segment resection are associated with larger cut surface area. These types of LLR have the highest scores for technical

complexity [10] and greater amount of liver parenchyma sacrificed.

In conclusion, the use of IOUS is indispensable for laparoscopic anatomic and non-anatomic resections. The ultrasound liver map technique allowed LLR to be performed safely. However, because the reproducibility of this technique is related to the surgeon's skills in IOUS, LLR teaching programs should include IOUS training. A solid background in open liver surgery and advanced laparoscopic surgery coupled with rigorous training in intraoperative liver ultrasound (via both open and laparoscopic approaches) can facilitate a linear increase in the complexity of LLR without compromising results.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Research involving human participants and/or animals All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Appropriate consent was obtained from all individual participant included in this study.

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