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The learning curve of laparoscopic liver resection after the Louisville statement 2008: Will it be more effective and smooth?

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Abstract

Background Laparoscopic liver resection (LLR) has been proven to be feasible and safe. However, it is a difficult and complex procedure with a steep learning curve. The aim of this study was to evaluate the learning curve of LLR at our institutions since 2008.

Methods One hundred and twenty-six consecutive LLRs were included from May 2008 to December 2014. Patient characteristics, operative data, and surgical outcomes were collected prospectively and analyzed.

Results The median tumor size was 25 mm (range 5–90 mm), and 96 % of the resected tumors were malignant. 41.3 % (52/126) of patients had pathologically proven liver cirrhosis. The median operation time was 216 min (range 40–602 min) with a median blood loss of 100 ml (range 20–2300 ml). The median length of hospital stay was 4 days (range 2–10 days). Six major postoperative complications occurred in this series, and there was no 90-day postoperative mortality. Regarding the incidence of major operative events including operation time longer than 300 min, perioperative blood loss above 500 ml, and major postoperative complications, the learning curve [as evaluated by the cumulative sum (CUSUM) technique] showed its first reverse after 22 cases. The indication of laparoscopic resection in this series extended after 60 cases to include tumors located in difficult locations (segments 4a, 7, 8) and major hepatectomy. CUSUM showed that the incidence of major operative events proceeded to increase again, and the second reverse was noted after an additional 40 cases of experience. Location of the tumor in a difficult area emerged as a significant predictor of major operative events.

Conclusions In carefully selected patients, CUSUM analysis showed 22 cases were needed to overcome the learning curve for minor LLR.

Keywords Laparoscopic · Liver resection · Hepatectomy · Hepatocellular carcinoma · Learning curve

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Since the first laparoscopic partial hepatectomy reported by Gagner et al. [1], an increasing number of publications have demonstrated the feasibility and safety of laparoscopic liver resection (LLR) [2–9]. However, LLR is still a difficult and complex procedure. It requires substantial training both in hepatobiliary surgery and in advanced laparoscopic technics. The learning curve of LLR is known to be steep but is not well evaluated. Cherqui et al. [10] analyzed 174 laparoscopic liver resections during a 12-year period and determined that a learning period of 60 cases was required for LLR by comparing the incidence of conversion to open in three different time frames. That series began in the initial stage of development of LLR in 1996. In the past two decades, the surgical techniques and energy devices utilized in LLR have shown significant improvement. Laparoscopic resection for liver tumors has become a reproducible and feasible procedure.

The first International Consensus Conference on laparoscopic liver surgery was held in Louisville [11]. It was concluded that LLR was feasible for tumors <5 cm and located in the peripheral liver. Laparoscopic lateral sectionectomy should be considered as a standard practice. Since then, the number of LLR performed worldwide has increased exponentially. LLR has now entered the exploration phase of surgical innovation, particularly at highly specialized centers. With adequate training in the surgical techniques and utilization of the new generation of energy devices, the learning of LLR should be more effective and smooth.

The rate of conversion to open surgery was typically used as an indicator of the quality of surgery and to evaluate the learning curve of laparoscopic operations [10, 12]. With careful patient selection and improvement of surgical techniques, the conversion rate of LLR gradually decreased [6, 7, 13]. On the basis of analysis of the perioperative outcomes at different time frames of Cherqui's group, they also demonstrated less blood loss, operative time, need for hepatic pedicle clamping, and shorter postoperative hospital stay in more recent cases. Indicators such as operation time, blood loss, and postoperative complication should be included for evaluating the learning curve of laparoscopic operation. LLR should be performed within reasonable time, with acceptable blood loss and smooth recovery without major postoperative complications. Operation time and blood loss were difficult to compare between the studies given the heterogeneous types of resections reported. Nguyen et al. [6] reviewed six studies, each with more than 100 patients, and found the average operative time ranged from 99 to 331 min and the blood loss ranged from 50 to 659 ml. In this study, operation time of more than 300 min, perioperative blood loss of more than 500 ml, or the presence of major postoperative complications were recorded as "major operative event" and indicated the inexperience of the surgeon.

The cumulative sum (CUSUM) technique was adopted to analyze the learning curve of surgical procedures in 1974 [14, 15]. However, the learning curve of LLR has not evaluated by this metric. The aim of this study was to evaluate the learning curve of LLR by analyzing the 6 years' single institutional experience of 126 consecutive operations. The surgical outcomes are assessed to evaluate the oncological feasibility, and the learning curve of LLR was analyzed utilizing the CUSUM technique.

Patient and inclusion criteria

Laparoscopic liver resection has been adopted in Koo Foundation Sun Yat-Sen Cancer Center, Taipei, Taiwan, since 2008. All patients eligible for liver resection were carefully selected for laparoscopic approach in the weekly multidisciplinary team meeting. The preoperative diagnosis of liver tumors was based on fine-needle biopsies or by clinical diagnostic criteria such as elevated tumor markers, diagnosis of chronic liver disease or liver cirrhosis, and imaging features suggestive of HCC or liver metastases from computed tomography scan (CT), magnetic resonance imaging (MRI), or angiography.

The indication and extent of LLR did not vary from the open group. The inclusion criteria of LLR were as follows (1) solitary tumor <5 cm in size. (2) Tumor located in peripheral liver (Couinaud segments 2, 3, 4b, 5, 6 or superficial part of other segments. (3) After the accumulation of 60 cases of experience, major hepatectomy and resection of tumors located in the superior-central area (segments 4a, 7, 8) were included for laparoscopic approach. Patient characteristics and operative results were prospectively collected and analyzed.

Complete blood counts and biochemistry data were routinely checked preoperatively. Patients with evident thrombocytopenia (platelet $< 50 \times 10^3$/uL) were considered as a contraindication for LLR because this typically coexists with liver cirrhosis and raises the risk of perioperative bleeding. For mild thrombocytopenia (platelet 50–100 $\times$ 10^3/uL), platelet transfusion was given preoperatively. CT, MRI, or angiography were used for diagnosis, evaluation of tumor location, and vascular anatomy. Tumor adjacent to major vessels was considered a contraindication for LLR. The extent of resection was dependent on tumor location and the patient's liver function. Most resections were intended to be anatomic and curative in order to resect the tumor's portal territory. However, in a few patients with superficial tumors located in a peripheral segment or with suboptimal liver function, subsegmenetctomies including the tumor and an adequate 1- to 2-cm margin were performed.

Definition

According to the conclusion of the 2008 Louisville statement, tumors located in the peripheral liver (segments 2, 3, 4b, 5, 6) were included in the early stage (before 60 cases) of this series and regarded as "easy location." Tumors located in the superior-central liver (segments 4a, 7, 8) were defined as "difficult location." Resection of tumors located in the peripheral liver and removal of less than two segments were recorded as "minor hepatectomy," whereas "major hepatectomy" was defined as right or left hemihepatectomy, central bisegmentectomy, or resection of more than three adjacent segments. LLR for tumors in difficult locations and major hepatectomy was defined as "advanced LLR." The surgical complications were documented according to the Clavien–Dindo classification [16]. Complications greater than grade III were recorded as "major complications."

After surgery, patients were seen in follow-up every 3 months at the outpatient department of the same institution. Liver function tests, tumor markers, and radiological study including ultrasound, CT, or MRI were performed.

Surgical procedures

For the resection of tumors located in the left or middle part of the liver, patients were placed in a supine position with the legs apart. The operating surgeon stood between the patient's legs, and assistants stood on two sides. For the resection of tumors located in the right posterior part of the liver, patients were placed in a left semi-decubitus position with the right arm elevated. The operating surgeon stood behind the patient with assistants standing on the opposite side. When the surgical table tilted to the left during the operation, the patients became poised in the left decubitus position. This position is helpful for the mobilization and exposure of the right posterior liver. Pneumoperitoneum was created using carbon dioxide, and the intraperitoneal pressure was maintained at 10–12 mmHg. The placement of trocars was based on tumor location. Five trocars were usually used: one 12-mm trocar around the umbilicus for the optic laparoscope, another 12-mm trocar for the application of surgical clip, ultrasound probe and linear stapler, and three additional 5-mm trocars for assistants' grasping or suction–irrigation. Intraoperative flexible laparoscopic ultrasound (5–10 MHz, ALOKA, Japan) was routinely used to identify the tumor and clarify its associations with blood vessels. Full mobilization of the right liver was crucial for tumors located in right posterior segments. After full mobilization of the right liver and incised falciform ligament, tilting the surgical table toward the left creates a "drop down" of the liver toward the left abdomen, creating enough space around the right posterior liver for surgery. The hepatoduodenal ligament was identified and encircled with a tape to prepare for portal triad clamping (Pringle's maneuver). Pringle's maneuver was not routinely used during liver parenchymal transection in this study series to minimize hepatic ischemic injury. If encountering bleeding that was not easy to control, intermittent portal triad clamping was performed following the rule of 15-min clamp and 5-min release to allow for the identification and control of the bleeding source. Once the bleeding was controlled, the tape around the hepatic hilum was released.

Hepatic parenchymal transection was mainly performed using ultrasonic shears or bipolar clamp. Usually, only small vessels and biliary branches are found in the superficial layer of hepatic parenchyma. Therefore, in this area, the liver parenchymal transection and sealing of vessels can be easily performed using energy devices. For vessels >3 mm in diameter, clips or bipolar electrocautery forceps were used for more secure control. When managing segmental Glissonian pedicle or major hepatic veins, a linear stapler was usually used.

After resection was completed, the intraperitoneal pressure was decreased to 4–6 mmHg in order to check for possible bleeding and bile leakage. One Jackson–Pratt drain was usually placed near the liver cut surface. The specimen was placed in a plastic tissue bag and removed via an extended umbilical incision or Pfannenstiel incision without fragmentation.

Statistical analysis

Statistical analyses were performed with the SAS software, version 9.1.3 (SAS Institute Inc., Cary, NC, USA). Continuous variables were compared between groups by Mann–Whitney *U* test, and categorical variables were compared by the Chi-square test. The p value of <0.05 was considered statistically significant in all tests.

The learning curve analysis was based on the expected probability of major operative events. Univariate analysis of the predictive factors of major operative event presence was performed. Comparison of the incidence of major operative events after adjusted potential confounders was performed by multivariate logistic regression analysis. The cumulative sum (CUSUM) technique [17] showed a presentation of the level of performance with departure or compliance from a defined level. The slope of CUSUM curve goes up when a laparoscopic liver resection was performed in a premature way with high expected probability of major operative events, and goes down when the surgery was performed successfully with low probability of major operative events.

Results

From May 2008 to December 2014, 126 consecutive LLRs were included in this study series. 96 % (121/126) of patients underwent surgery because of malignant disease including hepatocellular carcinoma (HCC), liver metastases, and cholangiocarcinoma (CCC). Only five tumors were benign (three focal nodular hyperplasia, one dysplastic nodule, and one pseudocyst). Patient characteristics are summarized and divided into four stages according to the results of CUSUM (Table 1). Regarding the comorbidity of patients especially liver cirrhosis and body mass index (BMI), there is no difference among the four groups. Seventy-two patients (57.1 %) had Hepatitis B, and 18 patients (14.3 %) had Hepatitis C. Defined by the Metavir fibrosis grade, 41.3 % of all 126 patients were proven to have cirrhotic liver and 56 % (52/93) of HCC/CCC

Table 1 Patient characteristics

Variables	Total	Stage 1 1st–22nd	Stage 2 23rd–60th	Stage 3 61st–100th	Stage 4 After 101st
Gender (M/F)	88/38	15/7	25/13	30/10	18/8
Age (years)	58 (26–88)	61	59	56	56.5
BMI (kg/m^2)	24 (17–32)	24	23.5	24	24
Liver cirrhosis	52 (41.3 %)	14	14	14	10
Tumor location					
Segments 2–3	56	8	18	20	10
Segment 4	13	1	4	5	3
Segment 5	22	3	10	5	4
Segment 6	30	9	8	6	7
Segment 7	10	1	2	4	3
Segment 8	7	0	1	3	3

The patients were divided into four stages according to the results of CUSUM

BMI body mass index, liver cirrhosis: pathology proved as Metavir F4; tumor location was recorded according to Couinaud segments

Table 2 Tumor pathology characteristics

Variables	Patients
Diagnosis [*n* (%)]	
HCC	87 (69.0)
CRM	14 (11.1)
Mets	14 (11.1)
CCC	6 (4.8)
Benign	5 (4.0)
Maximum diameter of tumor (mm)	25 (5–90)
Surgical margins (mm)	5 (1–40)

HCC hepatocellular carcinoma, *CRM* metastases from colorectal cancer, *Mets* metastases from other primary, *CCC* cholangiocarcinoma

patients. All resection margins were proved to be negative for malignancy by a pathologist. The tumor pathology characteristics are summarized in Table 2. The median operation time was 216 min (range 40–602), and median blood loss was 100 ml (range 20–2300). Blood transfusions with packed red blood cells were required for nine patients, and the median amount of blood transfusion was two units. Conversion to open surgery was required in three patients (conversion rate, 2.4 %) because of bleeding, inaccessible tumor location, or poor progress of the operation.

The postoperative wound pain was easily managed by oral or intravenous analgesics without the use of epidural infusion or patient-controlled analgesic devices. Six major postoperative complications occurred in this study series: intra-abdominal abscess in two, pneumonia in one, biliary fistula in one, postoperative bleeding in one, and transient cerebral ischemic stroke in one patient. All other patients recovered without complication, and the median hospital stay was 4 days (range 2–10). There was no 90-day postoperative mortality. The major morbidity and mortality rates were 4.8 and 0 %, respectively.

The event of "blood loss $>$ 500 ml" occurred in 18 (14.3 %) patients in this study series (Fig. 1A), "operation time $>$ 300 min" occurred in 28 (22 %) patients (Fig. 1B), and "major operative complication" occurred in six (4.8 %) patients (Fig. 1C). The operation time longer than 300 min, perioperative blood loss more than 500 ml, or the presence of major postoperative complication were recorded as "major operative event" and indicated the inexperience of the surgeon. There were 37 (29.4 %) events recorded in this series (Fig. 1D). The CUSUM analysis demonstrated that the probability of the occurrence of major operative events was increasing in the earlier period of this consecutive series prior to the 22nd patient and then decreased gradually (Fig. 2). The slope of CUSUM curve reversed after the 22nd consecutive patient. Regarding reasonable operation time, with acceptable perioperative blood loss and smooth postoperative recovery without major complications, the present study indicates a learning period of at least 22 cases was need for minor LLR.

We still respect and follow the conclusion of the study published by Cherqui et al. [10] which suggested 60 cases were needed to overcome the learning curve of LLR. The indication of LLR was not extended to include advanced LLR until the surgeon had accumulated 60 cases of experience. The CUSUM curve showed the incidence of major operative events increased again after the 61st cases and then decreased after the 100th cases (Fig. 2).

The operation characteristics were summarized and divided into four stages according to the results of CUSUM (Table 3). Major hepatectomies were performed more frequently in stage 3 and stage 4 (later stage, after 60th cases) ($p = 0.039$). The operation time was significantly

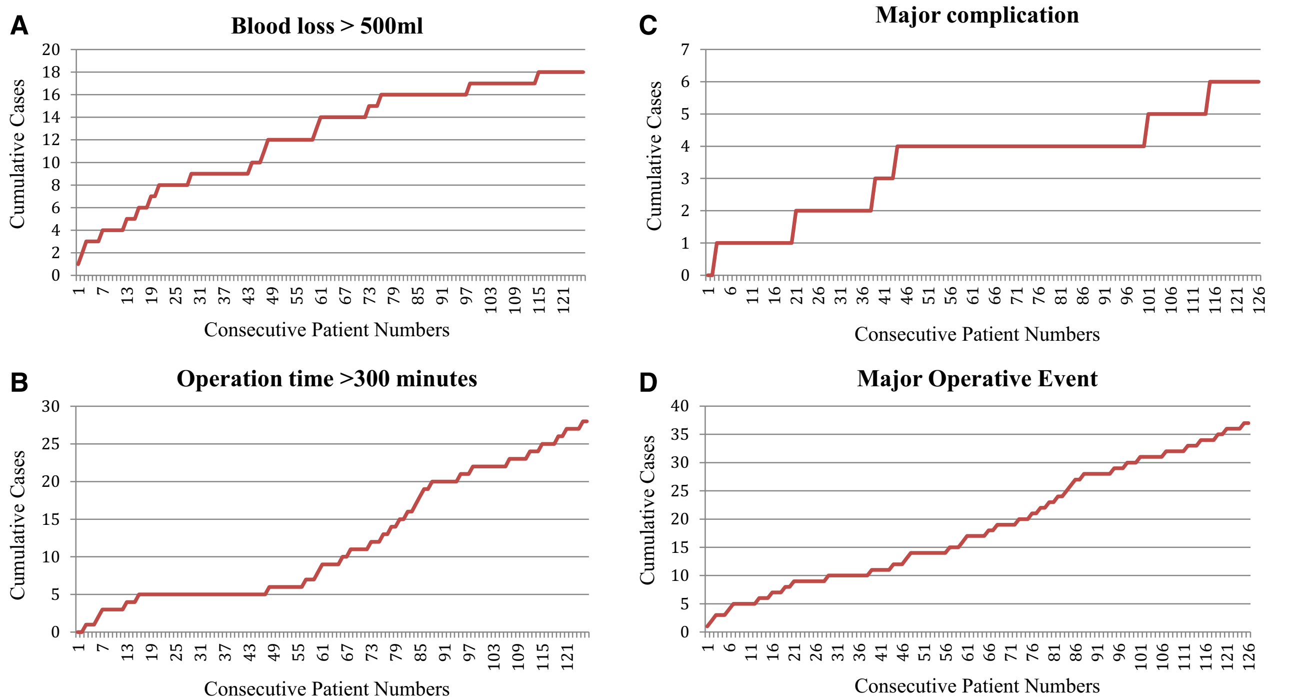

Fig. 1 Cumulative cases of major operative events: (**A**) blood loss > 500 ml; (**B**) operative time > 300 min; (**C**) major complication; (**D**) major operative event

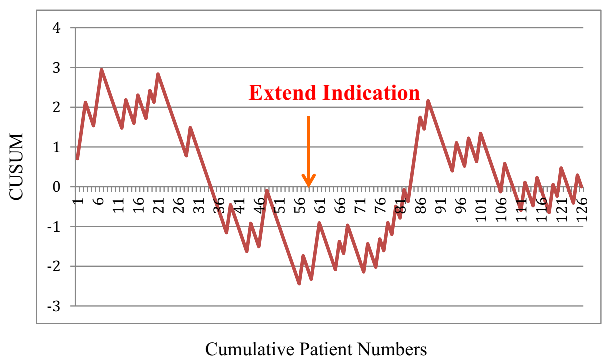

Fig. 2 CUSUM curve regarding the major operative events of the 126 consecutive laparoscopic liver resections. The CUSUM analysis was performed with following formula $S_n = \Sigma_{i=1}^{n}(X_i - p_0)$. p_0 indicated acceptable incidence of major operative events (p_0 was set as 0.2 in this study, reviewed and adapted from other published series). X_i indicated the outcome of surgery: $X_i = 1$ if major operative events occurred and $X_i = 0$ if did not

shorter in stage 2 compared to stage 1 (194 vs. 251 min, $p = 0.028$). The incidence of operation time longer than 300 min was significantly higher in the later stage ($p = 0.022$); however, the average blood loss and the incidence of blood loss >500 ml were significantly lower.

Univariate analysis (Table 4) for predictive factors of major operative events showed that tumors in difficult locations were associated with a significantly higher risk for the presence of major operative events ($p < 0.0001$, OR 0.1, 95 % CI 0.04–0.31). After adjusting for potentially confounding factors such as gender, age, liver cirrhosis, tumor size, and BMI, multivariate analysis (Table 5) showed that significant factors that decrease the incidence of major operative event were operation performed in the 23rd–60th patients ($p = 0.0469$, adjusted OR 0.271, 95 % CI 0.075–0.982) and tumors located in easy location ($p < 0.0001$, adjusted OR 0.097, 95 % CI 0.033–0.283) (Table 5).

Discussion

Since the first International Consensus Conference on laparoscopic liver surgery held in Louisville in 2008 [11], the number of LLR performed worldwide has increased exponentially. The so-called Louisville statement suggested that LLR is indicated for small tumors located in the peripheral liver. Surgeons embarking on LLR should begin with these minor resections. Laparoscopic major hepatectomy is more technically demanding, and it was recommended that it should be reserved for expert surgeons. Continued caution was recommended for the introduction of LLR. One of the conclusions from the second International Consensus Conference for laparoscopic liver resections [18] was that the need for a formal structure of education for those who are interested in performing LLR because of the steep learning curve.

Table 3 Operation characteristics

Variables	Stage 1	Stage 2	Stage 3	Stage 4	p value		
					Stage		
	1st–22nd	23rd–60th	61st–100th	After 101st	1 versus 2	3 versus 4	1 + 2 versus 3 + 4
Operation					0.0423	0.4605	0.4809
<1 segment (wedge resection)	6	10	8	4			
1 Segment	8	7	7	9			
2 Segment	0	8	6	2			
Left lateral sectionectomy	6	12	13	7			
Right posterior sectionectomy	2	0	1	0			
Central bisegmentectomy	0	0	0	1			
Left hemi-hepatectomy	0	0	1	2			
Right hemi-hepatectomy	0	0	2	1			
Type of resection [n (%)]					0.4429	0.3094	0.0399
Minor hepatectomy	22 (100)	37 (97.4)	37 (92.5)	22 (84.6)			
Major hepatectomy	0	1 (2.6)	3 (7.5)	4 (15.4)			
Location of tumor							
Easy location	19 (86.4)	33 (86.8)	32 (80)	19 (73.1)	0.9581	0.512	0.1728
Difficult location	3 (13.6)	5 (13.2)	8 (20)	7 (26.9)			
Operation time (minutes)	251	194	266	227	0.0284	0.1634	0.0541
>300 min [n (%)]	5 (22.7)	3 (7.9)	14 (35.0)	6 (23.1)	0.1034	0.3031	0.0221
Perioperative blood loss (ml)	512	273	239	145	0.0665	0.2064	0.0344
>500 ml [n (%)]	8 (36.4)	5 (13.2)	4 (10.0)	1 (3.9)	0.0355	0.3559	0.024
Major complications	2	2	0	2	0.3854	0.4315	0.5375
Tumor size (mm)	29.5	26.5	27.9	31.2	0.9041	0.5536	0.5679
Margin (mm)	7.5	7.8	9.1	7.7	0.5656	0.8493	0.0227
Major complication [n (%)]	2 (9.1)	2 (5.3)	0	2 (7.7)	0.5668	0.0749	0.3384
Hospital stay (days)	4.3	4.1	4.8	4.8	0.9581	0.512	0.1728

Operation was recorded according to Brisbane 2000 Terminology [31]; minor hepatectomy: wedge resection, ≤2 segments, lateral sectionectomy; major hepatectomy: central bisegmentectomy, right or left hemi-hepatectomy, >3 segments; easy location: segments 2, 3, 4b, 5, 6; difficult location: segments 4a, 7, 8; major complications: greater than Clavien–Dindo grade 3

Recent systematic reviews have indicated that LLR is associated with less blood loss, lower narcotic dose requirements, and shorter lengths of hospital stay, with no difference in the complication rates or oncological outcomes when compared to open hepatectomy [6, 19–23]. However, the potential benefits of LLR does not indicate a need to resect all liver tumors, especially small and asymptomatic benign tumors or simply for tissue diagnosis. In the present study, 96 % of patients underwent LLR because of malignant tumors.

In the study published by Cherqui et al. [10], they used conversion rate as the indicator to analyze the learning curve and suggested a learning period of 60 cases was required for LLR. However, with the improvement of LLR, the conversion rate has been decreasing. In the present series, only three patients needed conversion to open surgery. In this study, the conversion rate was too low to be an ideal indicator for evaluating the learning process of LLR. The majority of other studies arbitrarily split data into chronologic groups and perform simple statistics. Lin et al. [24] reviewed four groups each compared laparoscopic major hepatectomy outcomes for the early and later periods of their series which showed less operation time, less blood loss and shorter length of stay in the later period. A multicenter study including 210 laparoscopic major hepatectomies from six centers published by Dagher et al. [25] showed favorable surgical outcomes after the initial 15 cases. Pearce et al. [26] demonstrated a significantly lower conversion rate for laparoscopic right hepatectomy after 17 cases. A successful LLR should be completed within reasonable time, without too much blood loss and without major postoperative complications. In this study, the learning curve was evaluated using the CUSUM technique regarding operation time, perioperative blood loss, and complication rate.

The number of LLR performed worldwide after the Louisville Consensus Conference in 2008 has been exponentially increasing. By adopting surgical skills developed by expert surgeons and utilizing modern surgical devices,

Table 4 Univariate analysis for predictive factors of major operative events (blood loss > 500 ml, operation time > 5 h, presence of major complication)

Parameter	Event/number	%	*p* value	OR	95 % CI
Gender					
Male	25/88	28.4		1.0	0.5–2.7
Female	12/38	31.6	0.7200	1.2	
Age (year)					
<60	20/71	28.2		1.0	
≥60	17/55	30.9	0.7377	1.1	0.5–2.5
Cirrhosis					
No	22/74	29.7	0.9148	1.04	0.5–2.3
Yes	15/52	28.9		1.0	
Tumor size (cm)					
<3 cm	25/88	28.4		1.0	
≥3 cm	12/38	31.6	0.7200	1.2	0.5–2.7
BMI (kg/m^2)					
<25	22/82	26.8		1.0	
≥25	15/44	34.1	0.3945	1.4	0.6–3.1
Type of resection					
Minor	29/118	24.6			
Major	8/8	100			
Location of tumor					
Easy location	21/103	20.4		1.0	
Difficult location	16/23	69.6	<0.0001	8.9	3.3–24.5
Earlier or later period					
1st–22nd	9/22	40.9		1.0	
23rd–60th	7/38	18.4	0.063	0.3	0.1–1.1
61st–100th	14/40	35.0	0.6452	0.8	0.3–2.3
After 101st	7/26	28.9	0.3084	0.5	0.2–1.8

BMI body mass index; minor: wedge resection, lateral sectionectomy, ≤2 segments; major: central bisegmentectomy, right or left hemi-hepatectomy, >3 segments; easy location: segments 2, 3, 4b, 5, 6; difficult location: segments 4a, 7, 8

OR odds ratio, *CI* confidence interval

Table 5 Multivariate analysis for predictors of major events after adjusted for potential confounders

Parameter	Event/number	%	*p* value	OR adjusted*	95 % CI
Earlier or later period					
1st–22nd	9/22	40.9		1.0	
23rd–60th	7/38	18.4	*0.0469*	0.271	0.075–0.982
61st–100th	14/40	35.0	*0.4343*	0.628	0.2–2.0
After 101st	7/26	26.9	*0.1*	0.311	0.078–1.25
Location of tumor					
Easy	21/103	20.4	*<0.0001*	0.097	0.033–0.283
Difficult	16/23	69.6		1.0	

* By gender, age, cirrhosis, tumor size, body mass index (BMI)

Minor: wedge resection, lateral sectionectomy, ≤2 segments; major: central bisegmentectomy, right or left hemi-hepatectomy, >3 segments; easy location: segments 2, 3, 4b, 5, 6; difficult location: segments 4a, 7, 8

OR odds ratio, *CI* confidence interval

learning LLR should be more efficient and smooth. Furthermore, one of the beneficial characters of laparoscopic surgery is that the operation is video recorded. Surgeons who would like to learn laparoscopic surgery can easily access videos of procedures presented on the Web sites and conferences instead of oversea travel and observation in the operating room. By following standardized surgical procedures, using advanced instruments, and undergoing training program available in recent years, it was expected that the learning period of LLR could be decreased. In the present series starting from 2008, we proposed a learning period of 22 cases for minor LLR which is substantially shorter than previous reported.

An additional 40 cases of experience learning was observed in the present series after extending the indication of LLR for resection of tumors located in superior-central segments and major hepatectomy, however, not exclusive for that. It should be noted that only 33 % of operations in the later period (after 60 cases) were advanced LLR including seven major hepatectomies. This is insufficient to draw strong conclusions regarding the learning curve for advanced LLR.

The advanced LLR was performed more frequently after extending the indication of LLR in the later period (after 60 cases) of this series. Laparoscopic resections for tumors located in superior-central segments and major hepatectomy were more difficult and time-consuming than minor resections. In the present study, a higher incidence of operation time longer than 300 min was noted in these cases, whereas the average blood loss and the incidence of exceeding 500 ml were lower in the later period. Bleeding control during hepatic parenchymal transection was crucial in learning LLR. With adequate learning and the accumulation of experience, even longer operation time was required to perform advanced LLR, although the blood loss was lower in the later period.

The indication and patient selection were crucial factors for a successful LLR. Ban et al. [27] proposed a new scoring system to predict the difficulty of a LLR with the extent of liver resection, tumor location, tumor size, liver function, and tumor proximity to major vessels. In this study, the location of tumor in difficult area (segments 4a, 7, 8) is a significant predictor for the presence of major operative events by univariate and multivariate analyses. Although in experienced centers these lesions are increasingly managed laparoscopically [28–30], it is still a difficult and complex procedure that requires a longer training period. Surgeons embarking on LLR should begin with minor resections for tumors located in peripheral liver.

In conclusion, with careful selection of patients and sufficient training, 22 cases were needed to overcome the learning curve for minor LLR. More cases are needed to evaluate the learning period of advanced LLR.

Compliance with ethical standards

Disclosures Drs. Chung-Wei Lin, Tzu-Jung Tsai, Tsung-Yen Cheng, Hung-Kuang Wei, Chen-Fang Hung, Yin-Yin Chen, and Chii-Ming Chen have no conflicts of interest or financial ties to disclose.

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