SCIENTIFIC PAPER JSLS

Laparoscopic Liver Resection for Tumors in the Left Lateral Liver Section

Brian K. P. Goh, MBBS, MMed, MSc, Chung-Yip Chan, MBBS, MMed, MD, Ser-Yee Lee, MBBS, MMed, MSc, Victor T. W. Lee, MBBS, MMed, MSc, Peng-Chung Cheow, MBBS, Pierce K. H. Chow, MBBS, PhD, London L. P. J. Ooi, MBBS, MD, Alexander Y. F. Chung, MBBS

ABSTRACT

Background: The laparoscopic approach is increasingly adopted for liver resections today especially for lesions located in the left lateral liver section. This study was conducted to determine the impact of the introduction of laparoscopic liver resection (LLR) as a surgical option for suspected small- to medium-sized (<8 cm) tumors located in the left lateral section (LLS).

Methods: This is a retrospective review of 156 consecutive patients who underwent LLR or open liver resection (OLR) of tumors located in the LLS. The study was divided into 2 consecutive periods (period 1, January 2003 through September 2006, and period 2, October 2006 through April 2014); LLR was available as a surgical option only in the latter period. Comparisons made were LLR versus OLR, LLR versus OLR (in period 2 only), and resections performed in period 1 versus period 2.

Results: Forty-two patients underwent LLR with 4 conversions. LLR was significantly associated with a longer median operative time [167.5 minutes (range, 60–525) vs 105 minutes (range, 40–235); $P < .001$], decreased need for the Pringle maneuver [n = 1 (2%) vs 22 (19%); $P = .008$], and shorter postoperative stay [n = 4 (range, 1–10) days vs 5 days (range, 2–47); $P < .001$] compared with open resection. Comparison of the 42 patients who underwent LLR with the 64 contemporaneous patients who underwent OLR demonstrated similar outcomes. Again, LLR was associated with a significantly longer operation, decreased need for the Pringle maneuver, and shorter hospital stay.

Conclusion: LLR can be safely adopted to treat lesions in the LLS. The procedure is associated with a shorter postoperative stay and a decreased need for the Pringle maneuver, but longer operative time compared with that required for OLR.

Key Words: Laparoscopic hepatectomy, Laparoscopic liver resection, Left lateral sectionectomy, Left lateral segmentectomy, Outcome.

INTRODUCTION

Laparoscopy has become the approach of choice for many abdominal operations, such as cholecystectomy,[1] appendicectomy,[2] adrenalectomy,[3] and colectomy.[4] However, although laparoscopic liver resection (LLR) was first reported in 1992,[5] its widespread adoption has been hindered by the technical difficulty of the procedure, increased bleeding risk, and concerns about adequate oncologic margins.[6]

The first series of LLR was reported by Cherqui et al.[7] in 2000, and since then, an increasing number of investigators have demonstrated the feasibility and safety of the approach.[8,9] In 2008, a panel of international experts concluded that LLR is safe and effective in the hands of well-trained surgeons who are proficient in performing both hepatic and laparoscopic surgery.[9] These international experts further proposed that the laparoscopic approach be the standard one used when performing resections of lesions located in the left lateral section (LLS; segments II and III) of the liver.[9] Others have further proposed the use of the minimally invasive left lateral sectionectomy for live liver donation for transplantation.[10] However, it is important to note that these recommendations were made based on the results of several relatively small retrospective case series[10–12] in expert centers, with a high possibility of selection and publication bias.[9]

One of the major concerns about LLR is its reproducibility, because of the relatively long learning curve needed to achieve proficiency (reported to be ~60 cases by early adopters of the procedure during the pioneering phase).[6] During the learning phase, increased conversion rates, especially from bleeding could negate most of the benefits of laparoscopy and could even result in poorer perioper-

Department of Hepatopancreatobiliary and Transplantation Surgery, Singapore General Hospital, Singapore (all authors).

Duke-NUS Graduate Medical School, Durham, North Carolina, USA (Drs Goh, Chow, and Ooi).

Presented as an oral presentation in part at the 11th E-AHPBA Congress, Manchester

Address correspondence to: Brian K. P. Goh, MBBS, MMed, MSc, FRCSEd, Department of HPB and Transplant Surgery, Singapore General Hospital, Level 5, 20 College Road, Academia, Singapore 169856, E-mail: bsgkp@hotmail.com

DOI: 10.4293/JSLS.2015.00112

ative outcomes.[13,14] Further concerns raised include the possibility of compromised oncologic margins.[15] However, with the rapid advancements in laparoscopic equipment and standardization of surgical technique; many investigators have subsequently demonstrated that the learning curve can be shortened.[16,17] Nonetheless, a recent study reported that 43 cases were necessary to master LLR of the LLS.[16] Hence, at present; it remains debatable whether the adoption of LLR and its widespread application is safe, especially during the initial learning phase.

The initial impact of adopting LLR compared to the open approach has not been widely reported in the literature. In this study, we sought to determine the feasibility, safety, and impact of the introduction of LLR as a surgical option in a specific group of patients with tumors located in the LLS of the liver.

METHODS

All patients who underwent open or LLR of segments II, III, or both, from January 2003 through April 2014, were identified from a prospective surgical database. This study was approved by our center's Institutional Review Board.

All data were collected retrospectively from patients' clinical, radiology, and pathology records. Clinical data were collected from a prospective clinical database (Sunrise Clinical Manager, ver. 5.8; Eclipsys Corp., Atlanta, Georgia, USA) and patients' clinical charts. Surgical data were obtained from another prospective database (OTM 10; IBM, Armonk, New York, USA). For patients in the laparoscopic and open cohorts to be comparable, those with tumor size ≥8 cm or who had undergone emergency surgery, a previous liver resection, concomitant resection of other liver segments, or concomitant resection of extrahepatic organs were excluded (with the exception of cholecystectomies). One hundred fifty-six consecutive patients who met these criteria were identified.

To determine the impact of the introduction of LLR on our surgical practice, we divided the study into 2 periods: period 1 (January 2003 through September 2006), which was the period before the first LLR was performed for segment II/III at our institution, and period 2 (October 2006 through April 2014), after the introduction of LLR, when the laparoscopic approach became available as a surgical option. LLR was adopted at our institution in 2006 because of the increase in data in the literature that supported the feasibility and safety of the minimally invasive approach.[7,11,12] The type of surgical approach that we used after 2006 depended on various factors, including tumor characteristics, such as size and site, individual surgeon preference, and the individual patient's decision after a thorough discussion of the benefits and limitations of the laparoscopic versus open approach.

Relevant perioperative outcomes including operative time, estimated blood loss, blood transfusion, postoperative morbidity, and hospital length of stay were recorded. The comparisons were LLR versus OLR for the entire patient cohort, LLR versus OLR in period 2 (contemporaneous cohort), and operations in period 1 versus period 2.

In this study, various approaches to LLR were adopted, including the conventional totally laparoscopic multiport approach, hand-assisted laparoscopy, robot-assisted laparoscopy, and single-incision laparoscopy. The patient was placed supine, with or without the legs apart. The operating surgeon stood either between the patient's legs or on the right side. The liver parenchyma division was performed with various devices, including the Harmonic Scalpel (Ethicon Endosurgery, Cincinnati, Ohio, USA), Enseal (Ethicon Endosurgery), Ligasure (Covidien, Boulder, Colorado, USA), Thunderbeat (Olympus, Tokyo, Japan), or Cavitron Ultrasonic Surgical Aspirator (Valleylab, Boulder, Colorado, USA) depending on the individual surgeon's experience or preference. Large pedicles were stapled or clipped.

Statistical analyses were performed with the computer program Statistical Package for Social Sciences for Windows, version 21.0 (SPSS Inc, Chicago, Illinois, USA). The Mann-Whitney U test, χ^2 test, and Fisher's exact test were used to perform univariate analyses, as appropriate. All tests were 2 sided; $P < .05$ was considered statistically significant.

RESULTS

During the study period, 156 consecutive patients who met our study criteria underwent liver resection for tumors located in the LLS. There were 95 males (61%), with a median age of 61 years (range, 18–86). The median tumor size was 27 mm (range, 0–75). There were 42 (26.9%) LLRs, of which 4 (9.5%) required conversion to open. Of the 42 LLRs, 38 were conventional multiport, 1 was hand-assisted, 2 were robot-assisted, and 1 was single-incision.

The median operative time was 115 minutes (range, 40–525). One hundred resections involved 2 segments, and there were 79 anatomic resections. Twenty-five patients (16%) experienced postoperative morbidity, and there were no 90-day or in-hospital mortalities. Pathology of surgical specimens revealed 105 (67%) malignant neoplasms, including 67 hepatocellular carcinomas, 21 colorectal liver metastases, 6 intrahepatic cholangiocarcino-

Table 1.
Baseline Demographic and Perioperative Patient Data

	Laparoscopic (n = 42)	Open (n = 114)	Open period 2 (n = 64)	*P*	*P* [a]
Gender, male	25 (60)	70 (61)	37 (58)	.831	.861
Median age (range), years	59 (38–85)	62 (18–86)	63 (30–82)	.191	.055
Previous abdominal surgery	13 (31)	40 (35)	26 (41)	.629	.312
ASA score				.070	.055
1	6 (14)	16 (14)	8 (12.5)		
2	34 (81)	72 (63)	42 (66)		
3	2 (5)	24 (21)	14 (22)		
4	0	2 (2)	0		
Pathology				.100	.081
Benign	18 (43)	33 (29)	17 (27)		
Malignant	24 (57)	81 (71)	47 (73)		
Median tumor size, mm (range)	24.5 (8–70)	30 (0–75)	27 (0–70)	.155	.273
Concomitant surgery	10 (24)	14 (12)	7 (11)	.077	.077
Anatomic resection	19 (45)	60 (53)	32 (50)	.413	.631
Nonanatomic resection	25 (55)	54 (47)	32 (50)		
Segments resected				.271	.697
1	18 (43)	38 (33)	25 (39)		
2	24 (57)	76 (67)	39 (61)		
Background liver histology				.572	.902
Cirrhosis	12 (29)	38 (33)	19 (30)		

Data are number of patients (percentage of total study group), unless otherwise specified.
[a] Comparison of laparoscopic versus open liver resection in period 2. None of the differences was statistically significant ($P < .05$).

mas, and 11 other types. The 51 benign tumors included 11 hemangiomas, 10 focal nodular hyperplasias, 8 liver cysts, 4 adenomas, 4 cirrhotic nodules, and 14 various lesions. Fifty (32%) resections were performed in patients with histologically proven liver cirrhosis.

Laparoscopic Versus Open Liver Resection

There were no significant differences in the baseline demographic and preoperative data of patients who underwent LLR versus OLR (**Table 1**). Comparison of the outcomes of the 2 groups (**Table 2**) demonstrated that patients who underwent LLR had a significantly longer operative time but significantly shorter postoperative stay than did those who had OLR. The Pringle maneuver was significantly more likely to be applied in patients who underwent OLR. In the 2 approaches, there was no significant difference in blood loss, blood transfusion, or the frequency of an R1 resection.

LLR Versus OLR in Period 2

Comparison of LLR with OLR in the contemporaneous group of patients (**Tables 1** and **2**) also showed no difference in baseline features and demonstrated similar outcomes, showing that LLR was significantly associated with longer operative time but shorter postoperative stay.

Liver Resections Performed in Period 1 Versus Period 2

Comparison between the baseline characteristics of the patients between the 2 periods demonstrated no significant difference between most parameters other than the increased use of the laparoscopic approach in period 2 (**Table 3**). Forty percent of liver resections were performed via the minimally invasive approach in period 2. There was no difference between the 2 periods in the outcomes of the patients. A comparison of patients who underwent OLR in

Table 2.
Perioperative and Oncologic Outcomes of Patients

Parameter	Laparoscopic (n = 42)	Open (n = 114)	Open Period 2 (n = 64)	*P*	*P* [a]
Median operating time, min (range)	167.5 (60–525)	105 (40–235)	105 (55–235)	**<.001**	**<.001**
Median blood loss, mL (range)	0 (0–3000)	0 (0–4000)	100 (0–2000)	.747	.792
Perioperative blood transfusion	3 (7)	7 (6)	5 (8)	.821	1.000
Median blood transfusion, mL (range)	0 (0–2000)	0 (0–2000)	0 (0–2000)	.961	.927
Pringle maneuver applied	1 (2)	22 (19)	17 (27)	**.008**	**.001**
Median duration of Pringle maneuver, min (range)	0 (0–30)	0 (0–45)	0 (0–45)	**.010**	**.002**
Median postoperative stay, days (range)	4 (1–10)	5 (2–47)	5 (2–47)	**<.001**	**<.001**
Postoperative morbidity	6 (14)	19 (17)	14 (22)	.719	.329
Postoperative mortality	0	0	0	NA	NA
Resection margin <1 mm	4 (9.5)	7 (6)	3 (5)	.488	.431
Resection margin <1 mm in malignant tumors	0/24 (0)	3/81 (3.7)	2/47 (4.3)	1.000	.546
Median closest resection margin, mm (range)	5 (0–60)	8 (0–100)	7 (0–100)	.923	.798

Data are number of patients (percentage of total study group), unless otherwise specified.
[a] Comparison of LLR and OLR in period 2. Bold indicates statistical significance ($P < .05$).

the 2 periods demonstrated no difference in baseline characteristics and perioperative outcomes, other than the use of the Pringle maneuver (**Table 4**).

DISCUSSION

The results of the present study demonstrate that LLR can be safely adopted as a surgical option for tumors located in the LLS of the liver. Although LLR was associated with a longer surgical time compared with OLR, it did not translate into an increase in operative blood loss, need for blood transfusion, or postoperative morbidity. We postulate that the longer operative time associated with LLR is attributable to the effects of the learning curve, which is likely to decrease with increasing experience in our institution. It is important to add that other studies[10,11,18] have reported similarly longer operative times with LLR, especially during the learning phase, but have also demonstrated that shorter operative times were not crucial, given that they did not translate into improved perioperative outcomes, such as decreased blood loss or hospital stay.[10]

Based on our findings in this study, the benefits of the minimally invasive approach were obvious, even during the initial learning phase of our experience. Comparison of our first 42 LLRs with OLRs demonstrated that LLR was associated with a significantly shorter postoperative stay without compromising other outcomes, such as blood loss or postoperative morbidity, but at the expense of longer operative times. The early oncologic outcomes were also comparable to those of OLR, as evidenced by the similar rates of R0 resection and median resection margin length. None of the 24 malignant neoplasms in the laparoscopic arm had a resection margin <1 mm. We postulate that the shorter postoperative stay associated with LLR is probably not related to changes in clinical practice or surgeons' attitudes over time; comparison of OLR performed in period 1 versus period 2 demonstrated no significant difference in postoperative stay (**Table 4**). These findings are consistent with those in earlier studies in which it was shown that laparoscopic left lateral sectionectomy is associated with a shorter hospital stay, but longer operative time, compared with the open approach.[10,19–21]

In this study, the Pringle maneuver was applied less frequently during LLR, and there was no difference in blood loss compared with that occurring in OLR. This finding echoes those of Carswell et al,[15] who noted that portal clamping was required more frequently during OLR. This observation provides indirect support for the hypothesis that the positive pressure of pneumoperitoneum during LLR minimizes blood loss from the transected liver during parenchymal division.[15,22] However, it must be added that the frequency of use of the Pringle maneuver may be confounded by biases, such as an individual surgeon's preference in this nonrandomized study or selection of less technically difficult cases in the laparoscopic arm.

Table 3.
Surgical Characteristics and Outcomes in the 2 Study Periods

Operative Characteristics and Outcomes	Period 1 (n = 50)	Period 2 (n = 106)	*P*
Laparoscopic	0	42 (40)	**<.001**
Gender, male	23 (66)	62 (58)	.370
Median age, years (range)	59.5 (18–86)	61 (30–85)	.332
Previous abdominal surgery	14 (28)	39 (37)	.279
ASA score			.133
1	8 (16)	14 (13)	
2	30 (60)	76 (72)	
3	10 (20)	16 (15)	
4	2 (4)	0	
Pathology			.899
Benign	16 (32)	35 (33)	
Malignant	34 (68)	71 (67)	
Median tumor size, mm (range)	33.5 (0–75)	25.5 (0–70)	.175
Concomitant surgery	7 (14)	17 (16)	.742
Anatomic	28 (56)	51 (48)	.358
Nonanatomic	22 (44)	55 (52)	
Segments			.077
1	13 (26)	43 (41)	
2	37 (74)	63 (59)	
Background liver histology			.274
Cirrhosis	19 (38)	31 (29)	
Median operating time, min (range)	105 (40–210)	120 (55–525)	.058
Median blood loss, mL (range)	100 (0–4000)	100 (0–3000)	.881
Perioperative blood transfusion	2 (4)	8 (8)	.503
Median blood transfusion, mL (range)	0 (0–1800)	0 (0–2000)	.739
Pringle maneuver	5 (10)	18 (17)	.251
Median duration of Pringle maneuver, min (range)	0 (0–20)	0 (0–45)	.231
Median postoperative stay, days (range)	4.5 (3–13)	4 (1–47)	.949
Postoperative morbidity	5 (10)	20 (19)	.159
Resection margin <1 mm	4 (8)	7 (6.6)	.746
Median closest resection margin, mm (range)	8 (0–25)	6 (0–100)	.791

Data are number of patients (percentage of total study group), unless otherwise specified. Bold indicates statistical significance ($P < .05$).

More than half the patients who underwent LLR in our study had nonanatomic liver resection. Theoretical concerns have been raised about nonanatomic LLR and the possibility of compromised margins caused by the lack of tactile feedback. A study from Hong Kong demonstrated that anatomic laparoscopic left lateral sectionectomy is associated with wider resection margins than is laparoscopic wedge resection.[23] However, it must be emphasized that it is not known at present whether narrow but uninvolved resection margins compromise the prognosis of malignant liver tumors.[24] Our findings in the present study demonstrate that nonanatomic resections can be performed laparoscopically with a low incidence of margin involvement. This finding is especially important in

Table 4.
Characteristics and Outcomes of Patients Who Underwent Open Liver Resection

Operative Characteristics and Outcomes	Period 1 (n = 50)	Period 2 (n = 64)	P
Gender, male	33 (66)	37 (58)	.373
Median age, years (range)	59.5 (18–86)	63 (30–82)	.103
Previous abdominal surgery	14 (28)	26 (41)	.161
ASA score			.393
1	8 (16)	8 (12.5)	
2	30 (60)	42(66)	
3	10 (20)	14 (22)	
4	2 (4)	0	
Pathology			.525
Benign	16 (32)	17 (27)	
Malignant	34 (68)	47 (73)	
Median tumor size, mm (range)	33.5 (0–75)	27 (0–70)	.328
Concomitant surgery	7 (17)	7 (11)	.621
Anatomic	28 (56)	32 (50)	.524
Nonanatomic	22 (44)	32 (50)	
Segments resected			.142
1	13 (26)	25 (39)	
2	37 (74)	39 (61)	
Background liver histology			.350
Cirrhosis	19 (38)	19 (30)	
Median operating time, min (range)	105 (40–210)	105 (55–235)	.815
Median blood loss, mL (range)	100 (0–4000)	100 (0–2000)	.998
Perioperative blood transfusion	2 (4)	5 (8)	.400
Median blood transfusion, mL (range)	0 (0–1800)	0 (0–2000)	.728
Pringle maneuver	5 (10)	17 (27)	**.026**
Median Pringle duration, min (range)	0 (0–2)	0 (0–45)	**.024**
Median postoperative stay, days (range)	4.5 (3–13)	5 (2–47)	.058
Postoperative morbidity	5 (10)	14 (22)	.129
Resection margin <1 mm	4 (8)	3 (4.7)	.697
Median closest resection margin, mm (range)	8 (0–25)	7 (0–100)	.757

Data are number of patients (percentage of total study group), unless otherwise specified. Bold indicates statistical significance ($P < .05$)

patients in whom liver parenchymal preservation is essential, such as those with cirrhosis or resection for colorectal liver metastases.

This study was performed to evaluate and demonstrate the impact of introducing LLR as a surgical option for lesions located in the LLS of the liver. In this study, we compared patients who underwent surgery over 2 consecutive periods instead of using a case–control design, as in prior studies.[11,12,18,20] To determine whether some of these observations were owing to the confounding effect of historical case–control studies such as changes in institution and surgeons' practices and attitudes over time, we compared the outcomes of open resection between the 2 periods and between LLR and OLR in period 2 alone. Comparison of OLR between the 2 periods did not demonstrate any difference in operative time or hospital stay.

Table 5.
Selected Studies Comparing LLR With OLR of the Left Lateral Liver Section

Study	Country/Year	Laparoscopic	Open	Significant Outcomes Associated With Laparoscopy
Lesurtel et al.[12]	France, 2003	18	18	Inc op time, inc Pringles, dec blood loss
Tang et al.[11]	Hong Kong, 2005	10	7	Inc op time
Soubrane et al.[10]	France, 2006	16	14	Inc op time, dec blood loss
Aldrighetti et al.[18]	Italy, 2008	20	20	Inc op time, dec blood loss, dec LOS
Abu Hilal et al.[20]	United Kingdom, 2008	24	20	Dec blood loss, dec LOS
Carswell et al.[15]	United Kingdom, 2009	10	10	Dec LOS
Endo et al.[21]	Japan, 2009	10	11	Dec LOS
Campos et al.[25]	Spain, 2009	10 LLS	10 LLS	Dec LOS
		8 WR	8 WR	Inc op time
Dokmak et al.[26]	France, 2014	31	31	Dec op time, dec blood loss, dec LOS, dec cost
Present	Singapore	42	114	Inc op time, dec LOS, dec Pringles

dec, decreased; inc, increased; LLS, left lateral sectionectomy; LOS, length of stay; op, operative; WR, wedge resection.

However, comparison between LLR and OLR within period 2 still demonstrated the shorter postoperative stay and longer operative time associated with LLR. These findings suggest that the outcomes we observed were less likely to be related to the confounding effect associated with historical case–control studies. The studies[10–12,15,18,20,21,25,26] that have compared LLR versus OLR for tumors in the LLS are summarized in **Table 5**. The present study is one of the largest series to date to compare laparoscopic versus open resection for tumors in the LLS.

We acknowledge several potential limitations associated with this retrospective nonrandomized study. First, as in all such studies, selection bias is a potential confounding factor. Nonetheless, the baseline characteristics of patients in both the laparoscopic and open groups were similar, and we sought to diminish the bias with our inclusion and exclusion criteria. Second, institution referral bias may also be present, whereby smaller tumors entailing technically simpler resections may have been preferentially referred to surgeons who were more likely to perform LLR. Last, another limitation was that the design was not double-blind. Hence, biases may arise from both patients' and surgeons' attitudes and practices. The advantages of the laparoscopic approach observed in unblinded patients may be partly due to the placebo effect, which could cause patients to be more active after LLR, as they may perceive of themselves as having undergone a more minor "key-hole" surgery.[27] Unblinded clinicians may also contribute to the improved perioperative outcomes observed, as they may adopt different practices after LLR, such as earlier feeding and quicker dismissal from the hospital.[27] Hence, it cannot be ascertained definitively whether the benefits we experienced with the introduction of LLR are due to changes in surgeons' practices, to changes in patients' attitudes induced by laparoscopy, or to a true physiological advantage of laparoscopy. Nonetheless, the positive impact on perioperative outcomes associated with the introduction of LLR to our practice is clearly demonstrated in this study, although the level of evidence remains low. Only the performance of a well-designed double-blind randomized controlled trial can provide high-level clinical evidence to determine effectiveness of LLR compared with OLR.

In conclusion, this study demonstrates that LLR can be safely adopted to manage tumors located in the left lateral segments of the liver. The laparoscopic approach is associated with a shorter postoperative stay, a decreased need for the Pringle maneuver, but longer operative time compared with the open approach during the initial learning phase.

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