

# Laparoscopic liver resection: lessons learnt after 100 cases

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## ABSTRACT

**Objective:** To share our institutional experience in laparoscopic liver resection and our learning curve after the first 100 cases of laparoscopic liver resection.

**Design:** Case series with internal comparison.

**Setting:** A regional hospital in Hong Kong.

**Patients:** Our institution started performing laparoscopic liver resection since 2006. All patients who underwent laparoscopic liver resections from March 2006 to October 2012 were identified in a prospectively collected database. The demographic data and operative outcomes of these patients were extracted, and results of the early (from March 2006 to May 2010) and late (from June 2010 to October 2012) study periods were compared.

**Results:** Between March 2006 and October 2012, 100 laparoscopic liver resections were performed for 98 patients in the Department of Surgery, Kwong Wah Hospital, Hong Kong. They were 69 (70%) males and 29 (30%) females, and the median age was 65 years. The final histological diagnoses were as follows: hepatocellular carcinoma (n=72), colorectal liver

metastases (n=14), intrahepatic cholangiocarcinoma (n=4), and benign disease (n=10). There were more anatomical resections, major hepatectomies as well as resections of more anatomically challenging right-sided and posterosuperior lesions in the late versus the early period; however, operative outcomes remained comparable in both periods.

**Conclusion:** Laparoscopic hepatectomies are feasible with growing experience. Bearing in mind the diversity in the level of operative techniques with various types of laparoscopic liver resections, more experience is needed to overcome the learning curve.

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### New knowledge added by this study

- Laparoscopic hepatectomies are feasible in our hospital where operative skills and techniques improved over time with experience.

### Implications for clinical practice or policy

- Laparoscopic hepatectomies should be carried out in high-volume centres. Favourable results can be achieved with adequate experience, considering the steepness of the learning curve. The wide range of operative techniques for various types of laparoscopic hepatectomies implies that further exploration in training and learning curve effect is needed.

## Introduction

Since its inception in 1992, laparoscopic liver resection (LLR) has been increasingly employed as the new alternative to open liver resection.<sup>1</sup> Over 3000 cases of LLRs have been reported worldwide.<sup>2</sup> The safety and efficacy of the procedure have been shown in recent evidence to be comparable with open surgery. The advantages of LLR over traditional open surgery are less analgesic requirements, less operative blood loss, shorter hospital stay, accompanied with a low operative mortality and morbidity of 0.3% and 11%, respectively.<sup>3-6</sup> Laparoscopic left lateral sectionectomies and

wedge resections are now considered standardised operations performed routinely in dedicated centres.<sup>7</sup>

Laparoscopic hepatectomy is considered to be a complicated laparoscopic procedure. The surgeon should be experienced in both laparoscopic and liver surgery. Most of the studies on the learning curve effect show improved outcome with experience.<sup>8-11</sup> However, LLR is not a single procedure and the complexity of operation ranges from wedge resections to major hepatectomies involving anatomical resection of three or more segments. Experience in the complexity of procedure performed has not

been adequately studied. In Kwong Wah Hospital, our experience with laparoscopic liver surgery commenced in 2006, and since then the procedure has been performed in an increasing number of patients. Here we report our experience with the first 100 cases of LLR and the learning curve effect through the series of cases.

## Methods

All data including patient demographics, tumour characteristics, operative procedures, and outcomes were prospectively collected. All patients underwent chest radiography and contrast computed tomography (CT) of the abdomen. Magnetic resonance imaging and lipiodol arteriogram were performed in selected patients. Patients' preoperative liver function was assessed according to the Child-Pugh classification,<sup>12</sup> and with indocyanine green retention test and CT volumetric analysis, if necessary. Patients were selected for laparoscopic liver surgery if they were medically fit for the major operation, Child-Pugh class A or B liver cirrhosis with adequate liver remnant after resection. Our centre adopted a less stringent criterion in terms of patient selection; hence, patients were included if LLR was considered technically feasible after evaluating patients' history of surgical operations, tumour size, and location. In the later years, indications were expanded to include resection of more benign pathologies and cholangiocarcinoma, wherein resection was anticipated to be more difficult.<sup>13,14</sup>

## Operative techniques

All patients were operated on by specialist hepatobiliary surgeons with expertise in laparoscopic surgery. Hand-assisted or laparoscopic-assisted approaches were employed in the earlier period; however, the approach changed into total laparoscopy in the later period. Patient was put in Lloyd-Davis position for left hepatectomies and in semi-left lateral or left lateral position for right-sided lesion. Intra-operative laparoscopic ultrasound was used routinely. Five ports were used and placed according to tumour location. Parenchymal dissection was performed by Cavitron ultrasonic surgical aspirator (Valleylab Inc, Boulder [CO], US), Harmonic Scalpel (Harmonic ACE; Ethicon Endosurgery, Johnson & Johnson, Langhorne [PA], US) or LigaSure (Valleylab). Methods employed for haemostasis included bipolar diathermy, metal clips, Hem-o-lok (Weck Surgical Instruments, Teleflex Medical, Durham [NC], US) or endovascular staplers; the Pringle manoeuvre was not used routinely. Specimen was put inside a plastic bag and retrieved via a Pfannenstiel incision if the specimen was large or by extension of one of the port sites if the specimen was small. Pneumoperitoneum was re-established after

## 腹腔鏡肝臟切除手術：經驗100例手術後的分享

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目的：分享於本院進行了100例腹腔鏡肝臟切除手術後的一些經驗和學習曲線。

設計：病例系列的內部比較。

安排：香港一所分區醫院。

患者：本院自2006年起開始進行腹腔鏡肝臟切除術。從2006年3月至2012年10月期間所有曾接受腹腔鏡肝臟切除術的病例均被列入一個前瞻性收集數據庫。從數據庫取出口學資料和手術結果，並把前期（2006年3月至2010年5月）和後期（2010年6月至2012年10月）的手術結果進行了比較。

結果：2006年3月至2012年10月期間，於廣華醫院外科部共有98名患者（100例）接受腹腔鏡肝臟切除術。他們分別為69名男性（70%）和29名女性（30%）；年齡中位數為65歲。最後的病理診斷如下：肝細胞癌（72例）、結直腸癌肝轉移（14例）、肝內膽管細胞癌（4例）和良性病變（10例）。與前期相比，後期有較多解剖切除、肝大部份切除，以及更具挑戰性的解剖右路和後上病變的切除。然而，兩段時期的手術結果相若。

結論：隨著經驗的累積，腹腔鏡肝臟切除越可行。要注意的是，各種腹腔鏡肝臟切除手術須具不同程度的技術水平，如可延續先前經驗，很快便可克服學習曲線。

specimen retrieval at a pressure of 6 to 8 mm Hg to check for haemostasis. Tissue glue (Tisseel; Baxter, Vienna, Austria) was applied selectively. Abdominal drains were inserted as needed.

## Statistical analyses

Patients who underwent laparoscopic hepatectomies were divided chronologically into two periods for comparison. Those performed from March 2006 to May 2010 were classified into the 'early group' while those performed from June 2010 to October 2012 were classified into the 'late group'. All data including patient demographics, operative and postoperative parameters were retrieved from a prospectively collected database. Operative parameters included operation type, conversion, operating time, blood loss, transfusion requirement, duration of Pringle manoeuvre, and intra-operative complications. The postoperative parameters included resection margin, staging, medical and surgical complications, length of hospital stay, and operative mortality. Complications were recorded and classified according to the Clavien-Dindo classification.<sup>15</sup> Postoperative survival was measured using Kaplan-Meier estimates.

Statistical analyses were performed with the Statistical Package for the Social Sciences (Windows version 16.0; SPSS Inc, Chicago [IL], US). Numerical data were expressed as the median value. Mann-

TABLE 1. Summary of liver resections performed from March 2006 to October 2012

Total hepatectomies	Early (n=125)	Late (n=87)	P value
Laparoscopic hepatectomies	50/125 (40%)	50/87 (58%)	0.141
Major hepatectomies	10/50 (20%)	16/50 (32%)	0.171
Anatomical resections	25/50 (50%)	31/50 (62%)	0.108

TABLE 2. Patient and tumour characteristics, and indications of laparoscopic liver resection

Characteristic/indication	Data		P value
	Early (n=50)	Late (n=50)	
<b>Characteristic</b>			
Median age (years)	65	65	0.78
Gender (M/F)	37/13	33/17	0.38
<b>Child-Pugh score</b>			
A	49	48	0.56
B/C	1	2	
Median (range) tumour size (cm)	2.3 (1-10.5)	2.5 (0.25-13)	0.09
<b>No. of tumours*</b>			
1	42	42	
2	2	1	
3	2	0	
4	2	2	
5	1	1	
Cirrhosis on pathology	28/50	16/50	0.016
<b>Tumour location (segments)†</b>			
Anterior-inferior (segment 1-6)	40	46	0.01
Posterior-superior (segment 7-8)	13	17	0.38
Segment 7	4	13	0.017
<b>Indication of LLR</b>			
Hepatocellular carcinoma	40	32	
Cholangiocarcinoma	0	4	
Colorectal liver metastasis	7	7	
<b>Benign</b>			
Recurrent pyogenic cholangitis	1	3	
Haemangioma	0	1	
Adenoma	0	1	
Cirrhotic nodule	2	0	
Bile duct hamartoma	0	1	
Focal nodular hyperplasia	0	1	

Abbreviation: LLR = laparoscopic liver resections

\* Data of one case in early group and four cases in late group are missing due to pathologies of recurrent pyogenic cholangitis and cholangiocarcinoma

† Tumours located in the right lobe were counted in both anterior-inferior and posterior-superior categories

Whitney *U* test was used for comparing continuous variables. Chi squared test and Fisher's exact test were used for comparing categorical variables. Statistical significance was set at a P value of less than 0.05.

## Results

From March 2006 to October 2012, our unit performed a total of 212 hepatectomies. A laparoscopic approach was employed in 98 patients. The proportion of LLRs performed increased from 40% in the early group to 58% in the late group. There was an increasing proportion of laparoscopic major hepatectomies and anatomical resections in the late group versus the early group (Table 1).

A total of 98 patients who underwent LLRs were recruited during this study period. There were 69 (70%) male and 29 (30%) female patients; the median age was 65 years. Of the 98 patients, two underwent a second LLR, giving a total of 100 LLRs. Some of these patients had previously undergone conventional hepatectomy. The Eastern Cooperative Oncology Group status was 0 for all patients. The demographic data and tumour characteristics of the two groups are shown in Table 2. There were significantly more patients with cirrhosis in the early group ( $P=0.016$ ), and more patients had segment 7 tumour in the late group ( $P=0.017$ ).

Indications for liver resection are shown in Table 2. Overall, 72% of LLRs were performed for hepatocellular carcinoma, whereas benign pathologies accounted for 10% of all LLRs. There was an increase in the number of LLRs performed for benign pathologies and cholangiocarcinomas in the late versus the early period. The types of resection performed are listed in Table 3. The proportion of anatomical resections increased from 50% in the early period to 62% in the late period, including predominantly right hepatectomies (6% vs 16%) and right posterior sectionectomies (2% vs 8%). An increasing proportion of major hepatectomies, including right and left hepatectomies, as well as right posterior sectionectomies, were performed in the late period (20% vs 32%). In addition, more resections involving the posterosuperior segments (including segments 7 and 8) were performed in the late period (34% vs 26%); these are considered to be anatomically more difficult resections. Pure laparoscopic approach was employed in the majority of LLRs, and more LLRs were performed with a pure laparoscopic approach in the late period than in the early period (98% vs 88%) [Table 3].

A number of procedures were performed alongside with LLRs. These included two laparoscopic colectomies, two closures of ileostomies, one hepaticojejunostomy, one small bowel resection, and three radiofrequency ablation-assisted LLRs.

Table 4 shows the intra-operative results, postoperative complications, status of margin involvement, and hospital stay. Conversion rates were higher in the late period than in the early period (14% vs 2%) but did not reach statistical significance. Among the operations that required conversion to a standard approach ( $n=8$ ), three were

due to haemorrhage, and the rest were due to poor exposure, dense adhesions with resultant small bowel injury, anatomical limitations at posterior segment, and doubtful tumour margin during resection. There was no mortality in the early group and one in the late group. Complications were classified according to the Clavien-Dindo classification and are shown in Table 4. One patient in the early group who had situs inversus experienced complications in the form of bile leakage from a segment 4 branch after an anatomical right hepatectomy; this patient required laparotomy with T-tube insertion. One patient in the late group was found to have extensive bowel ischaemia on postoperative day 2 after a laparoscopic right hepatectomy; this patient required reoperation but did not survive. Two patients, one each from the early and late groups, developed bile leak postoperatively after laparoscopic right hepatectomies; they were managed with image-guided drainage and endobiliary stenting.

A subgroup analysis was conducted for patients receiving laparoscopic right hepatectomies. Between the early and late period, a total of 11 laparoscopic right hepatectomies were performed. Table 5 shows the peri-operative results of these patients. With increasing experience, the operating time, blood loss, transfusion rate and volume, as well as duration of hospital stay were significantly reduced.

The 2-year survival, according to Kaplan-Meier survival analysis, showed an overall survival of 89.1% in the early group versus 96.9% in the late group (log rank  $P=0.593$ ; Fig). Since the majority of the study population were recruited after 2008, 5-year survival data from this main bulk of patients were not available for this analysis.

## Discussion

Laparoscopic hepatectomies are technically demanding.<sup>16,17</sup> The difficulty lies in parenchymal transection with limited exposure and traction, thus requiring proficiency in both laparoscopic and liver surgery. The reproducibility and feasibility of the procedure have been questioned, preventing the procedure from being widely employed. Our current study demonstrated that, with growing experience, we could perform LLR safely, as demonstrated by the favourable overall outcome of LLR. The rates of overall mortality and major morbidity were 1% and 5%, respectively. Reoperation was required in two (2%) patients. For malignant indications, R0 resection rate (complete resection with no microscopic residual tumour) was 94% (85/90). The overall results are in accordance with reports in the literature.<sup>2,5</sup>

Blood transfusion was required in 21% of our patients and the conversion rate was 8%. We did not use the Pringle manoeuvre frequently because most of the bleeding occurred from hepatic veins.

TABLE 3. Types of laparoscopic liver resections

Item	Early (n=50)	Late (n=50)	P value
Type of resection			
Anatomical	25 (50%)	31 (62%)	0.108
Left hepatectomy	6 (12%)	4 (8%)	0.370
Right hepatectomy	3 (6%)	8 (16%)	0.200
Left lateral sectionectomy	7 (14%)	7 (14%)	1
Right posterior sectionectomy	1 (2%)	4 (8%)	0.362
Bisegmentectomies	1 (2%)	1 (2%)	1
Monosegmentectomy	7 (14%)	7 (14%)	1
Non-anatomical	25 (50%)	19 (38%)	
Additional procedures			
Colectomy	0	2	
Closure of ileostomy	1	1	
Hepaticojejunostomy	0	1	
Small bowel resection	0	1	
Radiofrequency ablation	1	2	
Laparoscopic approach			
Pure laparoscopic	44 (88%)	49 (98%)	0.140
Hand-assisted	1 (2%)	0 (0%)	
Laparoscopic-assisted	5 (10%)	1 (2%)	

Among these eight patients requiring conversion, three quarters were related to bleeding from branches of the hepatic vein. We preferred a pure laparoscopic approach because the use of a hand port caused interference with laparoscopic trocars and instruments.<sup>18</sup> It has been suggested that hand-assisted or hybrid approach offers speedy haemostasis but there is no solid evidence to support which single method is superior. We did not consider conversion to be a failure and hence, a higher conversion rate (14% vs 2%,  $P=0.06$ ) was observed with a lower blood transfusion rate (16% vs 26%,  $P=0.22$ ) in the late versus the early period. No strict transfusion criteria were implemented. The decision of blood transfusion was mostly made by individual anaesthetist intra-operatively. Early in our series, we tended to initiate transfusion early because we anticipated bleeding during LLR to be more difficult to control. With gaining experience, transfusion was given more judiciously. Thus, with similar median blood loss, there was a trend towards lower transfusion rate in the late group as compared with the early group.

We further analysed the outcomes of the LLRs performed in the early and late periods. The overall outcome parameters were comparable with no significant learning curve effect observed. We observed a slight increase in operating time (263 vs 240 mins,  $P=0.40$ ) and duration of hospital stay (6 vs 5 days,  $P=0.41$ ) during the later period, and we believe

TABLE 4. Comparison between early and late laparoscopic hepatectomies and complications classified according to the Clavien-Dindo classification

Characteristic/indication	No. or median (interquartile range)		P value
	Early (n=50)	Late (n=50)	
Comparison between early and late periods			
Blood loss (mL)	325 (95-1200)	300 (200-925)	0.50
Transfusion volume (mL)	0 (0-375)	0 (0-0)	0.10
Transfusion	13/50	8/50	0.22
Operating time (mins)	240 (167-323)	263 (168-426)	0.40
Conversion to open surgery	1/50	7/50	0.06
Positive margin	3/47	2/43	0.646
Pringle manoeuvre	2/50	2/50	1
Resection margin (mm)	5 (0-20)	7 (0-30)	0.50
Complications requiring reoperation	1/50	1/50	1
Complications requiring radiological intervention	1/50	2/50	0.56
Hospital stay (days)	5 (4-9)	6 (5-7.2)	0.41
Complications classified according to the Clavien-Dindo classification			
I			
Wound infection	1	0	0.315
Pleural effusion	2	1	0.558
Wound gapping	1	0	0.315
II			
Chest infection	0	2	0.153
Acute myocardial infarction	1	1	1
Arrhythmia	0	4	0.041
Urinary tract infection	0	1	0.315
III			
IIIa			
Bile leak	1	1	1
Upper gastro-intestinal bleed	1	0	0.315
Intra-abdominal collection	0	1	0.315
IIIb			
Bile leak	1	0	0.315
IVa			
Liver failure	1	0	0.315
V			
In-hospital mortality	0	1	0.315

that this was probably related to the increasing number of laparoscopic major hepatectomies and anatomical resections of right-sided lesions, as well as posterior segment LLRs performed in the later period.

With increasing experience in performing LLRs, we extended our indications of LLR from peripherally located tumours to posterosuperior lesions and from wedge resections to major resections, all reflecting an improvement in our

techniques of performing LLR. However, we believe that we are still on the learning curve for the more difficult LLRs because the operative outcomes did not improve much. We managed to perform more anatomical resections with time in order to secure oncological safety. However, 5-year survival and recurrence results of our patients are not available for comparison between these two study groups.

The subject of learning curve effect of laparoscopic hepatectomy has been investigated

TABLE 5. Comparison of laparoscopic right hepatectomies in the early and late period

Item	No. or median (interquartile range)		P value
	Early (n=3)	Late (n=8)	
Blood loss (mL)	1500 (1000-1800)	450 (220-875)	0.030
Transfusion volume (mL)	900 (600-1200)	0 (0-600)	0.033
Transfusion	3/3	2/8	0.026
Operating time (mins)	540 (520-665)	425 (344-472)	0.026
Conversion to open surgery	0/3	1/8	0.521
Positive margin	0/3	1/8	0.521
Pringle manoeuvre	1/3	0/8	0.087
Resection margin (mm)	1 (1-2.3)	5.5 (0-15)	0.280
Complications requiring reoperation	0/3	1/8	0.521
Complications requiring radiological intervention	1/3	1/8	0.425
Hospital stay (days)	20 (16-35)	7.5 (6.25-10)	0.002

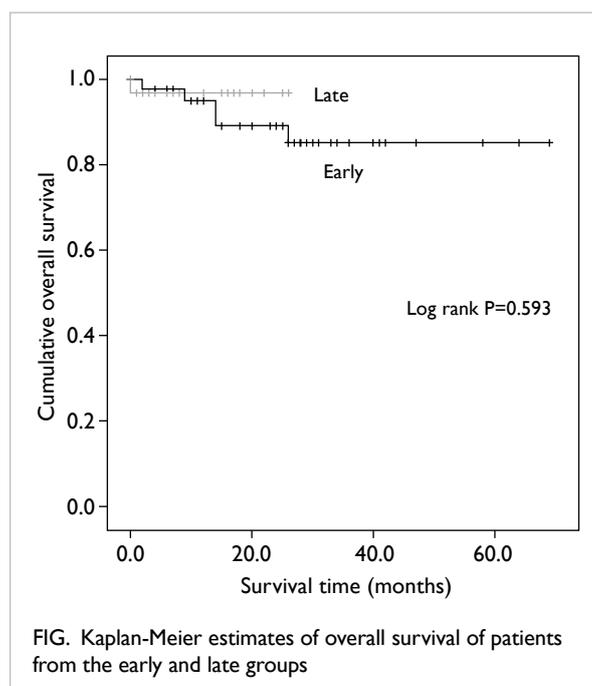


FIG. Kaplan-Meier estimates of overall survival of patients from the early and late groups

by several authors in the literature. Many studies attempted to identify the number of hepatectomies required to overcome the learning curve effect.<sup>8-11</sup> The 12-year experience of Vigano et al<sup>9</sup> demonstrated that after performing 60 consecutive cases of laparoscopic hepatectomies, operative outcomes in three consecutive periods in terms of conversion rate (15.5%, 10.3%, and 3.4%;  $P < 0.05$ ), operating time (210, 180, and 150 mins;  $P < 0.05$ ), blood loss (300, 200, and 200 mL;  $P < 0.05$ ), and morbidity (17.2%, 22.4%, and 3.4%;  $P < 0.05$ ) improved. They reported a steady increase in the proportion of LLRs

and a statistically significant increment in major and right hepatectomies in the later period of the study. The cumulative analysis of conversion rates in minor hepatectomies showed that at the 60th consecutive case, the conversion rate reached the average value and improved thereafter. A Korean group examined the results from their first 100 cases of laparoscopic liver surgery.<sup>8</sup> Their mean operating time was 220 minutes and the overall morbidity was 11%. They demonstrated a decrease in the volume of blood transfusion in the latter half of patients operated with a malignant pathology. Kluger et al<sup>11</sup> investigated the learning curve effect in laparoscopic major hepatectomy. Dividing their study results chronologically into three phases, they showed a steady increase in the proportion of major LLRs (1% vs 9%,  $P < 0.05$ ) and malignant lesions being resected at a later stage in the study period. Median operating time (150 vs 210 mins,  $P < 0.05$ ), blood loss (200 vs 300 mL,  $P < 0.05$ ), and clamping time (20 vs 45 mins,  $P < 0.05$ ) were significantly lower in the later study period. Morbidity rates also improved significantly with time (3% vs 17%,  $P < 0.05$ ). Their group concluded that a learning curve existed for both the operator and the institution, and a high-volume environment enables overcoming of the learning curve. The latest experience in the attempt to identify a learning curve came from a UK group.<sup>10</sup> Analysing their 37 LLRs, the researchers concluded that their results followed a learning curve whereby more complicated procedures could be performed in the latter part of their experience. They also emphasised the importance of achieving proficiency in laparoscopic hepatectomies via simulation and wet laboratories. From our experience, we agree that we could safely expand our indications from wedge resection of small tumours at anterior and

superior liver segments to major resections and posterosuperior lesions. However, the technical demand and learning path for wedge resections are entirely different from those of anatomical hemihepatectomies or monosegmentectomies. The training for LLR and learning curve issue is still an important unresolved topic that needs to be investigated further.

## Conclusion

Laparoscopic hepatectomies are feasible and safe with favourable patient outcomes. A learning curve is present and could be overcome with increasing experience. However, the long-term outcomes associated with the procedure require further study with longer follow-up.

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