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Outcomes of Repeat Laparoscopic Liver Resection Compared to the Primary Resection

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Abstract

Background Repeat laparoscopic liver resection (R-LLR) can be technically challenging. Data on this topic are scarce and many investigators would question its feasibility and outcomes. The aim of the present study was to evaluate the safety, feasibility, oncological efficiency and outcomes of R-LLR.

Methods We reviewed a prospectively collected database of 403 patients undergoing 422 laparoscopic liver resections (LLRs) from August 2003 to August 2013. Data of 19 patients undergoing R-LLR were analyzed and compared to the primary resection (P-LLR) in these patients. Demographic and clinical data were studied. A subgroup analysis was done for minor resections.

Results Twenty R-LLRs were performed in 19 patients (female 58 %; mean age: 57.5 years; age range: 23–79 years). Colorectal liver metastases (CRLM) were the commonest indication for R-LLR (60 %), followed by neuroendocrine tumor liver metastases (NETLM) (20 %) and hepatocellular carcinoma (HCC) (10 %). The majority (90 %) of resections were for malignant disease (18/20). There were three conversions (15 %), and two patients developed complications (10 %). The operative time ($p = 0.005$) and blood loss ($p = 0.03$) were both significantly greater in R-LLR compared to P-LLR, whereas length of stay (median 4 days; $p = 0.30$) and complications ($p = 0.58$) did not differ between the groups. R0 resection rates for P-LLR and R-LLR were 95 and 90 %, respectively ($p = 0.73$).

Conclusions Repeat LLR is safe, feasible, and can be performed with minimal morbidity. It appears to be technically more challenging than P-LLR, but without any increase in complications or length of hospital stay.

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Introduction

Laparoscopic liver resection (LLR) has evolved over the last two decades from an experimental procedure to a routine approach in the operative treatment of many liver lesions. Many groups have demonstrated the safety, feasibility, and oncological efficiency of the laparoscopic approach [1–10]. Advances in LLR have progressed in step with advancements in the oncological management of colorectal liver metastases (CRLM). Hence, multidisciplinary teams are frequently faced with recurrent metastatic disease deemed operable according to modern criteria. Repeat liver resection is considered the standard of care as it can positively impact survival [11]. Open repeat liver resection has traditionally been the routine approach, but it require considerable adhesiolysis and has up to 25 % morbidity [12–14]. Repeat laparoscopic liver resection (R-LLR) has not been fully assessed, with only a few reported small series [15–17]. Because of the increased technical challenges posed by R-LLR, more data are needed to confirm the safety and feasibility of the procedure. We herewith present our experience of R-LLR and compare outcomes of the primary and repeat procedure in the same group of patients, with focus on its feasibility, safety, and oncological efficiency.

Materials and methods

We reviewed a prospectively collected database of 403 patients undergoing 422 LLRs from August 2003 to August 2013; 20 of those patients underwent R-LLR. When we started considering patients for R-LLR, we agreed that the approach should not compromise the indication or the assessment process. Each new repeat liver resection was evaluated for number and distribution of metastases, disease-free interval, quality of life, extrahepatic disease, and future liver remnant. Demographic and clinical data pertinent to the current and past liver surgery were studied. We studied indications, operative time, blood loss and conversion to open surgery, length of stay, complications, oncological efficiency, and mortality.

Surgical technique

The surgical technique for the primary laparoscopic liver resection (P-LLR) for left lateral sectionectomy and right hemihepatectomy is described elsewhere [2, 18]. For other types of P-LLR, similar principles were employed. For R-LLR, patients are positioned in the supine position with the surgeon standing on the patient's right side for left-sided lesions and to the patient's left side for the right-sided lesions. For hemi-hepatectomy, the above position is occasionally substituted with the surgeon standing between the patient's legs. A 12 mm periumbilical port is placed for a 30 degree camera. Two more 10 mm ports and two 5 mm ports are inserted and this allows optimal mobilization and dissection of the liver. Port site adhesions and scarring can increase the risk of bowel injury. It is important that previous scarring does not drive the surgeon to move his port sites from the usual location, as this may render the second procedure technically difficult. Our first port is inserted with an open technique and the other ports are positioned under direct vision. According to adhesions, an occasional additional extra port has been used (six cases) to help in adhesiolysis. Laparoscopic ultrasonography is routinely used to locate the lesion(s), to check for proximity to the vasculature, and to mark the resection margins. Inflow control with a 5 mm nylon tape (for use of the intermittent Pringle maneuver) was routinely put in place for major hepatectomies or posterior–superior (not easily accessible) located lesions. Hepatic hilar adhesions can result from dissection and increase the risk of injury to the inflow of the future liver remnant; hence it is important that hilar dissection is minimized. Superficial parenchymal transection was achieved using LOTUS (Laparoscopic Operation by Tortional Ultrasound; S.R.A Developments, Ashburton, Devon, UK). Next, a combination of Cavitron Ultrasonic Surgical Aspirator (CUSA; Valleylab) and LOTUS was used to transect the deeper parenchyma with identification of vasculature and biliary structures. Clips or vascular staplers were used when required to divide major vessels. Hemostatic products such as collagen or fibrin glue (Evicel; Johnson & Johnson Wound Management) were routinely used on the cut surface. Prior to completion of the operation, hemostasis was checked again under the restored central venous pressure and Valsalva maneuver. The specimen was removed in a plastic endoscopy bag from a Pfannenstiel incision.

Classification

We use the Brisbane 2000 nomenclature classification to define liver resection [19]. A minor liver resection was defined as resection of up to two liver segments, and a major liver resection was defined as en-bloc resection of three or more liver segments. Indications of liver resection, operative time, blood loss, and conversion to open surgery are electronically captured for each patient during the operation. Length of stay was calculated from the date of surgery and date of discharge with both dates inclusive in the stay. Complications were graded according the Clavien-Dindo classification system [20]. Oncological efficiency was verified by histology result, and R1 resection was defined if margins were positive.

Statistics

We summarized patient characteristics and study results using proportions and means or medians with interquartile range (IQR). Normality distribution was checked with the Shapiro–Wilk test on SPSS software version 17. We used Student's t test to compare continuous variables between groups. For categorical variables, we used Chi square to determine differences in proportions between groups. Level of significance was kept at $p = 0.05$. Subgroup analysis was done for minor liver resection to determine whether type of resection influenced the outcome of R-LLR.

Results

Between August 2003 and August 2013, 422 laparoscopic liver resections in 403 patients were performed at our tertiary referral center. Nineteen patients with a mean age of 57.5 years (range: 23–79 years; female 58 %) underwent 20 R-LLRs with a CRLM as the commonest indication for R-LLR (60 %) followed by neuroendocrine tumor liver metastases (NETLM) (20 %) and hepatocellular carcinoma (HCC) (10 %). The majority of resections were for malignant disease (18/20). Of 12 patients with CRLM, 4 were treated in a two-stage hepatectomy and 8 were treated for recurrent disease. In four patients, we did a debulking liver resection for NETLM to control hormonal symptoms. The mean interval between the repeat and primary LLR was 10.5 months (range: 1–46 months). Fourteen minor resections (70 %) and six major (30 %) resections were done as R-LLR. The median tumor diameter was 28 mm (range: 10–90 mm).

Table 1 shows the comparison of P-LLR and R-LLR in the same group of patients. The American Society of Anesthesiology (ASA) status did not change over time for R-LLR patients. The operative time ($p = 0.005$) and blood loss ($p = 0.03$) were significantly greater in R-LLR compared to P-LLR. Length of stay ($p = 0.30$) and complications ($p = 0.58$) did not differ between the groups. The median length of stay in both groups was 4 days. The Pringle maneuver was used in six patients during the primary resection with median 15 min (range: 10–60 min) and in seven patients during repeat resection with median 30 min (range: 15–50 min). One patient in the P-LLR group (5 %) with CRLM had histologically positive margins, and two patients (10 %) (one each with CRLM and HCC) had positive margins during the R-LLR procedure ($p = 0.73$). There were no R2 resections in our series; nor were there any deaths.

Minor liver resection

Minor liver resection was the most common form of LLR in our series; 17/19 (89 %) in P-LLR group and 14/20 (70 %) in the R-LLR group. Operative time was significantly longer in the R-LLR group ($p = 0.03$) with minor resection [246 min (IQR 161–345 min) vs. 155 min (IQR 70–195 min)]. Blood loss ($p = 0.44$) and length of stay ($p = 0.28$) did not differ between the two groups. There were no complications in the P-LLR group versus one bile leak in the R-LLR minor group (7 %). Table 2 provides a summary of comparison for primary and repeat minor resections.

Major liver resection

Two major liver resections were done during the primary LLR, and six were done during R-LLR. Operative time was not significantly different in the two groups ($p = 0.87$). One patient required blood transfusion during P-LLR, and three patients required transfusions during R-LLR. In the

Table 1 Comparison of primary and repeat laparoscopic liver resection

	Primary LLR ($n = 19$)	Repeat LLR ($n = 20$)	p value
Type	17 minor (89 %)	14 minor (70 %)	1.0
	2 major (11 %)	6 major (30 %)	
Tumor diameter	Median 25 mm (9–75 mm)	Median 28 mm (10–80 mm)	0.5
Operative time	Median 165 min (IQR 90–203 min)	Median 285 min (IQR 195–360 min)	0.005
Blood loss	Median 100 ml (IQR 50–275 ml)	Median 400 ml (IQR 150–200 ml)	0.03
Conversion	Nil	3 (15 %)[b]	n.a
Complications	1 (5.2 %)	2 (10 %)	0.58
	postoperative bleed	1 pneumothorax	
		1 bile leak	
R1 resection	1 (5.2 %)[a]	2 (10 %)	0.73
Length of stay	Median 4 days (range 1–8 days)	Median 4 days (range 1–57 days)	0.30

LLR laparoscopic liver resection, *IQR* interquartile range

[a] This margin was re-resected at R-LLR

[b] Two due to bleeding and one to assess tumor invasion of diaphragm

Table 2 Comparison of primary and repeat laparoscopic minor liver resection

	Primary LLR minor ($n = 17$)	Repeat LLR minor ($n = 14$)	p value
Operative time	Mean 155 min (IQR 70–195 min)	Mean 246 min (IQR 161–345 min)	0.03
Blood loss	Mean 294 ml (IQR 56–287 ml)	Mean 452 ml (IQR 100–550 ml)	0.44
Conversion	Nil	1 (7 %) due to bleeding	n.a
Complications	Nil	1 (7 %) bile leak	n.a
R1 resection	1 (6 %)[a]	1 (7 %)	1.0
Length of stay	Median 4 days (range: 1–8 days)	Median 4 days (range: 1–57 days)	0.28

[a] This margin was re-resected at R-LLR

P-LLR group, one patient required reoperation for bleeding, and in the R-LLR group one patient had a pneumothorax. The average length of stay was 5.5 days in both groups. One patient with HCC in the R-LLR group had a positive margin.

Conversions

There were three conversions (15 %) in the R-LLR group. Two patients required conversion to control bleeding and one patient to achieve clear margins at segment 4A, where a CRLM was abutting the diaphragm. Both patients who required control of bleeding underwent a right-hemihepatectomy. This included a patient with HCC who had a bleeding from the right adrenal vein and a patient with CRLM and bleeding from middle hepatic vein territory.

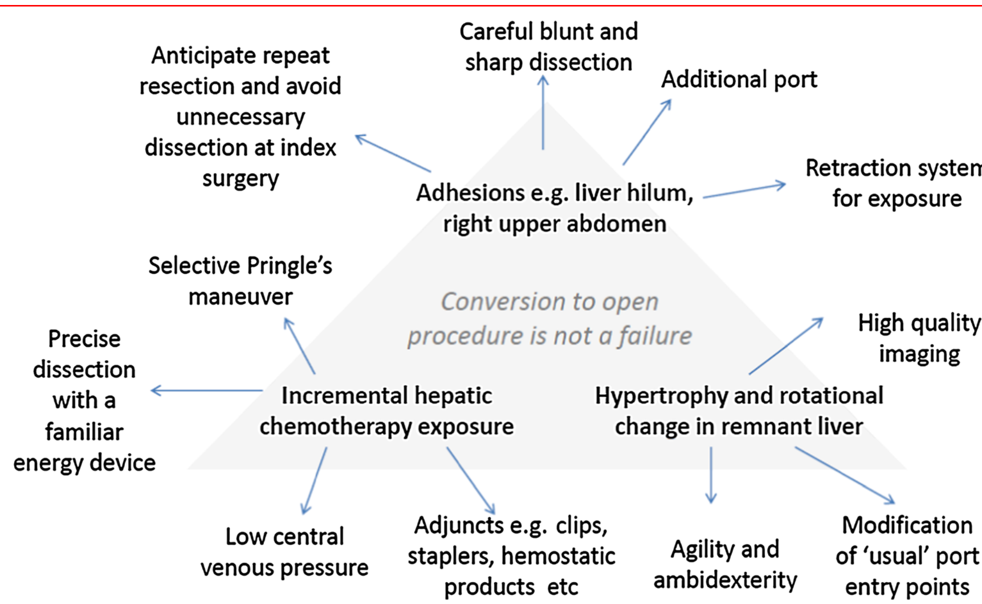
Complications after repeat laparoscopic liver resection

Two patients (10 %) developed complications after R-LLR. One patient with a HCC and previous multiple wedge resections developed an intraoperative pneumothorax during R-LLR right hemi-hepatectomy. In this patient, tumor was infiltrating the right hemi-diaphragm and hence there was a breach of the pleural cavity to achieve the negative margins. Another patient with CRLM who had one previous R-LLR right hemi-hepatectomy (i.e., two previous liver resections) 2 years earlier developed a bile leak following a wedge resection. This was managed conservatively.

Discussion

Repeat liver resections are increasingly being offered to patients due to multidisciplinary management of metastatic disease with improved chemotherapeutic regimens, improved imaging, and improved surgical technique, including parenchyma-sparing surgery, two-stage resections, and portal vein embolization [21]. We demonstrated that R-LLR is safe and feasible but technically more

Fig.1 Factors affecting repeat laparoscopic liver resection



challenging than P-LLR. Our results showed a longer operative time and increased blood loss in R-LLR, but without a negative impact on complication and length of hospital stay when compared to the P-LLR procedures performed on the same group of patients. This effect persisted in the subgroups of minor or major resections. Operative time and blood loss are likely increased from the interplay of three factors in R-LLR: adhesions, incremental hepatic chemotherapy exposure, challenging anatomy due to hypertrophy and rotational change in the liver. Figure 1 illustrates the role of these three factors and perioperative strategies to deal with them.

Conversion rates for P-LLR are 2.4–9.6 % in various published series [1, 3, 5, 10]. We had no conversions in our P-LLR group but three conversions (15 %) in the R-LLR group, one of which was in R-LLR minor. Shafaee et al. [17] had an overall conversion rate of 11 and 16 % (4/31) when R-LLR was done following a previous laparoscopic and open liver resection, respectively. It appears that P-LLR reduces conversion rates for R-LLR. This is most likely because of fewer adhesions and less scarring following a P-LLR compared to open liver resection. Belli et al. reported on safety and feasibility of laparoscopic reintervention (surgery and radiofrequency ablation) for HCC and cirrhotic patients. In their small series of 15 patients, they observed that patients who had previous LLR had fewer adhesions compared to patients with previous open liver surgery [15]. The perioperative complication rate is higher with lengthy preoperative chemotherapy and is likely related to the prolonged and sequential use of multiple regimens [22]. Two patients (10 %) developed complications following R-LLR; one patient (5.2 %), following P-LLR. This rate is lower than previously reports results in R-LLR [15, 17], but interestingly is in line with the 12.6–18 % rates published for P-LLR [1, 3, 5, 10].

There were no conversions in the P-LLR group, whereas one R-LLR procedure was converted. It has been suggested that loss of tactile feedback and inadequate visualization of posterior/superior segments of liver may compromise resection margins in LLR. However, our R0 resection rate is 90 % (excluding NETLM patients). Similar results were reported by Shafaee et al. (R1 rate of 8 %) [17]. One patient with a HCC requiring right hemi-hepatectomy had a positive margin. The other patient with a positive margin was a patient who had a previous R-LLR right hemi-hepatectomy (i.e., the third laparoscopic liver surgery for this patient) 2 years earlier for CRLM. Both these patients also required a conversion to open surgery for technical reasons. There was no difference in median length of stay in our two groups at 4 days, which is among the lowest reported for R-LLR [16, 17]. This is may reflect our tendency to encourage early discharge and our recent introduction of enhanced recovery program after liver surgery.

We recognize that this is a small, retrospective study, but understandably it is not easy to obtain large series as R-LLR is a demanding procedure with inherent technical challenges. It is not commonly performed, even in a high volume unit such as ours. Ours is the first study to compare primary and repeat LLR for minor resections in the same group of patients and by the same group of surgeons. However, larger multicenter reports are needed to confirm the findings and help in giving future guidance on indication and patient selection.

In conclusion, our results confirm that, even in expert hands, R-LLR is associated with significant intraoperative difficulties when compared to P-LLR. This is reflected by a higher operative time, blood loss, and conversion rate. Interestingly, it appears that R-LLR has no impact on postoperative outcomes, including mortality, morbidity, and hospital stay. Clearly, patient selection, advanced experience, and meticulous dissection techniques are essential pillars to ensure patients safety and good outcomes. With the increase seen in P-LLR, the use of R-LLR is likely to increase in the coming years.

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