Laparoscopic Liver Resection: Is There a Learning Curve?

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Abstract

Background: Laparoscopic liver resection (LLR) is becoming an accepted treatment option for resecting both benign and malignant tumours. However, it is critical that the laparoscopic approach does not compromise the technical quality of the liver resection. The aim of this paper was to review the learning curve of LLR in a specialist HPB unit. Methods: A prospective database was searched to identify patients undergoing LLR over a 4-year period. To assess the effect of the learning curve on outcome, the series was evaluated during two eras – early versus late. Results: Fifty-one (27 males, median age 68 years) patients were identified with 37 having LLR. The most common indication was for colorectal liver metastases, and the most common procedure was a non-anatomical metastectomy. Changes in management decisions (n = 14) occurred more frequently during the first era (9 vs. 5; p > 0.05). More patients underwent right hepatectomy in the late group (3 vs. 1; p < 0.05). There did not appear to be any difference in duration of surgery for laparoscopic left lateral resection between the eras (200 vs. 240 min; p > 0.05) which probably reflected trainees performing more operations during the late era. Left hepatectomy was most commonly performed in the early era compared to more right hepatectomies during the late era. Conclusion: LLR is associated with a learning curve, but once this has been overcome it can be safely utilised in the management of malignant liver lesions even for major resections, surgical training and simultaneous resections.

Key Words
Laparoscopic liver resection • Cirrhosis • Colorectal metastasis • Liver metastasis • Liver

Introduction

The first laparoscopic liver resection (LLR) for benign disease was described almost 20 years ago by Gagner et al. [1]. Since then, over 3,000 cases have been reported in the literature [2]. Initially, this procedure was limited to patients with symptomatic benign disease, but now it is becoming an accepted treatment for patients with malignant disease representing almost 50% of those reported in various case series [2, 3]. In 2008, an expert consensus conference was held to determine the role of LLR in contemporary practice. The conclusions of this meeting were that LLR can be safely performed in specialist HPB units, but the validity of the approach still needs to be carefully scrutinised [4].

In the West, the most common indication for liver resection is colorectal liver metastases (CRLM) with overall 5-year survival rates of 60% being reported [5–9]. Multi-
variate analysis has demonstrated that the ability to achieve an R0 resection is one of the most important prognostic variables in patients undergoing resection of CRLM [10, 11]. One study has addressed this in detail in a non-randomised study comparing 120 patients. There does not appear to be any difference in overall 5-year survival in those having either LLR or open resection in terms of disease free survival [12]. Most studies report no difference in R0 resection rates and no increased risk of a positive margin after LLR when compared to open resection [13]. Nonetheless, a recent meta-analysis suggests the risk of a resection margin of less than 1 cm is twice as high after LLR than for open resection, but no overall difference could be found in the number of positive margins compared to open resections [14]. Indeed, R1 resection rates of up to 43% have been reported [15], and non-segmental resections LLR may have higher recurrence rates when compared to anatomical resections (41.9 vs. 39%) [16]. A key requirement therefore when performing LLR is that the technical quality of the resection is not compromised by the choice of surgical approach. The aim of this study was to review the learning curve of LLR in our specialist HPB unit.

Methods

A prospectively maintained electronic database of patients entered into the Freeman Hospital laparoscopic liver program was identified (April 2007 to June 2011). Prior to surgery, all patients were discussed in a multidisciplinary team comprising surgeons, radiologists, histopathologists and oncologists. The choice of what type of resection to use was also discussed (e.g. LLR or open). Patients having deroofing of cystic liver lesions and intentional laparoscopic RFA at the time of listing were excluded from analysis. A further 41 patients having LLR by other HPB surgeons were excluded into the Freeman Hospital laparoscopic liver program was identified (April 2007 to June 2011). Prior to surgery, all patients were discussed in a multidisciplinary team comprising surgeons, radiologists, histopathologists and oncologists. The choice of what type of resection to use was also discussed (e.g. LLR or open). Patients having deroofing of cystic liver lesions and intentional laparoscopic RFA at the time of listing were excluded from analysis. A further 41 patients having LLR by other HPB surgeons were excluded from analysis. A total of 51 eligible patients were identified. In order to assess the role of the learning curve in developing the laparoscopic approach, the series was split into two halves with those operated on prior to 1 August 2009 being considered as the early group, whereas those operated on after this date were considered the late group.

For all patients, the extent of the hepatic resection, duration of surgery, conversion to open surgery, resection margins and perioperative complications were recorded. The latter were classified according to the Dindo and Clavien Classification [17].

Statistical Analysis

Numerical data are expressed as the median value (range). Categorical variables were compared with χ² test. Continuous data were compared with a two-tailed Mann Whitney U test. Statistical significance was set at a level of p = 0.05.

Results

Patient Characteristics

A series of 51 patients were identified (24 males, 27 females; median age 68 years, range 23–83 years). The most common indication for liver resection was CRLM (n = 38), lymphoma (n = 1), atypical on cross-sectional imaging, cholangiocarcinoma (n = 2) one found incidentally in a patient thought to have a CRLM, focal nodular hyperplasia (n = 4) in 2 patients having cholecystectomy with an adjacent liver abnormality and another patient with a previous history of colorectal cancer, hepatocellular cancer (n = 1), biliary cystadenoma formerly resected and not deroofed (n = 1), hepatic adenoma (n = 2), arteriovenous malformation (n = 1; not resected in a patient with previous colorectal carcinoma atypical on all preoperative imaging modalities), and haemangioma (n = 1) in a patient with a previous colonic carcinoma and despite MRI/CT and CEUS was considered atypical.

From the original 51 patients, operative decision-making was changed in 14 patients at the time of laparoscopy and prior to any liver transection. One patient did not tolerate a pneumoperitoneum and underwent ablative therapy at the same sitting (n = 1), 2 patients had tumours which were very posterior in segment VII (n = 2) and difficult to access both immediately converted to open, disease progression procedure abandoned (n = 3), tumour too big for lap resection both >10 cm (n = 2), laparoscopic ultrasound dysfunction (n = 1) therefore converted to open, prolonged laparoscopic anterior resection (CR), therefore simultaneous LLR abandoned in favour of ablative therapy (n = 1), absence of metastasis in a patient having had a previous anterior resection for colon cancer with laparoscopic ultrasound confirming an arteriovenous malformation (n = 1) and finally laparoscopic left lateral resection abandoned because of adhesions (n = 1). Only two patients were converted to open procedures during liver transection both because of concerns over the resection margin (both during era one). Changes in management decisions were less during the second era compared to the first, but did not reach statistical significance (9 vs. 5).

Surgical Procedures and Technique

The most common surgical procedure performed in both groups was a non-anatomical liver resection (metastectomy). Numbers were no different between eras (8 vs. 10). It is interesting to note that there were more left hepatectomies performed in the early group as compared to the late (3 vs. 0; p = 0.056), whilst in the late group more
patients underwent right hepatectomy (1 vs. 3; \( p < 0.05 \)). This is probably not surprising given that laparoscopic right hepatectomy is technically more demanding than left hepatectomy. Two of the right hepatectomies were hybrid procedures where all hilar dissection was completed laparoscopically and a small incision was made to assist parenchymal transection. In both these patients this was due to time constraints (beyond 5 h). All left hepatectomies were completed totally laparoscopically. The types of liver resections performed are summarised in table 1. Additional procedures performed simultaneously included laparoscopic right adrenalectomy, laparoscopic abdomino-perineal resection and a laparoscopic anterior resection. There was not any difference in operative duration for left lateral resections between eras; era 1, median 200 min (range 165–240) versus 240 min (range 120–300; \( p = 0.220 \)). However, as expected, major resections (left/ right hepatectomy) took significantly longer; median 420 min (range 270–510; \( p < 0.01 \)).

When undertaking resection of the left lateral segment or resection of lesions in the anterior segments (i.e. II, III, IV, V, VI), patients are generally positioned supine with the legs split to enable the operating surgeon to stand in between (fig. 1). It is our policy to preserve as much liver as possible, and therefore isolated metastases in the left lateral segment are treated by metastectomy as opposed to a formal left lateral resection as tumour recurrence in the right lobe could potentially limit subsequent resection options. For resection of lesions in the posterior segments, patients are positioned in the left lateral decubitus position (fig. 2), and sometimes the operating table is split to increase intra-abdominal operating space. The split legs position is also preferred when undertaking major hepatectomy; however, for a right hepatectomy it is useful to rotate the operating table slightly right side up and use a support wedge such that the patient’s right upper quadrant is slightly elevated.

When operating in the split leg position, an initial 12-mm port (ENDO PATH Xcel™, Ethicon Endosurgery, LLC, USA) is placed at the umbilicus using an open technique, and carbon dioxide pneumoperitoneum established at a pressure of 12 mm Hg. Pressures higher than this are generally avoided to reduce the risk of gas embol...

Table 1. Summary of types of liver resections performed

<table>
<thead>
<tr>
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<th>Early group (n = 18)</th>
<th>Late group (n = 19)</th>
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<tr>
<td>II/III (not full left lateral)</td>
<td>2</td>
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<tr>
<td>IV</td>
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<td>VI/VII</td>
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<td>VIII</td>
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<td>Left lateral sectionectomy(^a)</td>
<td>6</td>
<td>6</td>
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<tr>
<td>Left hemi-hepatectomy(^b)</td>
<td>3</td>
<td>0</td>
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<tr>
<td>Right hemi-hepatectomy(^b)</td>
<td>1</td>
<td>3</td>
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\(^a\) LLS + non anatomical resection (n = 3).

\(^b\) 2× laparoscopic assisted.

Fig. 1. Preferred position for most laparoscopic resections in the anterior segments.

Fig. 2. Position for tumours placed in the posterior segments.
lism but a slight rise during bleeding can aid haemostasis [18]. Sometimes, it is necessary to position the umbilical port higher up in patients where the distance between the umbilicus and Xiphoid is greater than 15 cm as the hepatic veins can be beyond the distance of acceptable camera visibility and instrumentation. Following placement of the umbilical port, a standard staging laparoscopy is performed to exclude the presence of significant extra-hepatic disease using a 30° laparoscope (EndoEye HD, Olympus Europa, Hamburg, Germany). Four other working ports are then usually placed as demonstrated in figure 3, i.e. a 12-mm port in both the right and left mid-clavicular line and a 5-mm port in both the right and left anterior axillary line. For right hepatectomy, ports are positioned to the right as far as the mid axillary line (fig. 4). For tumours located high up in the dome of the liver (VIII) near the diaphragm, an extra 10-mm port is often required at the Xiphisternum to allow for parenchymal transection with the CUSA (CUSA™, Integra, Saint Priest, France)

Following port placement, intra-operative ultrasound is performed utilising a laparoscopic probe (7.5 MHz, Aloka Co. Ltd., Tokyo, Japan) to locate the tumour and accurately assess its margins and also to locate any adjacent biliary/vascular structures. Next, the liver is retracted either utilising a Nathanson hook (5 mm) during the first era (as is used in a laparoscopic fundoplication), but now a laparoscopic retractor such as a Diamond Flex (Surgical Innovations Ltd., Leeds, UK) is more commonly used (5 mm). Once adequate exposure has been obtained, the pars lucida is opened and a nylon tape placed around the hepato-duodenal ligament with the aid of a ‘Gold finger’ (Gold finger™, Blunt Dissector and Suture Retrieval System, Ethicon Endosurgery, LLC, USA) as previously described [19]. A Pringle tape was placed in all but one patient. It was necessary to use this manoeuvre in only 15 of 37 patients (median 30 min, range 5–60 min). There was no difference in Pringle use between eras.

When undertaking a major hepatic resection, the hilum is dissected with extra-hepatic division of all major vascular structures with the aid of Hem-o-lok clips (Weck Closure, System, North Carolina, USA) (preferred method) or a reticulating vascular stapler (Endo TA, Covidien, Norwalk, Conn., USA). It is our preference to divide the bile duct intra-hepatically with a vascular stapler to avoid injury to the remnant hepatic duct [20]. Parenchymal dissection is performed with a cavitation ultrasonic aspirator (CUSA) in addition to a ACE harmonic scalpel (Ethicon Endosurgery Inc., Blue Ash, Ohio, USA) or more recently LOTUS torsion (SRA Developments Ltd., Devon, UK) or a Ligasure device (Covidien). Where necessary, large hepatic veins can be divided using either a roticulating vascular stapler or locking Hem-o-lok clips. Upon completion of parenchymal transection, and once haemostasis has been confirmed, the specimen is retrieved through a lower abdominal Pfannenstiel incision utilising an ENDO CATCH II bag (ENDO CATCH™, Covidien). If there are dense adhesions in the pelvis, then a portion of the old midline incision from the previous colectomy can sometimes be re-opened to remove the specimen.
Sometimes, a hand port is necessary to facilitate dissection, particularly during major hepatic resections e.g. right hepatectomy. When required this is normally placed in the right iliac fossa (fig. 5). They are also useful for controlling any bleeding and also to assist in major resections as the liver can be difficult to manipulate. However, a hand port was not used in this series.

**Combined Hepatic and Extra-Hepatic Procedures**

Up to 25% of patients presenting with a primary colorectal cancer have synchronous metastatic disease at the time of diagnosis [21]. In patients with resectable CRLM, either initially or after downstaging chemotherapy, one strategy for dealing with this is to perform a simultaneous liver and colonic resection [22, 23]. As our experience of LLR has increased, we have been able to utilise simultaneous liver and colorectal excision more effectively. Nonetheless, if surgery is prolonged management decisions may need to be changed. For example, one patient went on to have ablative therapy instead of LLR because of prolonged anaesthesia for the laparoscopic anterior resection.

**Patient Outcome**

There have been concerns raised regarding the status of resection margins during LLR. Indeed, early in the series the reason for conversion in 2 cases was the tumour lying close to major vascular structures and concern about the integrity of the margin. As the series has evolved, this has become less of a problem with a current R1 margin status of 7% for CRLM. This is because of better patient selection, avoiding tumours near major vascular structures and continued use of intra-operative ultrasound during parenchymal transection. In our series, tumour margins have been positive because of adjacent satellite lesions residing slightly away from the tumour that cannot be easily visualised on intra-operative ultrasound and where a tumour may extend down into a bile duct that is also not evident on intra-operative ultrasound. Tumours with extensive peri-neural or peri-vascular involvement can also be problematic. Figure 6 demonstrates overall survival in our series of patients with CRLM.

It is difficult to discuss the effect of LLR on reducing hospital stay. This is because some patients had multiple procedures which had an effect on overall stay. Most patients having metastasectomy or laparoscopic left lateral resection appear to have a reduced stay (median 3 days, range 1–15) when compared to those having more extensive resections (e.g. right and left hepatectomy). For major LLR, it is difficult to demonstrate any benefit in terms of hospital stay (median 11 days, range 3–23), although numbers are small (n = 7; p < 0.01). There were no deaths during either era. In those patients having a completed LLR, only 4 patients experienced a complication, 2 required laparoscopic washouts postoperatively (grade
IIIb), urinary tract infection (n = 1; grade II) and a bile leak treated conservatively (n = 1; grade II).

**Additional Procedures**

Some patients required additional resections. One patient who underwent laparoscopic clearing of CRLM in the left lateral segment underwent subsequent radiological portal vein embolisation, and extended right hepatectomy (open) 5 weeks later. Six (16%) other patients underwent repeat surgery ranging from 6 to 17 months later for recurrent disease, two of which were abandoned because of disease progression.

**Discussion**

As our experience with LLR has improved over time, we have been able to embark on more complicated procedures such as combined hepatic and colonic resections whilst achieving a reduction in the number of procedures that need to be converted to an open procedure or change in management decision. With advances in chemotherapy, more patients are becoming operable with their primary tumour still in situ, as their liver disease can be controlled, and it is likely that this cohort of patients will increase in the foreseeable future. In addition, our willingness to undertake more technically demanding laparoscopic right hepatectomy has increased during this series. However, without a hand port most authors still report operating times in excess of 6 h [24] for right hepatectomy. It is imperative that these patients have a very careful pre-operative assessment because of the need for a prolonged pneumoperitoneum.

Most studies of LLR report a learning curve. How long that learning curve is depends on the surgeon’s previous training and the types of resection. Small resections less than 2 cm require little additional skill to that needed for a complex laparoscopic cholecystectomy when positioned in the anterior segments V and IV or left lateral segment, on the proviso the surgeon has completed a recognised training program in HPB surgery and is a competent laparoscopic surgeon. For more major resections, e.g. right hepatectomy or left hepatectomy, the bar is significantly raised and should only be attempted by surgeons who regularly perform complex laparoscopic procedures, who are regarded as laparoscopic HPB specialists. The main limiting factor for these resections is technical difficulty and surgical access. Some would suggest that increasing size of tumour is not a limiting factor [25], but this is not what has been recommended in the Louisville guidelines [4], and in the authors’ experience larger tumours have proven to be more difficult to manipulate laparoscopically and require much larger incisions to remove them subsequently removing the benefits of a minimally invasive procedure.

It cannot be denied that not everyone is suitable for a LLR. Most centres suggest that up to 30% [26, 27] are suitable, although those centres performing more major resection regularly report higher rates of up to 80%, but these are often with the aid of hand-assisted techniques [28, 29]. From a previous series of 174 patients undergoing LLR, it has been demonstrated that increasing experience is associated with a reduction in operating time, conversion rate, blood loss and operative morbidity whilst at the same time performing more complex resections and more resections for malignant disease. Some authors suggest that a learning curve of approximately 60 cases is required to become fully familiar with the techniques of LLR [30] as suggested by others [26, 31]. However, more latterly some of the cases reported in the current series have been done by senior HPB surgical trainees under consultant supervision making the learning curve within this series more difficult to evaluate.

Once this learning curve has been overcome, we know from a recent meta-analysis that in appropriately selected patients, LLR is associated with reduced operative blood loss, fewer complications, a reduced hospital stay and a lower R1 resection rate when compared to open surgery although the operating time is often slightly longer [14, 32]. Nonetheless, in this series it was difficult to demonstrate any advantage in those patients who had major resection in terms of shorter hospital stay, although the numbers were perhaps too small to draw any useful conclusions.

The question therefore remains of how best to ensure surgeons are equipped to rapidly progress along the learning curve and become proficient at LLR. Various simulation models such as the LapSim virtual reality simulator, porcine or canine models have been developed in an attempt to address some of these issues and these are discussed in detail elsewhere [33–35]. An alternative approach which has been developed in Newcastle is the use of a cadaver training facility in a high specification ‘wet lab’. The advantages of this approach over other methods of simulation include similar tissue consistency and flexibility, identifying accurate anatomical landmarks and the ability to achieve near-perfect replication of critical operative steps. This ‘realistic’ training allows surgeons to find their equipoise when more complex cases such as right hepatectomy are being taught, in

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Harmonic Scalpel

Harmonic ACE®. The Harmonic Scalpel cuts and coagulates by using ultrasound and is good for going through the liver capsule at the start of LLR. Vessels are coapted (tamponaded) and sealed by a protein coagulum. Coagulation occurs by means of protein denaturation when the blade, vibrating at 55,500 Hz, couples with protein, denaturing it to form a coagulum that seals small coapted vessels. The newer Harmonic ACE version appears to be more effective in that it is faster and seals vessels up to 5 mm in diameter and seals up to twice systolic pressure. However, after a 15-second application, heat can reach 140°C up to 1 cm away from the tip causing significant lateral thermal damage away from the tissues being sealed [37]. Their powerful compression forces are directed at the tip of the device as well [38]. Newer generation devices include the LOTUS Torsion™ which uses torsional ultrasound which transfers less energy to adjacent structures. The torsional waveform is thought to be safer as there are only weak frictional forces at the tip of the active blade which reduces distal drilling and tissue charring. The device which utilises low voltage bi-polar radiofrequency energy seals vessels up to 7 mm in diameter up to 3 times systolic pressure and monitors changes in tissue impedance and adjusts the energy output accordingly causing less collateral tissue damage to within 1.5 mm of the grasping jaws [39]. Tissue Link works using transcollation (transforming collagen) technology sealing small biliary radicals with no charring and a bloodless field. This device delivers radiofrequency energy and salines simultaneously to achieve temperatures of 100°C [40]. A disadvantage is that it is slower than the ACE and LOTUS and is also more expensive. A cheap and effective method is bipolar diathermy which gives good haemostasis on the liver parenchyma using a power of up to 80 Watts. There have been concerns regarding argon beam coagulation and gas embolism [41] because of the stream of argon gas when the instrument is activated on the liver parenchyma adjacent to open blood vessels. It is strongly advisable not to use argon beam coagulation in this situation. Various techniques might be needed at different stages of the operation, and therefore a working knowledge of all available tools is useful.

In summary, LLR offers many advantages over conventional open surgical approaches in a select group of patients. Our experience, in keeping with that of others, is that this technique is associated with a learning curve that can be overcome by cadaver lab training in conjunction with progressive operative experience.

References

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