Laparoscopic liver resection for malignancy: A review of the literature

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Abstract

AIM: To review the published literature about laparoscopic liver resection for malignancy.

METHODS: A PubMed search was performed for original published studies until June 2013 and original series containing at least 30 patients were reviewed.

RESULTS: All forms of hepatic resections have been described ranging from simple wedge resections to extended right or left hepatectomies. The usual approach is pure laparoscopic, but hand-assisted, as well as robotic approaches have been described. Most studies showed comparable results to open resection in terms of operative blood loss, postoperative morbidity and mortality. Many of them showed decreased postoperative pain, shorter hospital stays, and even lower costs. Oncological results including resection margin status and long-term survival were not inferior to open resection.

CONCLUSION: In the hands of experienced surgeons, laparoscopic liver resection for malignant lesions is safe and offers some short-term advantages over open resection. Oncologically, similar survival rates have been observed in patients treated with the laparoscopic approach when compared to their open resection counterparts.

INTRODUCTION

Twenty-years after the first reported laparoscopic liver resection by Gagner et al., there has been an exponential growth of reports of laparoscopic liver resections but the results are yet to be fully elucidated.

Although initially described for benign and peripheral lesions, 50% of overall laparoscopic liver resections are now performed for malignant lesions and a growing number of centers are now performing major resections, including right and left hepatectomies, in North America, Europe, and Asia.

The purpose of this study is to review the published literature on laparoscopic liver resection for malignant lesions. We will discuss the different types of resection, the most common as well as the innovative techniques, the surgical outcomes, postoperative complications, and oncologic results.
MATERIALS AND METHODS
A PubMed search was performed for original published studies until June 2013. Articles were selected using the indexing terms “hepatectomy”, “laparoscopy”, and “liver neoplasm/surgery”. Keyword search for “laparoscopy”, “laparoscopic”, “hepatectomy”, “resection”, “liver cancer”, “liver neoplasm”, “liver tumor”, “hepatic cancer”, and “hepatic neoplasm”. Large series with more than 30 patients with malignant lesions were included. Reported procedure other than resection, such as radiofrequency ablation and cyst fenestration were excluded.

RESULTS
About 43 studies with more than 30 patients who underwent laparoscopic resection for liver malignancy were identified. No randomized clinical trials were available. Most data were reported as case series or case-control studies. Although the first large series was in 2002, the vast majority of reports were published in and after 2009. In this review, we analyzed preoperative findings such as indications and tumor size, intraoperative findings like blood loss and operative time, short-term outcomes, as well as oncologic outcomes (Table 1).

DISCUSSION

Indications and contraindications of laparoscopic liver resection
As with open surgery, hepatocellular carcinoma (HCC) and colorectal metastasis (CRM) are the main indications of malignant tumor resection [2,16,18]. Much less commonly, resections of cholangiocarcinoma, lymphoma, and non-colorectal liver metastasis (e.g., neuroendocrine tumors, breast cancer, and renal cell carcinoma) have been performed [2,13,15,18].

In patients who cannot tolerate pneumoperitonium due to their cardiopulmonary status and those with adhesions that cannot be lysed laparoscopically, laparoscopic liver resection is contraindicated. Relative contraindications are in patients with lesions adjacent to the inferior vena cava or major vessels, in whom there is a need for biliary and/or vascular reconstruction, those with hilar lesions or in those with resections that require an extensive portal lymphadenectomy [15,19,20]. Although considered a contraindication for laparoscopic resection by a large number of surgeons, successful minimally invasive approach to gallbladder cancer has been performed in 7 patients published in two papers with no reports of port site metastasis [20,28].

Minor resection
Minor resections including segmentectomy, subsegmentectomy, and wedge resections are the most common type of laparoscopic liver resection performed. Left lateral sectionectomy (LLS) which was first reported by Azagra et al. [21], is by far the most frequently reported anatomic resection given easy visualization of the lesions with laparoscopy, peripheral location of the intended resection area, and the ease of controlling the left hepatic vein. Inagaki et al. [22] reported 30 LLS for hepatocellular carcinoma using Hand-assisted technique. They postulated 2 advantages to the Hand-assisted technique; First, better visualization of the surgical field and the transected margin with direct manipulation by the surgeon’s hand, and second, immediate hemostasis by depressing the bleeding point and proper application of hemostatic instruments.

Major resection
After the first reported cases of laparoscopic major hepatectomy by Hüscher et al. [23] in 1998, an increasing number of series describing major resections have been reported [6,13,14,17,23,25-27,47,48].

In the largest series of major hepatectomies of 210 patients, 136 with right hepatectomies and 74 with left hepatectomies, Dagher et al. [24] showed a mean operative time of 250 min, with mean EBL of 300 mL. The mortality in that series was 1%.

Gumbs et al. [49,50] reported the first laparoscopic extended left hepatectomy as well as the first laparoscopic extended right hepatectomy in 2008. The patient who underwent laparoscopic extended right hepatectomy had gallbladder adenocarcinoma and underwent preoperative portal vein embolization followed by totally laparoscopic extended right hepatic resection with preservation of segment IVa and the left half of IVb due to concerns of postoperative hepatic reserve. A total of 3 patients underwent laparoscopic extended left hepatectomy. One patient suffered a bile leak that was treated with endoscopic biliary stents.

Three large series have also included patients who underwent extended hepatectomy [14,26,28]. The papers showed that extended hepatectomy can be safely performed when undertaken by experienced surgeons and with careful patient selection.

Uncommon resections and novel approaches
While laparoscopic resection of lesions in segments 2-6, the so called “laparoscopic liver segments” have been widely performed, posterior and superior lesions have been classically unamenable to laparoscopic resection. This has changed in the last 6 years.

In a series of 300 patients, including 103 with malignant liver tumors, Koffron et al. [48] reported 8 caudate lobectomies, 2 of which were for cancer. Cho et al. [51] documented 10 right posterior segmentectomies in a series of 71 patients with hepatocellular carcinoma and colorectal metastasis.

Abu Hilal et al. [52] reported 2 cases of pure laparoscopic en bloc left hemihepatectomy and caudate lobe resection for intrahepatic cholangiocarcinoma. The first patient’s operative time was 360 min and blood loss was 390 mL. The second patient’s operative time was 310 min and blood loss was 300 mL.

Hu et al. [53] reported a case of multiple hepatic colorec-
| Year | Ref. | n   | HCC | CRM | GB | CA | Cholangiocarcinoma | Length of stay (d) | Margin (cm) |
|------|------|-----|-----|-----|----|----|--------------------|-------------------|-------------|
| 2013 | [23] | 57  | 55  | 55  | 53 | 53 | 53                 | 15.6              | 12          |
| 2012 | [21] | 62  | 62  | 62  | 62 | 62 | 62                 | 15.6              | 12          |
| 2012 | [23] | 62  | 62  | 62  | 62 | 62 | 62                 | 15.6              | 12          |
| 2012 | [21] | 62  | 62  | 62  | 62 | 62 | 62                 | 15.6              | 12          |
| 2012 | [21] | 62  | 62  | 62  | 62 | 62 | 62                 | 15.6              | 12          |
| 2012 | [21] | 62  | 62  | 62  | 62 | 62 | 62                 | 15.6              | 12          |
| 2012 | [21] | 62  | 62  | 62  | 62 | 62 | 62                 | 15.6              | 12          |
| 2012 | [21] | 62  | 62  | 62  | 62 | 62 | 62                 | 15.6              | 12          |
| 2012 | [21] | 62  | 62  | 62  | 62 | 62 | 62                 | 15.6              | 12          |
| 2012 | [21] | 62  | 62  | 62  | 62 | 62 | 62                 | 15.6              | 12          |
| 2012 | [21] | 62  | 62  | 62  | 62 | 62 | 62                 | 15.6              | 12          |

**Table 1.** Published studies of laparoscopic liver resection for malignancy

- **Ref.**: Reference number
- **n**: Number of patients
- **HCC**: Hepatocellular carcinoma
- **CRM**: Cholesterolosis
- **GB**: Gallbladder adenocarcinoma
- **CA**: Cholangiocarcinoma
- **Length of stay (d)**: Days
- **Margin (cm)**: Millimeters

Operative time; LOS: Length of stay; Margin: Resection margin size; Pos: Positive margin rate; R0: R0 resection rate.
ental metastases of the left lateral and right posterior segments who underwent laparoscopic partial hepatectomy of the right posterior segment using a retroperitoneal approach, followed by laparoscopic hepatic left-lateral segmentectomy using a transabdominal approach. The operative time was 120 min, blood loss volume was 150 mL and the patient was discharged on postoperative day 9.

**Hand-assisted technique**

Hand-assisted technique entails the creation of a 7-8 cm incision that would allow the operating surgeons’ hand access to the abdominal cavity through a gas-tight port. The theoretical advantages of the hand-assisted technique is the ability to apply liver traction and mobilization, palpate the liver with tactile feedback, and help achieve hemostasis by applying compression.

The Hand-assisted technique has been proposed to provide a safer and more attainable approach to laparoscopic resection. The application of the hand-assisted technique has been proposed to help with difficult resections like those involving the posterior-superior segments. In their published series in 2007, Koffron et al. reported 103 patients with laparoscopic liver resection. In 6% of the patients a conversion from a totally laparoscopic to hand-assisted surgery was necessary while the conversion to open surgery was nil. They suggested that the use of hand-assistance may help prevent conversion to open surgery. However, there is no consensus on the usefulness of the hand-assisted technique as other authors have doubted its usefulness.

**Robotic resection**

Robotic laparoscopic resections are now well reported in the literature. While the technique of port placement is different from laparoscopic surgery, most studies have showed encouraging results with comparable results to laparoscopic approach. In a series of 70 patients, 42 of which had malignant lesions, Giulianiotti et al. reported 4 conversions to open surgery (5.7%), a median operative time for a major resection of 313 min and 198 min for minor resection, median blood loss of 150 mL for minor resection and 300 mL for major resection. The rate of complications was 21%, while the mortality rate was 0%.

In a matched analysis study, Daouadi et al. showed that patients undergoing robotic liver resection had longer operative times when compared to laparoscopic resection (253 min vs 199 min), however, the robotic approach increased the percentage of major hepatectomies that were completed in a purely minimally invasive approach. There was no difference between the two groups in terms of other surgical outcomes like blood loss, resection margin, and 3-mo mortality.

**Outcomes of laparoscopic liver resection**

**Operative blood loss**: Due to the heterogeneity of the reported cases, blood loss was highly variable in different studies. Average blood loss ranged between 50 to 700 mL. Daghet et al. and Otsuka et al. showed that with late experience, blood loss was significantly lower than in early cases, i.e., surgeons had lower blood loss during laparoscopic resection with more procedure performed. Six studies have showed that laparoscopic resection was associated with lower blood loss than open surgery. Martin et al. showed lower rates of transfusions in laparoscopic resections when compared to open resections (10% vs 48%).

**Operative time**: In terms of Operative time, the average operative time ranged from 95 to 280 min. Although one study showed increased operative time when compared to open surgery, 3 studies demonstrated decreased operative time in laparoscopic surgery. Daghet et al. showed decreased operative times when early experience is compared to an established technique period. (270 ± 143 min vs 171 ± 95 min, P < 0.001), which points out that there is a learning curve with laparoscopic liver resection.
Conversion to open surgery and length of stay: Conversion to laparotomy rates in the literature ranged from 0% to 19.4%. Koffron et al\(^\text{[35]}\) converted to Hand-assisted technique in 6% of the resections and had 0% conversion to open surgery which signifies that the use of the hand-assisted technique may decrease the rate of conversion to open surgery. Ikeda et al\(^\text{[33]}\) had a 0% conversion rate in a series of 30 patients. In the series published after 2011, conversion rates never exceeded 6%, which also may point to a learning curve effect in laparoscopic liver surgery. The main reasons for conversion were bleeding, adhesions, and inability to complete the resection laparoscopically due to technical or anatomical considerations.

The average length of stay ranged from 4.8 to 13 d in the studies and many of them found a shorter length of stay when compared to open surgery\(^\text{[4,6,24,26,40]}\).

Morbidity and mortality: The average morbidity rate was 5.5% to 27.5%. Common complications included bile leak, liver abscess, and transient hepatic failure. General complications included pleural effusions, pneumonia, urinary tract infection, and cardiac arrhythmia. Lower morbidity as compared to open surgery was observed in many studies\(^\text{[4,6,24,26,40]}\).

Inagaki et al\(^\text{[38]}\) showed markedly decreased rate of pulmonary complications in the patients who underwent laparoscopic resection as compared to open surgery (3% vs 17%).

Mortality rate varied between 0% and 3.7%. Reported causes of death included liver failure\(^\text{[28,30]}\), cerebral infarction secondary to hypotension\(^\text{[1]}\), postoperative hepatorenal failure\(^\text{[7]}\), pseudomembranous colitis, technical clip failure leading to massive hemorrhage\(^\text{[14]}\), acute respiratory distress syndrome\(^\text{[26,31]}\), bleeding from esophageal varices\(^\text{[13]}\), and multi-organ failure\(^\text{[35]}\).

Potential disadvantages: While the safety of laparoscopic liver resection has been documented, possible limitations include the significant learning curve\(^\text{[4]}\), loss of tactile feedback and inability to manually palpate the liver that may cause missing other lesions, and potential bleeding that may be harder to control laparoscopically\(^\text{[2]}\).

Oncologic results

Resection margin: The surgical margins were free of cancer in 87% to 100% of patients in the published studies. The Size of the margin varied with an average ranging between 0.3 cm to 2.08 cm. Topal et al\(^\text{[59]}\) showed a lower rate of positive surgical margin with laparoscopic surgery as opposed to open resection; 1.2% vs 2.1%.

Castaing also showed higher rate of R0 resection with laparoscopic resection 87% compared to open surgery 72%\(^\text{[14]}\). The addition of intraoperative ultrasound was associated with lower rate of positive margins\(^\text{[9]}\). Buell et al\(^\text{[5]}\) reported the only case of port site metastasis in the literature which was in a patient who underwent laparoscopic resection for CRM.

Hepatocellular carcinoma: Hepatocellular carcinoma is the most common primary liver malignancy. 52% of reported laparoscopic liver resections done for malignancy are performed for HCC\(^\text{[3]}\). In the literature, the 3-year disease-free survival was 51% to 62% and the overall 3-year survival ranged from 66.4% to 90.4%. The 5-year disease-free survival ranged from 32% to 46.4%, while 5-year overall survival was 50% to 85.9% (Table 2).

Three studies found no difference in survival between patients with hepatocellular carcinoma who were treated with laparoscopic resection when compared to open resection\(^\text{[32,33,52]}\).

Belli et al\(^\text{[39]}\) showed reduced morbidity, especially postoperative ascites, and a shorter length of stay in cirrhotic patients who underwent laparoscopic resection for hepatocellular carcinoma when compared to those who underwent open resection.

In the largest series of 163 patients with hepatocellular carcinoma treated at 3 European centers by Dagher et al\(^\text{[29]}\), the mean operative time was 180 min, mean estimated blood loss was 250 mL, the mortality rate was 1.2% and the mean resection margin was 1.2 cm. The researchers also found that there has been a decrease in operative time and blood loss, increase in the size of tumors re-

| Ref. | Disease-free survival | Overall survival |
|------|-----------------------|-----------------|
|      | 1 yr | 2 yr | 3 yr | 5 yr | 1 yr | 2 yr | 3 yr | 5 yr |
| Gigot et al\(^\text{[4]}\) | 43.70% |      |      |      | 85.4% | 94.7% | 62.50% |      |
| Chen et al\(^\text{[4]}\) |      | 60.90% | 45.60% |      |      | 66.4% | 74.2% | 59.4% |
| Tranchart et al\(^\text{[4]}\) |      | 60.40% |      |      |      | 90.40% |      |      |
| Yoon et al\(^\text{[6]}\) | 85% | 47% | 38% |      | 96% | 67% | 52% |      |
| Lai et al\(^\text{[4]}\) | 81% | 62% | 32% |      | 95% | 70% | 55% |      |
| Truant et al\(^\text{[4]}\) | 78.80% | 51% | 45.30% |      | 86.90% | 81.80% | 70% |      |
| Lee et al\(^\text{[4]}\) |      |      |      | 70% |      |      |      |      |
| Hu et al\(^\text{[4]}\) | 71% |      |      |      | 81% |      |      |      |
| Yoon et al\(^\text{[5]}\) |      | 52.90% | 46.40% |      | 93.30% | 85.90% |      |      |
| Choi et al\(^\text{[4]}\) |      |      |      | 79.30% |      |      |      |      |

Table 2  Reported survival after laparoscopic resection for hepatocellular carcinoma
sected, and lower rate of morbidity in patients who were operated on in the later experience series[30].

**Colorectal liver metastasis**

Surgery is the only curative option for metastatic colorectal cancer to the liver. 35% of laparoscopic liver resections for malignancy are performed for CRM[30].

The goal of resection in patients with CRM is resection of all liver metastasis with a negative margin but at the same time preserving adequate post-resection liver volume. Liver resection offers long-term survival in up to 60% of patients with CRM[61].

Disease-free survival at 1 year was 61.3% to 81%, but dropped at 5 years to 30% to 42%. Overall survival at 1 year was 88% to 100%, at 3 years ranged from 82% to 88%, and at 5 years ranged from 51% to 64% (Table 3).

Nguyen *et al*[29] reported the largest series of 109 patients with laparoscopic resection for CRM. The mean estimated blood loss was 200 mL, the transfusion rate was 10%, the average length of operation was 234 min, the resection margin was negative in 94.4%, and the conversion rate was 3.7%. Conversion was due to hemorrhage.

Shafae et al[32] showed that the survival rates for patients undergoing repeat hepatectomy laparoscopically were equivalent or even superior to the long-term outcomes of patients undergoing open resection. Two other studies have shown no statistical difference in disease-free and overall survival rates between laparoscopic and open surgery[13,24].

**CONCLUSION**

In conclusion, although laparoscopic liver surgery requires a great deal of experience by hepatobiliary surgeons, this approach is deemed safe for malignant liver lesions with comparable oncological results to open surgery. In addition, it offers better short term results including shorter hospital stay, lower costs, less postoperative pain, and lower complication rates. While operative blood loss has been a major concern with laparoscopic resection, a number of reports is showing that minimally invasive approach is associated with lower risk of bleeding and transfusions. Tumor size is no longer an obstacle to laparoscopic resection, although laparoscopic major hepatectomy is still limited to experienced centers. The disadvantages of the laparoscopic approach are the loss of tactile sensation and palpation of the liver as well as the learning curve that is associated with laparoscopic resection. It should be noted that there has been no randomized clinical trials involving laparoscopic liver resection for malignancy and such trial is needed to clarify the risks vs benefits and help standardize the approach.

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