

ORIGINAL ARTICLE

Laparoscopic liver resection for malignant liver tumors, why not more?

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Purpose: The precise role of laparoscopic liver resection in liver malignancies remains controversial despite an increasing number of publications that have used the laparoscopic resection of benign liver tumors. This study was performed to assess the feasibility, safety, and outcome of laparoscopic liver resection for malignant liver tumors. **Methods:** This study is a retrospective review of the profiles, pathology, surgery and outcome performed on 61 patients who had undergone laparoscopic liver resection for liver malignancies between January 2004 and March 2011. **Results:** Among the 61 patients, 34 patients had hepatocellular carcinoma (HCC), 24 patients had liver metastasis. The mean tumor size was 2.8 ± 2.0 cm (mean \pm standard deviation). Tumors located at Couinaud segment number 2 to 8. The resection included 36 anatomical resections, 25 wedge resections. The mean surgical time was 209.7 ± 108.9 minutes. There was one operation that resulted in death. Postoperative complications occurred in 9 patients (14%). There were 2 conversions to laparotomy (3%). The mean postoperative hospital stay was 9.0 ± 4.4 days. Blood transfusion was needed in 11 patients (18%). The mean surgical margin was 1.3 ± 1.2 cm. The mean follow-up period was 18.1 ± 11.1 months. The three-year overall survival rate was 87% for patients with HCC and 95% for patients having liver metastases from colorectal cancer. **Conclusion:** Even though laparoscopic liver resection requires a learning curve, it produced acceptable outcomes even in patients who had a malignant liver tumor. This study provides evidence to support further investigation and the establishment of laparoscopic liver resection for malignant liver tumors.

Key Words: Laparoscopy, Hepatectomy, Liver neoplasms

INTRODUCTION

Over the past two decades, tremendous achievements have been made in laparoscopic surgery including laparoscopic liver resection. Some skilled surgeons with extensive experience both in hepatic and laparoscopic surgery have demonstrated the feasibility and safety of laparoscopic liver resection in selected patients. However, laparoscopic liver resection for malignant tumors has not

gained wide spread use due to the long learning curve with technical difficulty and its oncologic safety. Nevertheless some experts have reported the usefulness of laparoscopic liver resection even in liver malignancy, which is a minimally invasive technique [1-4].

The purpose of the present study was to analyze the feasibility, safety, and outcome of 61 patients who underwent laparoscopic resection for liver malignancies in Yeungnam University Medical Center between January 2004 and

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METHODS

Patients

From January 2004 to March 2011, 111 patients underwent laparoscopic liver resection in Yeungnam University Medical Center. Among the 111 patients, 61 patients with malignant liver tumors were included in this study.

Surgical technique

All procedures were performed under general endotracheal anesthesia after obtaining informed consent. All procedures were performed under the supine or left lateral decubitus position. The pneumoperitoneum with carbon dioxide was introduced after the placement of a 12 mm trocar through a subumbilical incision. Intraabdominal pressure was monitored and maintained at less than 14 mmHg. Three or four additional trocars were positioned, depending on the surgical requirements. The trocar insertion sites depended on the locations of the lesion.

A flexible laparoscopic ultrasound probe was used to localize the tumor and determine the transection line before parenchymal dissection. One to 2 cm depth of liver paren-

chyma was transected using a Harmonic Scalpel (Ethicon Endo-Surgery Inc., Cincinnati, OH, USA). An ultrasonic dissector (CUSA Excel; Integra Lifesciences Co., Plainboro, NJ, USA) was used to dissect deep portions of the liver to skeletonize the portal and hepatic vein [5-7]. An endoclip was used to control larger structures. We did not apply the Pringle maneuver to control blood flow to the liver. The specimen was extracted using a vinyl bag. An argon beam coagulator was used on the cut liver surface to control bleeding with ventilation due to the risk of air embolism. Finally, fibrin glue was applied to the cut surface.

Statistical analysis

Variables analyzed included operation time, surgical margin, blood transfusion, conversion rate to laparotomy, postoperative hospital stay, postoperative complication, operation related death, mean follow-up period, overall survival and disease free survival. Overall and disease free survival rates were calculated using the Kaplan-Meier method. Survival curves were created using the Graph pad prism. Numeric variables were expressed as mean \pm standard deviation (SD).

RESULTS

Patient characteristics are summarized in Table 1. There

Table 1. Patients and tumor characteristics

Characteristic	Value
Age (yr), mean \pm SD	59.1 \pm 9.8
Gender (M/F)	43/18
Histology of cancers	
Primary liver malignancies	
Hepatocellular carcinoma	34
Intrahepatic cholangiocarcinoma	3
Secondary liver malignancies	
Liver metastasis from colorectal cancer	23
Liver metastasis form breast cancer	1
Tumor size (cm), mean \pm SD	
Hepatocellular carcinoma	2.6 \pm 1.4
Metastatic tumor	2.5 \pm 1.2
Single/multiple	56/5
Liver function (ICG R ₁₅)	
Hepatocellular carcinoma	18.1 \pm 16.5
Metastatic tumor	9.9 \pm 7.3
Intrahepatic cholangiocarcinoma	28.9 \pm 36.1

ICG, indocyanin green.

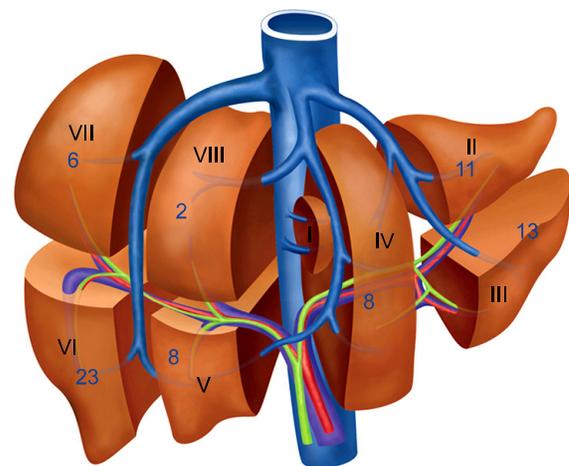


Fig. 1. Schematic illustration of tumor location.

was a single tumor in 56 patients and multiple tumors in 5 patients. The liver function was assessed by indocyanin green R₁₅. The tumor location according to the Couinaud classification is shown in Fig. 1. Types of laparoscopic liver resection are provided in Table 2.

The mean operating time was 209.7 ± 108.9 (mean \pm SD) minutes and mean resection margin was 1.3 ± 1.2 cm. Blood transfusion was needed in 11 patients (18%). There were two conversions to laparotomy (3%) because of tumor rupture and bleeding. The mean postoperative hospital stay was 9.0 ± 4.4 days. Postoperative complications occurred in 9 patients (14%), including acute renal failure, wound infection, pleural effusion, etc. However, all problems were resolved with conservative treatment. There was one unexpected operation related death due to esoph-

Table 2. Types of operation

	HCC	Metastatic tumor ^{a)}	ICC	Total
Right hemihepatectomy	1	1		2
Left hemihepatectomy	2			2
Right posterior sectionectomy	3			3
Left lateral sectionectomy	8	9	2	19
Segmentectomy	9	1		10
Wedge resection	11 ^{b)}	13 ^{b)}	1	25
Total	34	24	3	61

HCC, hepatocellular carcinoma; ICC, intrahepatic cholangiocarcinoma.

^{a)}Metastasis from colorectal cancer or breast cancer. ^{b)}Associated with microwave cauterization in each of HCC and metastasis.

Table 3. Surgical outcomes of the laparoscopic resection for liver malignancy

	HCC (n = 34)	Metastatic tumor (n = 23) ^{a)}	ICC (n = 3)
Operation time (min)	200.6 ± 106.9	203.9 ± 99.7	265.0 ± 109.6
Resection margin (cm)	1.3 ± 1.3	1.4 ± 1.3	0.7 ± 1.1
Conversion to laparotomy	2	0	0
Hospital stay (day)	9.1 ± 3.8	9.2 ± 5.4	9.7 ± 4.7
Complication	5	3	1

HCC, hepatocellular carcinoma; ICC, intrahepatic cholangiocarcinoma.

^{a)}Metastasis from colorectal cancer or breast cancer.

ageal variceal bleeding at postoperative day 3.

At a mean follow-up period of 18.1 ± 11.1 months, no port site recurrence had developed in any of the 61 patients. During the follow-up period, recurrences were detected in 14 patients. A comparison of surgical outcomes and recurrence for patients with HCC and those with metastasis and those with intrahepatic cholangiocarcinoma (ICC) is summarized in Table 3. Three ICC were diagnosed after operation. In one case, the initial diagnosis was a 10 cm sized huge hemorrhagic cyst on the left lobe of the liver. This patient had undergone left lateral sectionectomy in 2004 and the tumor recurred in the pancreas at 3 years after the operation. In another case, the initial diagnosis was HCC. In this patient, transarterial chemoembolization was performed at first because of severe cirrhotic liver and then a wedge resection was performed. The tumor locally recurred after 5 months of operation and the patient died because of esophageal variceal bleeding. In another case, the diagnosis was confused between hepatocellular carcinoma and cholangiocellular carcinoma but postoperative histological diagnosis was ICC. The tumor was located at segment 4 and the tumor size was 2.4 cm and gross type was mass forming. This patient underwent wedge resection and was disease free at 27 months after operation.

The mean follow-up period of HCC was 18.9 ± 11.7 months and that of metastasis was 16.6 ± 7.5 months. The three-year overall survival rates were 87% in HCC and 95% in metastasis (Fig. 2), and the three-year disease free survival rates were 57% in HCC and 90% in metastasis

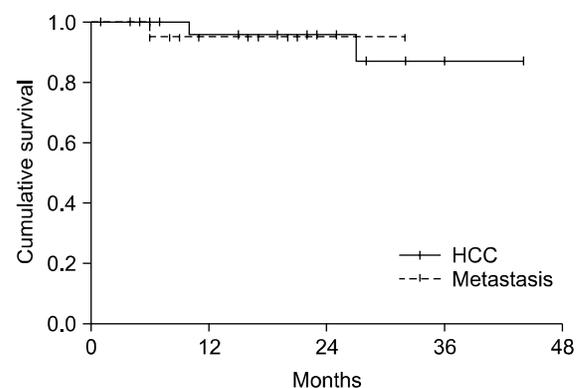


Fig. 2. Three-year overall survival rates were 87% in hepatocellular carcinoma (HCC) and 95% in metastatic tumors.

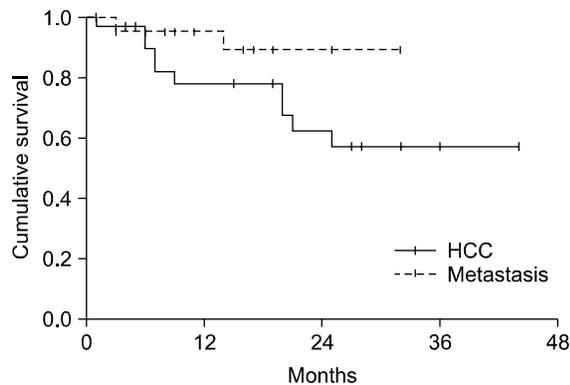


Fig. 3. Three-year disease free survival rates were 57% in hepatocellular carcinoma (HCC) and 90% in metastatic tumors.

(Fig. 3). The three-year overall and disease free survival rate of metastasis are better than those of HCC ($P < 0.05$).

DISCUSSION

The widespread success of laparoscopic surgery in many surgical fields has also extended to liver surgery. Laparoscopic liver resections have several advantages, such as causing minimal damage to the abdominal wall, earlier postoperative recovery and fewer complications. Furthermore, Simillis and colleagues have found that laparoscopic liver resection results in less blood loss and a faster recovery than open procedures [8].

One of the main concerns during hepatectomy is minimizing blood loss and avoidance of blood transfusion, which may be achieved by hypotensive anesthesia and vascular clamping, despite the drawback of ischemic injury to the liver parenchyma. Intraoperative blood loss was consistently lower in the laparoscopic hepatic resection group than in the open hepatic resection group, but this finding did not clinically manifest in the need for blood transfusions, which was comparable between the groups. The use of ultrasonic scalpel, and the hemostatic effect of the pneumoperitoneum improved intraoperative blood loss [8].

Another advantage of laparoscopy is lower adhesion after operation. This is advantageous to patients with HCC or liver metastasis who are likely to undergo subsequent abdominal surgery, such as repeat hepatectomy for re-

current cancer or subsequent liver transplantation. Other advantages in cancer patients may include greater preservation of the immune function, with some authors advocating a possible enhancement in the antineoplasm response and earlier access to adjuvant treatment for an earlier recovery. At the beginning, many surgeons were skeptical of using this procedure because of concerns regarding bleeding, bile leakage and air embolism [9]. However, laparoscopic surgery may provide better visualization of deep vascular structures and possibly a more precise and accurate surgery.

With development of open, laparoscopic surgical skills and instruments, many skilled surgeons are trying laparoscopic liver resection, although there are still have some limitations associated with this approach. Currently, in a selected group of patients, when liver and laparoscopic surgery is appropriately performed by an experienced surgical team, the technique appears to be safe with an acceptable complication rate and mortality.

The best indication for laparoscopic liver resection for malignancy seems to be solitary lesions, 5 cm or less, located in the peripheral liver segments (segments: II to VI) [10]. In this study, we included patients with small tumors located in the periphery or left lobe of the liver and excluded patients with poor liver function (child C), lymph node metastasis, large tumors, or patients with tumors located in the central portion of the right lobe, close to the portal bifurcation or suprahepatic junction.

However, application of this technique to liver malignancies remains controversial because of its oncologic safety. In laparoscopic liver resection for liver malignancies, the same oncologic surgical principles as used in open surgery should be applied, including tumor free radical resection, anatomical resection or achievement of a 1 cm free resection margin [11]. Although parenchymal-sparing resection is required by the presence of underlying liver disease, anatomic resection has been shown to reduce local recurrence and improve survival in HCC patients when compared with nonanatomic wedge resections. This attributed to the mode of dissemination of HCC through microvascular portal invasion, which justifies anatomic resection of a portal territory around the tumor.

Based on our experience of laparoscopic liver resection,

we could do an anatomical liver resection, if the tumor is located in the left lobe of the liver (segment II to IV). Otherwise (segment V to VIII), we would attempt to resect it with an adequate resection margin of more than 1 cm, which is difficult because of the loss of tactile sensation. To achieve the 1 cm free surgical margin, we used laparoscopic ultrasonography.

Regarding air embolism, we fortunately have had no complications related to air embolism. To prevent air embolism, we do not try to lower the central venous pressure below 3 cmH₂O, as is conducted in open surgery.

Oncologic clearance is also an important issue. Tumor cell seeding and port site metastasis have been addressed by several reports in other types of gastrointestinal malignancy [12,13]. We only have one case of tumor seeding because of tumor rupture during surgery. But we believe, we can minimize the tumor seeding and port site metastasis by careful manipulation of tumor and use of a vinyl bag to retrieve the specimen.

Despite the limited number of cases studied, case selected and short follow-up period, we have good early surgical outcome in HCC and colorectal liver metastasis. In a large series of open resected HCC on cirrhotic liver, the overall 1- and 2-year survival rates were 68 to 80% and 55 to 68% [14-16]. And recent case-matched analysis between laparoscopic and open liver resection in Korea also revealed no survival difference in HCC [17]. Choti et al. [18] and Abdalla et al. [19] also reported that survival rates after laparoscopic liver resection for colorectal liver metastasis were similar to those for the open surgery.

In our series of laparoscopically resected HCC, the overall 3-year survival rate was 87%. For patients with open resected colorectal liver metastasis, the overall 1- and 2-year survival rates were 89 to 93% and 62 to 73% [20]. In our series of laparoscopically resected colorectal liver metastasis, the overall 3-year survival rate was 95%. The complication rate was relatively higher and overall survival rate was lower in HCC than in colorectal metastasis ($P < 0.05$). It seems to be related to the poor preoperative liver function and natural course of HCC after surgery. R₁₅ ICC has no statistical significance because the case of ICC was too small. In this short-term study, no significant differences between open and laparoscopic surgery in liver malig-

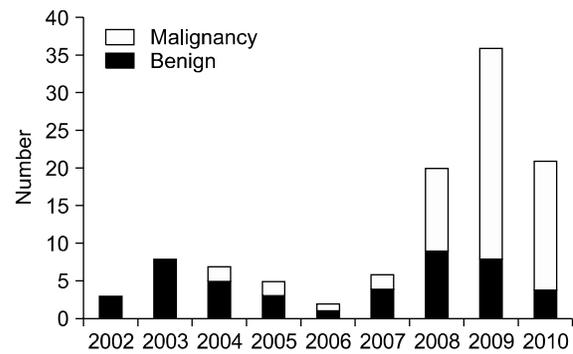


Fig. 4. Annual cases of laparoscopic liver resection for benign and malignant liver tumor in our institution.

nancies were observed, which indicates that the laparoscopic approach is oncologically safe. Regarding cholangiocellular carcinoma, it seems not to be a good indication for laparoscopy except small size and mass forming type tumors. In this study, only three cases of post-operatively diagnosed cholangiocellular carcinoma were included. One patient who had a small size and mass forming type tumor is 27 months disease free.

Although laparoscopic liver resection is known to need more learning curve than laparoscopic surgery for the other organs, there are no reports about the learning curve according to the proficiency [21]. Our institution is not a big center, main purposes of this review were to encourage ourselves for laparoscopic liver resection for malignancy and find rationale to go further in our institution. Fortunately we have a good result and we want to encourage the same volume center to start laparoscopic liver resection for malignancy. Our annual cases of laparoscopic liver resection for benign and malignancy are listed in Fig. 4.

In conclusion, even though laparoscopic liver resection requires a learning curve and only a limited number of patients were included in this study, laparoscopic liver resection is a feasible approach with reasonable surgical outcome even in patients who had malignant liver tumor especially in HCC and liver metastasis from colorectal cancer. Based on the findings of this study, laparoscopic resection warrants further study for the treatment of malignant liver tumors.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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