Review Article



# Minimally invasive liver resections for malignancies: where is the limit?

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**Abstract:** Laparoscopic liver resection (LLR) has been disseminated in the last two decades because of the development of devices and improvement of techniques. Its effectiveness and safety have already been reported. In addition, oncological outcomes in LLR for hepatocellular carcinoma and colorectal liver metastases were reported to be similar to those of open surgery in selected cases. The indications for LLR have gradually expanded, and currently, highly challenging procedures including major hepatectomy are applied. However, there are several limitations to LLR in terms of technical aspects, tumor characteristics, and so on because much prolongation of the operation time and increase in the risks should not be permitted. For hepatectomy in which severe complications easily develop, it is most significant to minimize the operative complications. The indication criteria for LLR should be rigorously determined with an understanding of the limitations of laparoscopic surgery.

**Keywords:** Laparoscopic liver resection (LLR); minimally invasive liver resection; indication

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## Introduction

Laparoscopic liver resection (LLR) was first reported in 1991 (1). Since then, LLR has been gradually prevalent, and its efficacy and feasibility have already been reported (2-5). The indications for LLR have been expanded according to the development of laparoscopic instruments, devices, and technical refinements.

The First and Second International Consensus Conference on Laparoscopic Liver Surgery held in Louisville (in 2009) (6) and Morioka (in 2014) (7) showed the evolution of LLR and numerous recommendations. LLR has several superior advantages to open liver resection (OLR) other than cosmetic benefits. A laparoscopic magnified caudo-dorsal view provides excellent visibility of structures including the vessels and enables more meticulous procedures and unique approaches that are different from open surgery (8-13). Additionally, pneumoperitoneal pressure potentially reduces bleeding from the hepatic veins during liver parenchymal transection. However, LLR may have some disadvantages, such as direction misidentification, lack of tactile sense, device movement restriction, risk of tumor exposure, and less controllability for emergency bleeding. The optimal indications for LLR are mandatory to obtain the true benefit of minimally invasive surgery.

## Type of procedure

The Second International Consensus Conference concluded that the minor LLR was a standard practice; however, the major LLR, defined as trisectionectomy, bisectionectomy, hemihepatectomy, and resection of the posterosuperior segments, remains an innovative procedure and is still in the exploratory learning phase (7).

Laparoscopic partial resection and left lateral sectionectomy already have widespread use and are commonly performed. In experienced institutes, various laparoscopic anatomic resections, including hemihepatectomy, sectionectomy, segmentectomy, and smaller anatomic resections, so-called cone unit resection (14), have been performed successfully (4,15-21). Although many types of laparoscopic anatomic hepatectomy procedures without resection of the hilar vessels or extrahepatic bile duct resection have been standardized (9-13), the indications for these should be well discussed, considering malignant potential such as tumor type and vascular invasion.

## Liver function

In terms of liver function, the indication criteria for LLR are basically the same as those for OLR. The Makuuchi criteria (22) are widely used as the indication criteria according to an estimated volume of resected liver, which were categorized using the hepatectomy types, including limited resection. The most common malignancies treated by liver resection are hepatocellular carcinoma (HCC) and colorectal liver metastasis (CRLM). HCC usually develops in patients with chronic liver diseases, such as hepatitis B and C viral infection, alcoholic liver injury, or steatohepatitis, while the liver of patients with CRLM has often been damaged by chemotherapy (23,24). The LLR feasibility and efficacy for patients with liver cirrhosis (LC) have been reported (25-31). A systemic review and meta-analysis showed that LLR for patients with HCC and chronic liver disease achieved fewer postoperative complications and comparable oncological long-term outcomes (32). In this study, it was concluded that postoperative ascites and liver failure were reduced with LLR.

During LLR, the abdominal wall destruction is minimized, and liver mobilization can often be minimized (13). In cases with LC, by avoiding the destruction of the collateral veins and lymphatic vessels around the liver, postoperative ascites can be decreased, and consequently, the liver function can be maintained. LLR may expand the indications for liver resection in patients with LC. The surgical indications for LLR must be considered more carefully than those for OLR in patients with LC because there are risks for intraoperative bleeding due to coagulopathy disorders and portal hypertension and postoperative complications, such as refractory ascites, hemorrhage, and liver failure (33). Further experiences and studies are required to address this issue.

## Tumor characteristics

The indication for LLR is decided by referring to tumor type, location, size, number, vascular invasion, and so forth. Acceptable indication criteria for LLR recommended in the First International Consensus Conference were solitary lesions, a size of 5 cm or less, and location in liver segments 2 to 6 (6). Since then, these criteria have been extended with the remarkable development of LLR.

### *Tumor type*

LLR is most commonly performed for HCC, followed by CRLM. Several large studies, including systematic reviews and meta-analyses, have already been conducted. They all reported that LLR for HCC or CRLM was associated with better short-term outcomes such as less blood loss, shorter hospital stays, and less morbidity than OLR and comparable oncological and long-term outcomes (34-42). Based on these results, HCC and CRLM are both good indications for LLR. The following are mainly described for other tumor types.

#### Metastatic tumors

The indication criteria for liver resection for metastatic tumors depend on their original malignancies. Currently, liver resections for various kinds of metastatic tumors other than CRLM, such as neuroendocrine neoplasm (NEN) (43-47), gastric cancer (48-50), and other tumors (51), have been reported to have better prognoses. The number of liver resections for metastatic tumors is increasing as a part of the multidisciplinary treatment because of the development of chemotherapy and interventional radiology. Particularly for NEN, LLR was associated with better short-term outcomes than OLR and comparable oncological and long-term outcomes, similar to CRLM (43,52-56).

Partial liver resection, which is familiar to LLR, is usually employed for metastatic liver tumors as a parenchyma-sparing liver resection (57,58). LLR is often feasible even in repeat hepatectomy (55); however, it takes a much longer operation time for multiple resections than OLR. LLR is sometimes performed simultaneously with resection of the primary site (59). Synchronous liver and colorectal resection usually require complex procedures and long operation times. In particular, major hepatectomy with low anterior rectal resection not only takes a long operation time but also leads to increased surgical risks. The timing of liver

resection should be carefully decided, considering surgical risks and oncological efficacy.

**Intrahepatic cholangiocarcinoma (ICC)**

ICC is the second most common primary liver tumor (60). Regarding LLR for ICC, there are a few reports that showed better short-term outcomes than OLR and comparable oncological and long-term outcomes in selected patients (61-65). Most reports excluded tumors that had invaded into the blood vessels or bile duct in the hepatic hilum (hilar invasion). However, ICC had a higher malignant potential, and lymph node metastasis developed in 30–40% of patients (66). Although the necessity of routine lymphadenectomy is controversial, especially for tumors without hilar invasion (66) because there are some technical problems with lymphadenectomy in laparoscopic surgery, inadequate nodal evaluation can hinder accurate staging (67). LLR should be carefully performed for ICC, paying attention to the surgical margin.

**Perihilar cholangiocarcinoma**

For perihilar cholangiocarcinoma, a few reports described LLR (68-71). In general, perihilar cholangiocarcinoma requires major hepatectomy combined with caudate lobe resection, extrahepatic bile duct resection, regional lymphadenectomy, and biliary reconstruction (72). In most cases, the surgical margin in the dissection planes cannot be secured without tactile sensation, and it is difficult to determine an appropriate portion to cut the bile duct on the remnant liver side. Even if each procedure is technically available via a laparoscopic approach in some limited cases, it takes a much longer time to secure the surgical margin as well as complete biliary reconstruction precisely. The surgeon who does not know how difficult it is to secure the surgical margin in the dissection planes and bile duct stumps or how significant it is to prevent stenosis and leakage of the biliary anastomosis in this surgery may attempt to perform via a laparoscopic approach.

**Gallbladder cancer (GBC)**

For advanced GBC, laparoscopic extended cholecystectomy, in which the gallbladder is removed with gallbladder bed regional lymph nodes and, sometimes, common bile duct, followed by biliary reconstruction, may be an option in expert centers (70,73-77). Similar to patients with perihilar cholangiocarcinoma, patients with GBC involving the hepatoduodenal ligament should not undergo laparoscopic surgery.

***Location***

Currently, the tumor locations, even difficult ones like segments 1, 7, and 8, do not limit the indications for LLR in expert institutes (78). Liver resection of segments 1 and 7 have been standardized by utilizing the laparoscopic unique approach in the caudo-dorsal view (10,79), and that of segment 8 has been standardized by using intercostal trocars (13).

***Size***

A large tumor may obstruct the laparoscopic view, making it difficult to handle, as well as increase the risk of tumor exposure and rupture. Previous reports described that large tumors >5 cm could be approached laparoscopically without increased complications compared with OLR, but tumors >10 cm in size showed greater blood loss and longer operative time (80-82). Additionally, the conversion rate to OLR was slightly higher (9.3% to 15.4%). In patients with large tumors, especially those over 10 cm, LLR should be carefully selected.

***Number***

To remove several lesions, sparing the liver parenchyma and major blood vessels as much as possible, multiple resections with careful parenchymal dissection are required. If it is performed via a laparoscopic approach, it requires a longer operation time. Furthermore, to identify and remove all lesions without tumor exposure, detailed intraoperative ultrasonography and palpation, which are difficult to provide in LLR, are helpful. The limited number of tumors for LLR should be judged in each case referring to the patient's condition, such as cardiac or renal function, as well as the surgeon's skill. Hand-assisted laparoscopic surgery (HALS) or hybrid techniques may be useful for managing these intraoperative difficulties (83).

***Vascular invasion***

Similar to perihilar cholangiocarcinoma or GBC, the tumor suspected to invade the hepatic hilum should not be applicable for LLR.

## Repeat hepatectomy

Recently, repeat hepatectomy has been aggressively

performed to improve prognosis, and the results regarding HCC and CRLM have been reported (84-88). Repeat hepatectomy has also been increasingly performed via a laparoscopic approach. Wakabayashi *et al.* (89) reported in a systematic review and meta-analysis that laparoscopic repeat hepatectomy showed favorable short-term outcomes without mortality in highly selected patients although the rate of conversion to open surgery, HALS, or tumor ablation was relatively high (11%). As a previous hepatectomy, OLR was associated with longer operation time and greater blood loss than LLR. Another meta-analysis regarding repeat hepatectomy reported by Peng *et al.* (90) showed that LLR had similar operation time, less blood loss, fewer major complications, and shorter hospital stays compared with OLR. However, compared with LLR as a first hepatectomy, laparoscopic repeat hepatectomy took longer operation time, while the blood loss amount and transfusion rates, R0 resection, conversion, postoperative complications, and mortality were similar between the two groups.

The technical difficulty of repeat hepatectomy is caused by not only postoperative adhesion but also by the difficulty in recognizing anatomic landmarks due to a deformation of the liver derived from the previous hepatectomy, which increases during LLR because of easy disorientation in a laparoscopic narrow field. Particularly in cases that have been dissected around the hepatic hilum or have undergone mobilization of the right liver with exposure of the inferior vena cava in previous hepatectomy, if the portion around the hepatic hilum is dissected again, the risk of injury of important structures is higher in LLR than in OLR. Around the hepatic hilum, even to apply the Pringle maneuver is sometimes difficult. However, in general, adhesions after laparoscopic surgery are mild and easier to dissect. In addition, by utilizing some unique laparoscopic approaches, the hepatic hilum can remain untouched, and liver mobilization can be minimized in LLR (10,13). The indication for LLR in repeat hepatectomy should be determined by considering the estimated operation time and surgical risk associated with the tumor location and previous hepatectomy.

## Conclusions

Recently, LLRs requiring highly difficult and complicated procedures have been increasingly performed in cases of malignant disorders. Although LLR is useful for properly selected cases, its indication criteria should not be expanded immoderately. The true goal of laparoscopic surgery is to provide minimal invasiveness to the patient. For hepatectomy in which severe complications easily develop, it is most significant to minimize the operative complications but not surgical incisions.

The indication criteria for LLR should be rigorously determined with an understanding of the limitations of laparoscopic surgery.

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