

## Is the Indication of Liver Resection for Hepatocellular Carcinoma Expanding with the Application of Laparoscopic Approach?

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### Abstract

Liver resection (LR) for the patients of hepatocellular carcinoma, often with chronic liver disease, have high risks of developing significant postoperative complications and multicentric metachronous repeat lesions with the need of repeat treatments. Reduction of surgery-induced parenchymal injury and destruction of the collateral blood/lymphatic flow, which leads to less post-operative ascites production, and facilitation of repeat LR with less adhesion and improved vision/manipulation between adhesions are among the advantages of laparoscopic LR. These characteristics of laparoscopic LR may lead to expanding indication of LR.

**Keywords:** Liver resection; Laparoscopic hepatectomy; Hepatocellular carcinoma; Chronic liver disease; Repeat hepatectomy

### Introduction

Hepatocellular carcinoma (HCC) is the fifth most common primary cancer and the third most common cause of cancer-related deaths worldwide [1,2]. The treatment options for HCC include liver resection (LR) [3], liver transplantation [4], transarterial chemoembolization (TACE), and local ablation therapy [5]. Among them, LR and liver transplantation are thought to be the best hopes for cure. Although liver transplantation should be adapted to patients with deteriorating liver function and HCC within the Milan criteria [6], LR should be considered as a primary therapy in the other patients [7,8]. However, most patients with HCC have underlying chronic liver disease (CLD). Therefore, there are high risks of developing significant postoperative complications and also multicentric metachronous repeat lesions occurring in chronically injured liver after LR with the need of repeat treatments. When considering the treatment of HCC in patients with CLD, the degree of invasive surgical stress, especially to the impaired liver, should be considered in addition to the oncological therapeutic effects. Patients with severe CLD have various (overt and preliminary) symptoms, such as: (1) deteriorations of protein synthesis and metabolism; (2) GI tract congestion, ascites, pancytopenia due to portal hypertension and hypersplenism; and (3) susceptibility to infectious diseases and hepatopulmonary syndrome (hypoxaemia) due to increased shunt vessels [9]. Cirrhotic patients have high morbidity and mortality following anesthesia and surgery [10] and the risk of abdominal operations increases according to the preoperative Child-Pugh class of the patients [11]. Even limited small volume LR for severe cirrhotic patients often develops refractory ascites, which leads to fatal complications [12,13].

Since the first successful report in 1992 [14], laparoscopic LR is thought to be a less invasive procedure than conventional open LR for the treatment of hepatic lesions [15]. In a comprehensive meta-analysis study, laparoscopic LR was compared to open in 1678 patients across 26 studies [16]. While it is associated with longer operating times and no differences in oncological outcomes, it is advantageous in

several aspects. Laparoscopic LR is associated with reduced blood loss, decreased portal clamp time, decreases in overall and liver-specific complications, and shorter post-operative hospital stays. Furthermore, recent technological development of devices and accumulation of experiences have facilitated the expansion of the indication of the procedure [17,18]. For those patients with HCC and CLD who are not able to undergo usual treatment modalities due to liver function, tumor size and/or localization, "less invasive" pure laparoscopic hepatectomy may provide a good option, especially after repeat treatments for the disease with multicentric metachronous lesions occurring in chronically injured liver.

Under open surgery, even limited LR for severe CLD patients often develops refractory ascites leading to fatal complications [12,13]. Laparoscopic LR may be particularly advantageous for those patients, given the potential for lower levels of parietal and hepatic injury and the preservation of venous and lymphatic collateral circulation in cirrhotic patients. The safety and feasibility of the laparoscopic approach and its short-term benefits for HCC patients with CLD have been demonstrated by several series. The studies have investigated the major differences between laparoscopic and open LR [19-29]. Favorable short-term results, including fewer incidences of ascites and liver failure, and shorter postoperative hospital stay correlate with the laparoscopic procedure. Tranchart et al. reported laparoscopic LR of HCC for selected patients resulted in better postoperative outcomes without long- and short-term oncologic consequences [30]. Also in our experience [31], we reported the favorable perioperative course of the patients with severe CLD (Child B/C and ICG R15 of 40% or above) who underwent pure laparoscopic LR, which is comparable to that of the patients with mild/moderate CLD (Child A and ICG R15 of 10.1-27.4%). This study showed that laparoscopic LR has the advantage of minimal ascites [31] due to preservation of venous and lymphatic collateral circulation, which leads to lower risk of disturbance in water and/or electrolyte balance and hypoproteinemia that could trigger fatal liver failure. This feature could be the most remarkable specific advantage for laparoscopic LR. Patients who undergo LR are exposed three different types of stresses: 1) general, whole-body surgical stress, 2) reduced liver function due to resected liver volume, 3) surgery-

induced injuries for liver parenchyma and environment around the liver, such as parenchymal injury by compression of the liver and destruction of the collateral blood/lymphatic flow by laparotomy plus mobilization of the liver. Reduction of the third mentioned stress by laparoscopic LR should lower the risk for HCC patients with severe CLD. Among these patients with severe CLD in our series, one underwent living-related liver transplantation 20 months after hepatectomy [32]. The procedure could also be an advantageous option in bridging therapy to liver transplantation for certain HCC patients with severe CLD. Furthermore, our experience showed laparoscopic LR also results in improved vision and manipulation in a small operative field under several conditions, such as repeat hepatectomy with adhesions [32]. In addition to smaller extend of adhesion after laparoscopic than open LR, this feature of laparoscopic LR facilitates the repeat LR for the patients with multicentric metachronous lesions occurring in chronically injured liver. Also,

some novel approach of LR (for example, caudal, not anterior as open, approach for oncologically appropriate posterior sectorectomy and right hepatectomy [33]) is also possible laparoscopically, using the laparoscope-specific view/approach (such as good view from caudal and dorsal sides of the liver) and by changing position of the patients for the use of the gravity to dissection and handling large-volumed liver/tumors.

These characteristics of laparoscopic LR listed above may indicate it is a superior method when compared to open LR under certain conditions and its application may lead to expanding indication of LR. Table 1 is summary of recent reports of comparative studies of laparoscopic LR and open LR for HCC, which show favorable results for laparoscopic LR. However, there is no controlled study comparing laparoscopic LR and open LR, liver transplantation, ablation therapies etc. to data. Further investigations are needed.

Study		Ascites		Liver failure		Hospital stay (days, mean ± SD)		Mortality	
Author	Year Ref No.	LLR	OLR	LLR	OLR	LLR	OLR	LLR	OLR
Lai	2009 [34]	NA	NA	NA	NA	NA	NA	0/25	1/33
Aldrighetti	2010 [35]	0/16	1/16	NA	NA	6.3 ± 1.7	9 ± 3.8	0/16	0/16
Trancharat	2010 [30]	3/42	11/42	0/36	4/53	6.7 ± 5.9	9.6 ± 3.4	1/42	1/42
Kim	2011 [36]	0/26	1/29	NA	NA	11.08 ± 4.96	16.07 ± 10.697	0/26	0/29
Lee	2011 [37]	0/33	2/50	NA	NA	NA	NA	0/33	0/50
Truant	2011 [38]	5/36	12/53	NA	NA	6.5 ± 2.7	9.5 ± 4.8	0/36	4/53
Ker	2011 [27]	2/116	26/208	NA	NA	6.2 ± 3	12.4 ± 6.8	0/116	6/208

**Table 1:** Recent reports of laparoscopic (LLR) and open liver resection (OLR) comparative studies for HCC

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