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Laparoscopic liver resection for hepatocellular carcinoma

Massimo Giacca, Daniel Cherqui

Hepatobiliary Center, Paul Brousse Hospital-Assistance Publique-Hopitaux de Paris, Universite' Paris Sud, Villejuif 94800, France.

Correspondence to: Dr. Massimo Giacca, Hepatobiliary Center, Paul Brousse Hospital-Assistance Publique-Hopitaux de Paris, Universite' Paris Sud, Villejuif 94800, France. E-mail: massimogiacca4@gmail.com

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Abstract

Hepatocellular carcinoma (HCC) represents the most common indication of laparoscopic liver resection (LLR). It must be acknowledged that most series concern minor hepatectomies for peripheral lesions located in favorable segments, and such procedures are now performed in the majority of HPB centers. However, there are growing reports concerning major hepatectomies (i.e., 3 segments or more) and complex resections such as anatomical resections in difficult segments (i.e., postero-superior). Retrospective comparative studies, including some with propensity score matching, and meta-analyses showed that LLR is associated with short-term benefits including reduced blood loss, length of stay and morbidity with identical oncological results and survival rates. In addition, laparoscopy leads to less post-operative abdominal adhesions, improving operative outcomes in case of repeat hepatectomy or secondary liver transplantation. Despite the lack of results of randomized-controlled trials in HCC, a consensus exists that the laparoscopic approach can improve the outcome of major liver resections, provided it is performed in experienced centers. This requires specific high-quality training.

Keywords: Laparoscopy, hepatocellular carcinoma, cirrhosis, hepatectomy, liver resection

INTRODUCTION

Since 2000, when the first case-series was published^[1], laparoscopic liver resection (LLR) has represented a growing challenge. The number of resections and the extension to major hepatectomies and difficult locations have increased worldwide over the last 10 years. In contrast with other procedures, liver resections address



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various diseases including primary and secondary liver cancer on normal or diseased underlying liver. Furthermore, different types of resections including major and minor hepatectomies can be performed, which include various procedures according to tumor type and location in the liver segments. The only available Randomized Control Trial (RCT) concerns LLR for colorectal liver metastases^[2]. Results from this RCT confirmed previous retrospective reviews and meta-analyses by demonstrating benefits of LLR compared to open resection, such as reduced blood loss, morbidity and hospital stay. Two international consensus conferences on laparoscopic liver surgery were held in Louisville (USA) in 2008 and in Morioka (Japan) in 2014^[3,4]. The conclusions of the Morioka meeting validated minor LLRs as standard practice in surgery, while complex anatomical resections and major LLRs were still in an exploratory phase. The Morioka consensus also focused on underlining how major LLRs require high-level skills and emphasizing that a structured training should be performed, together with the establishment of a scoring system to evaluate difficulty before surgery. Currently, a laparoscopic approach seems applicable in 20%-50% of liver resections, certainly depending on local experience and skills^[5]. Authors of the largest review and meta-analysis published so far^[6], with data from 9000 patients, propose LLRs as a feasible alternative to open liver resection (OLR) mainly in patients undergoing a minor resection or in those undergoing a major liver resection without biliary or vascular reconstruction. At present, LLR is accepted worldwide, with favorable outcomes compared to OLR, mainly in terms of length of stay, blood loss and post-operative complications, with comparable oncological and survival outcomes.

Almost 90% of HCCs evolve from chronic liver disease, with different prevalent etiologies in the Eastern and Western world. Several medical and surgical approaches or, more often, combinations of these, are used to treat HCC, but surgical resection and liver transplant play the main role. Sixty-five percent of LLRs are performed for malignant disease, with HCC remaining the main indication. This is in part attributable to the large contribution of Asian literature where HCC resection is very common, and also the accurate surveillance and screening programs which allow detection, in a growing number of cases, of small single tumors which are the best candidates for LLR^[5].

OPERATIVE AND POST-OPERATIVE OUTCOMES

The first series of LLRs for HCC on cirrhosis studying both short-term outcomes and survival rates was published in 2006^[7]. It concluded that LLR in selected patients with peripheral HCC on chronic liver disease was a safe procedure with good midterm results. More recent studies confirmed these results especially in cirrhotic patients^[8-14]. Meta-analyses proved that patients with HCC undergoing LLR have reduced intra-operative blood loss and length of stay when compared to those undergoing OLR^[15,16]. A systematic review and meta-analysis on LLR vs. OLR for HCC was published in 2013 by Yin *et al.*^[11] This study included 1238 patients from 15 studies, all requiring left lateral or right peripheral resection. Together with reduced intra-operative blood loss, it showed a lower rate of post-operative morbidity in patients undergoing laparoscopic resections. There was no significant difference in terms of survival, both overall survival (OS) and disease-free survival (DFS). Two studies comparing laparoscopic and open resections for HCC using the propensity score were published in 2015^[17,18]. The one by Han *et al.*^[17] showed no inferiority of LLR, with similar 1, 3 and 5-year OS and DFS rates, lower post-operative morbidity and post-operative transient liver failure. These groups of patients had comparable operative times. A study by Takahara *et al.*^[18] showed similar results with reduced blood loss, post-operative morbidity, ascites and liver failure in patients who underwent LLR. In this group of patients operative time was longer and oncological results comparable.

MAJOR HEPATECTOMIES

In recent years the laparoscopic approach has extended to major hepatectomies. In 2017, Yoon *et al.*^[13] in a propensity-score analysis comparing patients who had laparoscopic and open right hepatectomy for HCC

on cirrhosis, demonstrated better results in the laparoscopic group for length of hospital stay, level of post-operative pain and ascites. Rate of incisional hernia was also lower in this group. These authors used the comprehensive complication index (CCI) to prove a significantly less severe overall morbidity. They showed no significant difference in terms of intra-operative blood loss. None of the patients in both groups required transfusions. In the Yoon's cohort of patients, operative time was significantly shorter in the open group. The main limits of this study are that it is not an RCT and that the great majority of patients (more than 90%) had HBV-related cirrhosis. We are of the opinion that patients with HCC on chronic hepatitis B may offer a less challenging setting for resection and less post-operative complications when compared to other etiologies of cirrhosis^[19].

Another recent propensity-score study by Xu *et al.*^[20] compared the laparoscopic and open approaches for major hepatectomies to treat HCC on cirrhosis. This study, which included 103 patients, confirmed a lower occurrence of post-operative ascites and showed no difference in all other medical and surgical post-operative complications. A lower post-operative occurrence of ascites had already been observed by other authors and described in meta-analyses^[15,16,21]. Also in the Xu's series, the open group had significantly lower operative and Pringle times, while the laparoscopic group showed a significantly shorter length of stay and a higher overall cost of hospitalization.

A study that aimed at comparing laparoscopic and OLR for HCC following sequential trans-arterial chemoembolization (TACE)-portal vein embolization (PVE) was published by Goumard *et al.*^[22] The results from this study showed no difference in oncological radicality in terms of R0 resections and tumor margins. LLRs were proven to offer shorter length of stay and fewer grade B post-operative liver failures.

Results from the first Asia Pacific consensus meeting of LLR for HCC were published in 2018^[23]. The meeting of experts produced 22 recommendations, concluding that minor LLRs should be performed in experienced centers and major LLRs in centers of excellence. In these selected centers LLR with portal vein reconstruction is also possible if vascular involvement only targets the left lateral branches. The meeting's conclusions also mention some of the new frontiers of LLRs, such as the use of indocyanine green fluorescence and robotic resection, which could become high-quality tools to optimize surgery in the near future.

CONVERSION RATES

Another main-point of interest in evaluating the feasibility of LLRs for HCC is conversion rate. Goumard *et al.*^[22] had a higher conversion rate compared to the other studies, reaching 25% but never in an emergency setting. These authors defined conversion criteria as: significant bleeding, failure to accurately recognize the biliary anatomy and poor exposure leading to failure or slow progression during parenchymal transection. Work from other authors showed conversion rates ranging from 5% to 13%^[14,17,24]. The largest available case series in all LLRs for HCC is a retrospective analysis by Dagher *et al.*^[25], which presented a conversion rate of 10%. A recent retrospective analysis of 2861 cases of LLRs by Halls *et al.*^[26] showed a conversion rate of 7.8%, in which bleeding was the most common cause. Almost 19% of conversions were due to adhesions. In this series, 11.5% of patients had cirrhosis and a conversion rate of 11.1%, which turned out to be statistically significant when compared to the conversion rate of 7.3% in non-cirrhotic patients.

ONCOLOGICAL OUTCOMES

In all studies, there was no evidence of inferiority of LLR in terms of oncological results and survival rates, both OS and DFS^[13,14,17,18,20,27]. Moreover, the work by Han *et al.*^[17] compared the laparoscopic and open groups in terms of pathological liver status, tumor size and satellites, microvascular and capsular invasion, tumor grade and stage. No significant difference was found. Recently, a retrospective study by

Woo-Hyoung *et al.*^[28] analyzed 234 patients undergoing anatomical LLR for HCC: DFS was 67.5% and 55.3%, OS was 91.7% and 87.1% at 3 and 5 years respectively. In this work anatomical resection emerged as a good prognostic factor for HCC recurrence, but had no impact on the OS. Another recent study by Guro *et al.*^[29] considered retrospectively 177 patients who underwent major LLR or OLR, finding the early (< 1 year) recurrence rate to be significantly higher in the open group, with similar OS and DFS rates. Population in this study also showed a larger tumor size in the open group, which could explain the better results in the laparoscopic one.

FEASIBILITY OF LLR

Although postero-superior segments (1, 4a, 7 and 8) are known to be the less accessible ones, recent literature leans toward the concept that tumor location should no longer be a criteria for patient selection in laparoscopic surgery^[30,31]. Already in 2010, Yoon *et al.*^[32] published a retrospective study comparing postero-superior (PS) and antero-lateral (AL) resections for HCC. The study concluded that PS patients had longer operative time and length of hospital stay, but no significant difference in terms of post-operative morbidity, recurrence or survival. A non-significant tendency towards a higher rate of conversion was shown in PS patients.

In 2012, Ishizawa *et al.*^[33] analyzed 62 patients who had resections in all segments, confirming that PS resections require longer operative time and are also affected by higher blood loss. The authors proved accurate LLR to be feasible in all segments, but considered PS resections as “difficult segmentectomies” which should be performed by surgeons with advanced open and laparoscopic experience.

Last, the laparoscopic approach reduces the formation of post-operative adhesions. This appeared, in the case of repeat hepatectomy, to reduce operative time and difficulty of the adhesiolysis which could impact on peri-operative morbidity in terms of bleeding and bowel or other organ injuries^[13,34]. This suggests that LLRs should be preferred, when feasible, considering the risk of recurrence and especially in potential candidates for liver transplant^[35].

LLR VS. ABLATION

Regarding single small HCCs, several authors have debated whether to perform laparoscopic resection or local ablation. OLR was shown to be associated to higher rate of complications, greater blood loss and longer hospital stay compared to radiofrequency ablation (RFA)^[23,36,37]. These disadvantages are likely to be reduced in laparoscopic resections. LLR seems to have better oncological results, in terms of lower recurrence rates, when compared to RFA for the treatment of small (< 3 cm) HCCs^[23,38-40]. OS in the two procedures do not differ significantly^[39,41].

The main limitations of this study are that it was a single-center non-systematic review.

CONCLUSION

In conclusion, data have been accumulated in the recent literature in favor of safety and reliability of LLR for HCC, especially in a cirrhotic setting. Currently, while LLR is the standard practice for patients requiring minor hepatectomies, evidence regarding the feasibility of major LLRs is growing. Several studies also show short-term benefits of LLR for major hepatectomies, with identical oncological results. A particular advantage in the cirrhotic patient is a lower risk of postoperative decompensation and ascites. Still, these operations are mainly performed in experienced centers. The next challenge will be the dispatch and training of surgeons in accordance to these procedures, in order to achieve a meaningful improvement in patient care and clinical outcomes.

DECLARATIONS

Authors' contributions

Concept and design of study or acquisition of data or analysis and interpretation of data; drafting the article or revising it critically for important intellectual content; final approval of the version to be published: Giacca M, Cherqui D

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Both authors declared that there are no conflicts of interest.

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Not applicable.

Consent for publication

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