Laparoscopic Hepatectomy for Hepatocellular Carcinoma

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Abstract. With the evolving of times, treatment strategies for laparoscopic hepatectomy are constantly evolving. However the result and indication of laparoscopic liver resection(LLR) is still controversial. This review assess the efficacy and outcomes of LLR through preoperative and postoperative factors. Most of article manifest that LLR is associated with the better improvement of operation. Nonetheless many difficulties are complicated and need to be captured.

Keywords: Laparoscopic Hepatectomy; Hepatocellular Carcinoma; Minimally Invasive Liver Surgery; Postoperative Outcomes.

1. Introduction

Liver cancer is the sixth-most-common cancer in the world, and the second-most-common reason of cancer-related death(1). Over 90% of liver cancer cases are hepatocellular carcinomas (HCCs). One of the reasons of high mortality is that there is still no particularly effective therapy for HCC at present.

In 2014 Kota Katanoda etc, published a review showed that in all the age group, the maximum mortality is 40% and that for older-aged-group is less than 10%(2).For the surgeon the usual options for therapy of that were chemotherapy and immunotherapy(3). For early stage HCC surgical resection and liver transplantation are usually the curative therapy. Abolition sometimes may also be applied to early stage patients(4). Although the overall survival rate for middle and advanced caner(CNLC IIb, IIIa, IIIb)is unsatisfactory, surgical resection can still benefit most of patients in the absence of other effective therapy(5). Before the first laparoscopic hepatectomy reported in1990s, patients can only choose open hepatectomy as surgical treatment of liver tumor(6). As time goes on, the benefits of laparoscopic were discovered by surgeon such as less venous bleeding, more accessible to the liver inside the rib cage, and better magnified view(7).After the 2nd International Consensus Conference on Laparoscopic Liver Resection, laparoscopic liver resection has been spread explosively in North America, Europe and East Asia(8).At the same time many surgeons start to use Indocyanine Green Fluorescence Imaging as a tactile mimicking visual tool(9).

Caelán M. Haney etc, published a review to compare laparoscopic and open liver resection in 2021, which included 80 articles and 1114 patients. Overall complication with laparoscopic and open liver resection rate is 125 per 1 and 253 per 1, respectively. The mean hospital stay was 2.9 days lower in Laparoscopic Liver Resection. The mean blood loss was 115.41ml lower in Laparoscopic Liver Resection. The large number of reports in this review were important for the demonstration of feasibility and better prognosis(10). But Kevin Tri Nguyen pointed out potential limitations and disadvantages of laparoscopic liver resection. including limitation to the size of tumor, potential bleeding, and those with vascular invasion(11).

Liver cirrhosis is a frequent consequence of the long clinical course of all chronic liver diseases. Characteristics of cirrhosis in histology is irreversible remodeling of architecture and cause hepatocellular nodules. Among these nodules, dysplastic nodules are premalignant(12).Regardless of root cause, cirrhosis is widely regarded as precursor of HCC(13).In a review among 91,666 autopsies, the prevalence rate of HCC patients with cirrhosis(7.4%-23%) is much higher than in patients without cirrhosis(0.3%)(14).

Cirrhosis is also a big challenge in surgery even for practiced surgeon. Because it may bring complications, such as lower platelet counts and portal hypertension, so it is important to select cirrhotic HCC patients before LLR(15) .According to review of Marco Vivarelli ,they introduced a

prophylaxis which can lower the incidence of postoperative thromboembolic complications safely(16).

In this review, we will summarize and stress the application and limitation for LLR for HCC. Then we will focus on the perioperative period and postoperative survival of patients.

2. Current Application of LLR in Liver Cancer

2.1 Small HCC and Large HCC

Small HCC is referring to a single nodule with a maximum diameter of 5cm(including) and minimum diameter of 2cm, without obvious symptoms and signs according to Chinese medicine association. Laparoscopic hepatectomy, percutaneous radiofrequency ablation and open hepatectomy is the mainstream surgery method of small HCC(17). In a study matched 108 patients (no significant differences in the demographic or operative characteristics) demonstrated that LLR have lower invasiveness and better safety(18). Another study published by Wenda Liu, included 87 open hepatectomy (OH) patients,133 laparoscopic hepatectomy (LH) and 60 MWA (microwave ablation) patients with no significative difference before treatment. MWA provide better short-term outcome but high risk of recurrence, LH not only provide familiar long-term result with OH but also provide fewer complications and less Hospital stay time(19). Also through the case report from Yukio Iwashita ,even Cirrhosis patients use laparoscopic hepatocellular of paracaval portion of liver with hand-assist method can be safe(20).In comparison with laparoscopic and open sugary, LLR is more preferable option of small HCC, which is reflected in disease-free and overall survival curves(21).

Large HCC is about 5-10cm in size which mentioned in the Southampton Consensus guidelines. It also mentioned that comparing to small HCC and more-tiny-tumor, large HCC laparoscopic surgery brings longer operative time and more blood loss. These phenomena are also referred in the Morioka guidelines(11, 22).So some difference exist in LLR using of large HCC, but only limited in cohort study. In a research published by Eunmi Gil including 45 patient with large HCC, long operation time truly exists (23). The same conclusion is also reached in other smaller retrospective studies, but in consideration of lager size of tumor longer operation time is predictable, however further study for long-term survival was absent and need to validate all these conclusion(24).After consideration, LLR is safe to large HCC patients. What cannot be ignored is lager tumor and different location may make surgeon hard to approach the area flexibly, such as around the caudate lobe and caval ligament(23, 25).Therefore, although LLR is applicable to large HCC, surgeons expertise is also limited its application.

2.2 Colorectal Carcinoma Liver Metastases

Carcinoma liver metastases is very common to be observed in various patients with cancer(26). Gastric and gallbladder carcinoma are particularly prevalent source of liver metastases among them(27). In addition of these, hepatic metastasis of colorectal carcinoma is one of the reasons of hepatocellular carcinoma. Nearly 15-25 percent of colorectal cancer patients encounter synchronous liver metastases. The best surgical management is synchronously surgical resection of both colorectal and liver cancer (28). Among patients who is bale to undergo a complete margin negative resection can have 50% 5-year overall survival rate(29). As early as in 2004, the study published by Abraham demonstrated that LLR is more efficient in short-term outcomes compared with conventional open resection(30).In a research which analyzed 61 patients with LLR, and most of them were small HCC patients. The conclusion of research showed that laparoscopic simultaneous resections would not influence the risk of postoperative complication compared to laparoscopic surgery alone(31).

2.3 Multiple Hepatocellular Carcinoma

Except for the tumors above, multiple liver cancer is the focus of attention in LLR. In 2018 the guidelines of European Association for the Study of the Liver, ablation or liver transplantation was the best choice of multifocal non-metastatic within Milan criteria(32).An early research about partial

hepatectomy written by Lei Yin, showed better overall survival of partial hepatectomy in multiple liver cancer, compared with the overall survival of radiofrequency or TACE, but it also cost the high recurrence rate of 68.9%(33). Recent research published in 2022 confirmed the feasibility of simultaneous multiple LLR. In this series surgery, including 463 patients which were divided into three group based on their tumor status. The result proved that this hundreds of patients with more than three LLR done during the same surgery, and has also shown its safety in terms of postoperative outcomes and quality of oncologic resection(34).

2.4 Difficulties in Using LLR for HCC

Lots of causes limited LLR using for HCC. Except for the substantial learning curve of laparoscopic surgeons, tumor size and location make great affect of LLR(35, 36). In The Southampton Consensus Guidelines, with the increase of incubation time, operative time, conversion rate, blood loss, morbidity, and hospital stay could be significantly improved(35).The guidelines also described the learning curve of major and minor resections which can be reduced by surgeons assisting each other, and emphasized the importance of training by a current and up-to-date knowledge of literature mentors and trainer(22).

Different procedures have different technical complexity(37). Therefore, in the laparoscopic hepatectomy, lots of standards and difficulty score emerged. In such a situation, Ban and colleagues have attempted to classify difficulty of LLR through a score with multiple variables such as tumor size, location and liver function(38).But these variables were confined, so Yoshikuni improved scoring system based on theirs. Yoshikuni use various characters except liver function, and stratified the difficulty of each LLR. Namely, lesions which are small and distant to major vessels (low score in Ban system) are mostly removed using wedge resection(37). Nearly five years to 2020, about 4500 difficult LLR has successfully completed. Most of difficult LLR procedures have become safe and feasible in specialized centers(39).

3. Perioperative Outcomes

3.1 Operation Result

3.1.1 Blood Loss and Transfusion

Due to the heterogeneity of each patient, the average blood loss ranged in 207ml of LLR and 441ml of open hepatectomy. In an analysis with 11 trails published by Li Xing showed that laparoscopic surgery had significantly less blood loss (SMD = −0.56,95% CI −0.99 to −0.12; P = 0.01)(40).And Cai's fixed effects model also prove the less blood loss of laparoscopic hepatectomy, which may have absolutely benefited the patients 'recovery(41).The conclusion of other six studies reported that comparing to open resections, laparoscopic resection was more associated with lower blood loss(42).Transfusion is closely related to blood loss, 11 studies included 562 open resections and 441 LLRs for solitary HCC which conducted in Europe found that with equal operative time between the groups, no matter blood loss or transfusion was favored a laparoscopic approach(43).

3.1.2 R-0 resection

A study reported the R-0 resection from five researches showed that R-0 resection rate was higher in LLR, but that was no difference in HCC and metastases cancer(44). Castaing showed the visual rate of R-0 resection, it is 87% in LLR and 72% in open surgery(45). Other two control experiments draw the conclusion that in the final histopathological report no difference exists in both two groups(46, 47). In conclusion, comparing LLR with open resection, no significant negative effect on R-0 resection was found in current study.

3.1.3 Time of Operation

Wakabayashi summarized eight studies which median operative time range 120 to 413min.The article also mentioned open resection take longer time than LLR(48).But some other studies gives

completely different outcomes, in these studies operating time of LLR was significantly longer than open resection, however most of articles emphasized the short-term clinical advantages was incomparable with open resection, such as less blood loss, lower postsurgical morbidity in HCC(42, 49-51).In a Parenchymal-sparing hepatectomies (PSH) study, the median operating time was 189 min(range 125-369)(42).Both in PSH, Chen compared outcomes between anatomic and non-anatomic. He found a significantly longer operating time(52).In different position of liver, outcomes were different. Compare left and posterosuperior segments, longer operating time were observed in the posterosuperior segment resections(53).

3.1.4 Postoperative Survival

Part of studies were observed no differences between the approaches in overall or disease-free survival at 1,3,5 years(43).But LLR, like open surgery, was still in the risk of recurrence. So it was inevitable for part of patients to experience reoperation. Shelat etc. compared the outcome of primary LLR (P-LLR) with the outcome of repeat LLR (R-LLR), they showed that although even in expert hands, R-LLR have higher operative time, blood loss, and conversion rate. R-LLR has no impact on postoperative outcomes. Clearly, it proved the importance of meticulous dissection techniques which played an essential role in postoperative survival(54).

4. Conclusion

In conclusion, LLR is under constant development during last thirty years. With the advance in surgical techniques and accumulation of experience, LLR of HCC is safe and can offer more short-term advantages over open resection including transplanted patien·t (55). But learning curve and professional should remain the first factor of LLR outcomes. And some unfavorable tumor locations have been better choices to offer the benefits of laparoscopic surgery. Therefore, LLR have comparable postoperative and economic outcomes in comparison with open liver surgery. Though LLR still have a high development space, and may be the first choice of HCC. Moreover, selection of appropriate candidates and satisfactory perioperative preparation are the key points to ensure the success of the approach.

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