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Review Article

Laparoscopic Liver Resection in Ruptured Hepatocellular Carcinoma [with Video]

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ABSTRACT

Laparoscopic liver resection (LLR) has emerged as a valuable treatment option for managing ruptured hepatocellular carcinoma (HCC). As surgery is one curative treatment of HCC in selected patients, LLR offers advantages over open liver resection (OLR) in terms of reduced blood loss, shorter hospital stays, and comparable postoperative outcomes. While LLR is feasible for non-ruptured HCC, its role in resections of ruptured HCC remains a controversial issue. The primary and secondary aims of this article were to review the current role of LLR, and provide patient selection criteria for ruptured HCC. To date, only 10 cases with good postoperative outcomes have been reported in patients having undergone LLR for ruptured HCC. Patient selection is crucial, along with individualized assessment; based on hemodynamic status, tumor burden and liver function, to guide treatment decisions. In highly selected patients with ruptured tumor, LLR in an experienced center can provide a minimally invasive alternative to OLR; leading to improved patient outcomes. As current evidence relies exclusively on minor hepatectomy case series, further studies are necessary to refine indications and optimize outcomes in this specific context.

Keywords: Hepatectomy; hepatocellular carcinoma; laparoscopy; laparoscopic hepatectomy; minimally invasive liver resection; ruptured hepatocellular carcinoma

INTRODUCTION

Despite advancements in treatment modalities and development of new targeted drugs[1], hepatocellular carcinoma (HCC) is still the third most common cause of cancer-related death[2]. The incidence of ruptured HCC has been reported as 10% to 15% in Asian countries[3]. In addition, the mortality rate in ruptured HCC remains high (25-75%) owing to intraperitoneal hemorrhage and liver failure that occurs in 12% to 42% during the acute phase[4]. Hence, the management of this life-threatening condition

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is still challenging in the current era. Curative treatment of HCC includes: liver transplantation, liver resection, and local ablation. Nevertheless, ruptured tumors are considered to be one of the contraindications for liver transplantation[5]. While subcapsular, exophytic, and large tumors (>5 cm) are risk factors for rupture[3], they are also contraindications for ablation. Hence, surgical resection is the only chance for curative treatment in ruptured HCC.

As of the first reported laparoscopic liver resection (LLR) for HCC, published in 1995[6], LLR has played a crucial role in the management of HCC; even in cases of ruptured tumors. LLR is increasingly performed worldwide as a curative surgical option for liver tumors, because it offers advantages; such as less blood loss, fewer blood transfusions, lower postoperative complications and shorter hospital stay, compared to open hepatectomy[7]. Additionally, a laparoscopic procedure seems to lower the risk of postoperative ascites, or liver failure; even in patients with cirrhosis[8]. Furthermore, the results from a randomized controlled trial in patients with HCC showed LLR is preferable over open liver resection (OLR), with a noticeably shorter hospital stay and no compromise to oncological outcomes[9]. Nevertheless, the use of LLR in ruptured HCC is still in the exploratory stages due to the complexity of tumors and patient circumstances.

An electronic search of articles published before February 2024 was carried out on MEDLINE and EMBASE (Supplementary Video 1) https://drive.google.com/file/d/1R2vZXygU2uvXMRNLUXGVXKUVODzKVMUc/view?usp=sharing.

A manual search of the references was undertaken for additional articles. This review aimed to discuss the current role and limitations of LLR in ruptured HCC, based on the available evidence and experience of the author.

Current role of laparoscopic liver resection in HCC

More than three decades ago, the first laparoscopic hepatectomy was reported[10]. Additionally, three international consensuses on laparoscopic liver surgery have greatly contributed to the application, education, and adoption of minimally invasive hepatectomy[11-13].

In reference to the Asia Pacific consensus recommendations, which primarily focused on the treatment of HCC, patient selection for a laparoscopic approach included: a liver function evaluation, tumor size and tumor location[14]. The preferable selection criteria for LLR in HCC includes: peripheral segments, minor liver resection, preservation of liver function and tumor size ≤5 cm. Any tumors that are: a) located in difficult locations, b) >5 cm, or c) require major hepatectomy should be carefully selected to undergo LLR in centers of excellence given the chances of oncological compromise, insufficient margin clearance, and risk of rupture during manipulation[14].

Oncological outcome is a major concern when LLR is used in cases of a primary liver tumor that could easily rupture, as in patients with HCC. One study has demonstrated that the pattern of recurrent HCC after LLR or OLR was not different between the two groups, without any port site metastasis in the LLR group[15]. A multicenter propensity score matching analysis was performed between patients having undergone LLR or OLR in selected HCC patients, with mean tumor sizes of 2.8 cm, difficult locations in 21.2%, and major hepatectomy in 10.9%. Patients having undergone LLR had fewer postoperative morbidities than patients that underwent OLR; additionally, the LLR patients exhibited comparable long-term outcomes[16]. Outcomes from a meta-analysis of propensity score matching analyses in patients with HCC that underwent laparoscopic right hepatectomy revealed significantly reduced severity of complications in the LLR group, with comparable 2-year disease free survival and OS[17]. Furthermore, the laparoscopic approach in minor hepatectomy is the only independent factor associated with reduction in the complication rate for HCC[18]. In a specific group of patients with cirrhosis, LLR significantly reduced postoperative ascites and liver failure[8], and a 26% reduction in hazard ratio of death was observed[19].

Growing evidence has elucidated the benefits of the laparoscopic approach in patients with HCC. Additionally, the accumulating experience of liver surgeons and the knowledge of liver anatomy have contributed to the widespread adoption of LLR; not only in minor non-anatomical resections (NAR) but also in major or anatomical hepatectomy[20].

Various techniques for LLR have been developed; including pure laparoscopic, hand-assisted and hybrid approaches. Among these, pure laparoscopy has been increasingly adopted over the past decade, particularly for complex procedures[21]. Hepatic inflow control in LLR typically involves three methods: intermittent total inflow occlusion (Pringle's maneuver), hemihepatic control, and the Glissonian approach. While the Pringle's maneuver is technically simple, it carries a risk of global hepatic ischemia and related complications[22]. In contrast, the Glissonian approach enables precise anatomical resections[23] including hemihepatectomy, segmentectomy, and subsegmentectomy with better preservation of uninvolved liver tissue. Comparative studies have shown that the Glissonian technique offers advantages; such as reduced operative time, lower blood loss, fewer positive margins[24], shorter hospital stay and improved perioperative outcomes[25]. Moreover, anatomical resection aligned with portal distribution provides superior oncologic control without increasing morbidity or mortality[26].

Role of laparoscopic liver resection in ruptured HCC

The precise mechanism of spontaneous rupture in HCC is still not fully understood; although, several hypotheses have been proposed[3]. Tumors situated subcapsularly or within anatomically constrained regions; such as the left hepatic lobe or caudate lobe, appear particularly vulnerable due to limited surrounding parenchyma, which provides insufficient structural support and resistance to tumor expansion[27]. Rapid tumor proliferation, intratumoral necrosis, and local vascular invasion may lead to obstruction of hepatic vein branches, resulting in elevated intratumoral pressure and venous congestion[4]. These hemodynamic disturbances are thought to precipitate vascular dysfunction by accelerating the degradation of elastin and type IV collagen, thereby rendering blood vessels rigid and fragile[28] conditions that predispose them to rupture under minimal external force or systemic hypertension. Additionally, the frequent coexistence of liver cirrhosis in HCC patients compromises hepatic synthetic capacity; including the production of coagulation factors. In the event of rupture and hemorrhage, resulting hypoperfusion further impairs hepatic function and exacerbates coagulopathy; thereby, increasing the likelihood of persistent or recurrent bleeding[29]. The pathophysiological mechanisms underlying ruptured HCC are illustrated in Figure 1.

Spontaneously ruptured HCC has been a significant subgroup of patients having undergone hepatectomy: accounting for 9.8-11.5% of all operable HCCs[30,31]. In patients presenting with spontaneously ruptured HCC, the aims of initial management should focus on resuscitation and hemostasis, followed by definitive treatment. Emergency 1-stage resection is associated with high inpatient mortality (16.5-100%); however, staged hepatic resection mortality is approximately 9%[3,32]. In this circumstance, the most accepted approach is the sequential transarterial embolization (TAE) or transarterial chemoembolization (TACE), followed by hepatectomy; which is the so called staged hepatic resection[33,34]. The poor outcomes associated with emergency hepatectomy are likely linked to unclear liver function reserve and hemorrhagic shock. Therefore, emphasis needs to be placed on the importance of patient selection as well as optimization of liver function prior to surgery.

A staged hepatectomy can be carried out either by the open or laparoscopic approach (Supplementary Video 1). Patient selection for LLR should follow the same indications as OLR, with additional criteria based on the center's experience[14]. Accordingly, patients that undergo LLR could at least achieve the general

benefits of this minimally invasive approach. However, awareness of the limitations for laparoscopy in ruptured HCC must be underscored; such as limited visibility due to hemoperitoneum, exacerbation of hemorrhagic shock from pneumoperitoneum and prolonged operating times. LLR should only be performed in hemodynamically stable patients with good liver function, accessible tumors, and low difficulty scores. Key concerns include: the risk of gas embolism[35], inadequate hemorrhage control and compromised oncologic outcomes due to involved surgical margins. Advanced laparoscopic skills and experience in hepatobiliary disease management are crucial. Although peritoneal metastasis is a concern in LLR, the occurrence is rare[15,36], and complete resection may lead to long-term survival[36]. In addition, the laparoscopic approach allows comprehensive evaluation of the peritoneal cavity and early detection of disseminated nodules, enabling timely systemic treatment[37,38]. Beyond enabling early detection of dissemination, the laparoscopic approach requires mitigation strategies; such as minimal manipulation and protected specimen extraction, to improve patient outcomes. A study of 42 patients with ruptured HCC having undergone OLR showed a 14.3% rate of postoperative liver failure; a 30-day mortality rate of 2.4%, with a reported 5-year OS rate of 52%[31]. Significant predicting factors of worse OS were also identified; such as large tumor size, vascular invasion and positive margin. A recent study of 91 patients also confirmed a significant difference in 5-year OS in surgery (55.1%) versus a non-surgery group (0%) regardless of prior treatment with TACE[39].

To our knowledge, only 10 cases have been reported in the literature of patients with ruptured HCC having undergone LLR (Table 1). The first report of LLR in ruptured HCC was in 2009. This included two laparoscopic AR (i.e., laparoscopic lateral sectionectomy) and one laparoscopic NAR (i.e., laparoscopic wedge resection of segment 6). In this series, the operative times ranged from 100 to 150 minutes, and postoperative hospital stays ranged from 5 to 7 days. One patient experienced peritoneal recurrence at 18 months postoperatively, while the other two patients remained disease-free at 24 and 27 months[32]. The only major LLR was reported in 2018, which was a left hepatectomy, in a 66-year-old male with HCC in non-hepatitis and non-cirrhotic liver. This parient

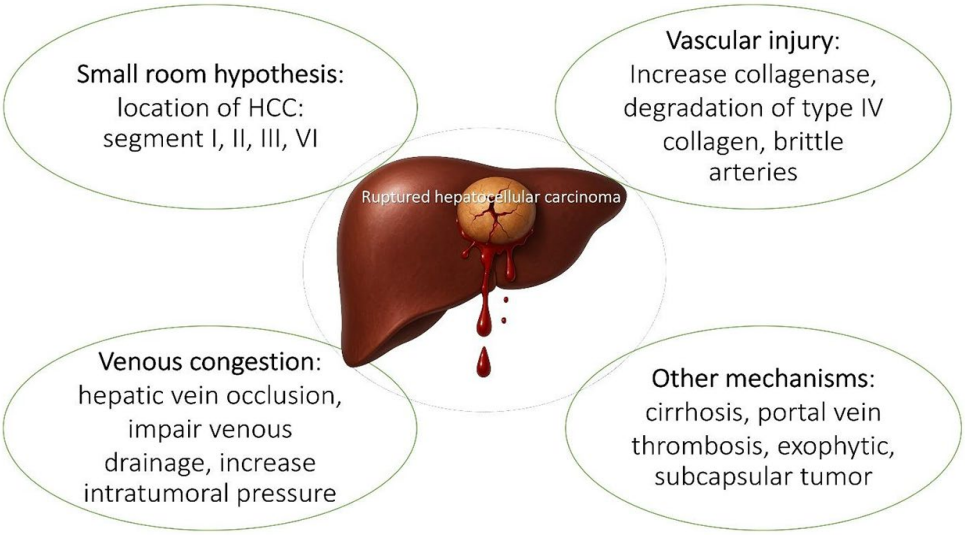


Figure 1 The pathophysiological mechanisms of ruptured hepatocellular carcinoma

Table 1 Summary of case reports on laparoscopic liver resection of spontaneously ruptured hepatocellular carcinoma

Study (Year)	No.	Age (Years)	Timing of surgery[†]	Preoperative TAE or TACE	Type of operation	Tumor size (cm)	Operative time (m)	Cirrhosis	Complications	Recurrenc[‡] (Months)
Belgaumkar et al.[34] (2009)	1	39	4	No	LLS	8.5	110	No	None	No (27)
	2	44	12	TAE	LLS, wedge segment 5	13	150	No	None	No (24)
	3	51	21	No	Wedge segment 6	8	100	No	None	Yes (18)
Yoshiya et al.[39] (2018)	4	66	110	TAE	Left hepatectomy	6	194	No	None	NA
Kabir et al.[40] (2019)	5	69	1–12	No	HA–wedge segment 6	4.5–12.5	165	Yes[§]	None	NA
	6	51	1–12	No	Wedge segment 5/6	4.5–12.5	170	No	None	NA
	7	81	1–12	No	Wedge segment 6/7	4.5–12.5	215	No	None	NA
	8	81	1–12	No	Wedge segment 5/6	4.5–12.5	215	No	None	NA
	9	88	1–12	No	Open conversion to wedge segment 5/6	4.5–12.5	230	No	Yes, minor	NA
Khairuddin et al.[41] (2020)	10	55	1.25	No	Wedge segment 2/3	10	180	No	None	NA

[†]Parenthesis indicates days after onset of rupture; [‡]Outcomes at the last follow–up; [§]reported one in five cases; TAE=trans–arterial embolization; TACE=trans–arterial chemoembolization; m=minutes; LLS=left lateral sectionectomy; N/A=not available; HA=hand assisted

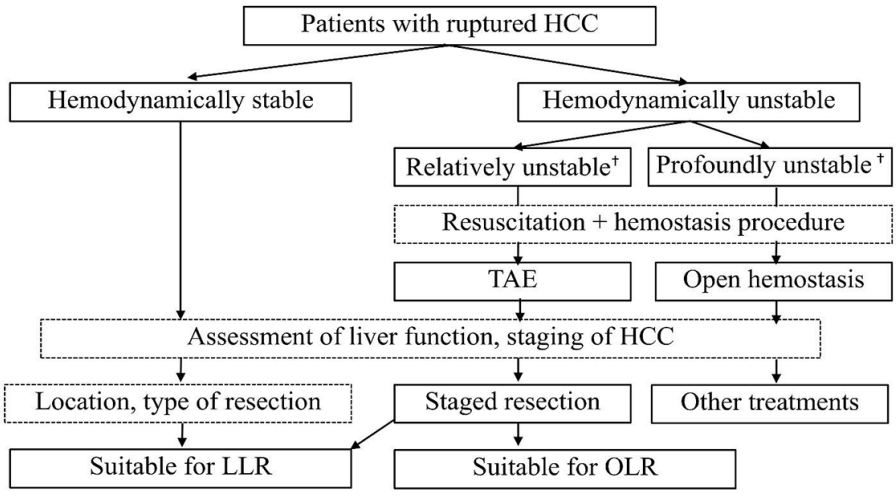
successfully underwent staged hepatectomy 110 days after TAE. Due to the tumor and hematoma location, only a left hepatectomy allowed *en bloc* resection. The authors stated that the longer interval led to reduced intraperitoneal hemorrhage, which potentially enabled pure laparoscopic surgery of the left hepatectomy. The postoperative course was uneventful, and the patient was discharged on day 6[37]. In 2019, the largest series of LLR for ruptured HCC reported five LLR patients that were matched to 10 cases of OLR for ruptured HCC. Additionally, a distinct cohort undergoing LLR for non–ruptured HCC was compared with the laparoscopic group[40]. The authors believed that since early laparoscopic hepatectomy could possibly reduce a recurrent rupture event and the risk of tumor recurrence, 4 out of 5 patients underwent a semi–emergency LLR within the index admission. It is important to note that the authors had extensive experience with LLR. They carefully selected hemodynamically stable patients with good liver function and peripherally located tumors. Despite the high inpatient mortality rate reported in emergency surgery[3], the authors achieved no 90–day mortality. Interestingly, when LLR was compared to OLR for ruptured HCC, no significant differences in perioperative outcomes were observed in median operating time, blood loss, blood transfusion, length of stay; overall complication rates, major complication rates and 90–day mortality rates. In addition, comparable outcomes were observed in LLR for ruptured HCC compared to LLR in non–ruptured HCC. The latest report of LLR for ruptured HCC was in 2020. In this case, the authors performed an uneventful emergency laparoscopic wedge resection of segment 2/3 for a 10 cm tumor. The same selection criteria were applied, which included: hemodynamically stable, no ongoing bleeding and good functional liver reserve[41]. Notably, all patients were hemodynamically stable, and the majority had non–cirrhotic liver disease with preserved liver function. Additionally, 9 out

of 10 hepatectomies were minor resections, 7 out of 10 were NAR, and all (10 out of 10) involved peripherally located tumors. These findings highlight the importance of careful patient selection based on liver function, type of resection, and tumor location, all of which are critical for achieving favorable surgical outcomes. A summary of the key selection criteria and surgical considerations is presented in Table 2. The summarized surgical technique, derived from previously reported cases[32,37, 40–42], involved positioning patients in the supine and reverse Trendelenburg positions to optimize surgical visualization and reduce central venous pressure (CVP). Port placement was performed using the open Hasson technique, so as to minimize the risk of vascular injury. A 12 mm supraumbilical port was inserted for the laparoscope, along with additional 5–12 mm working ports placed in the epigastrium, bilateral hypochondria, and lateral abdomen. In selected cases, the umbilical port site was extended to facilitate specimen retrieval. Intraoperative ultrasonography (IOUS) was utilized to assess the future liver remnant, localize lesions, and delineate resection margins. Parenchymal transection was performed using a caudal-to-cranial approach, employing a combination of the Harmonic scalpel, ultrasonic dissector (CUSA), and soft coagulation; under intermittent inflow control via the Pringle's maneuver. Small vessels were sealed using energy devices, while larger structures including branches of the Glissonian pedicle and major hepatic veins were divided with clips and staplers. Based on the available evidence, we propose a management algorithm for ruptured HCC: as illustrated in Figure 2.

Table 2 Key selection criteria and surgical considerations

Hemodynamic stable
Non-cirrhotic liver with preserved liver function
Minor liver resection (90%)†
Non-anatomical liver resection (70%)†
Peripheral location of tumor (100%)†

†Proportion of patients based on reported cases



TAE=transarterial embolization; LLR=laparoscopic liver resection; OLR=open liver resection

Figure 2 Management algorithm for ruptured hepatocellular carcinoma (HCC); other treatments include: transarterial chemoembolization, ablation, and systemic therapy. †: Profound instability: refractory hypotension and hypoperfusion, despite resuscitation. Relative instability: responsive to resuscitation, permitting definitive assessment and intervention

Conclusion and future perspectives

LLR in ruptured HCC is feasible; however, the evidence in this area remains limited. To date, a consensus recommendation has not been reported. The selection criteria, based on the existing evidence for LLR in highly selected patients that require minor resection are: preserved liver function, hemodynamic stability, no ongoing bleeding, and small and peripherally located tumors without macrovascular invasion. In this group of patients, perioperative outcomes seem to be comparable to OLR in ruptured HCC. Additionally, the outcomes with LLR in ruptured HCC appear to be comparable with LLR in non-ruptured HCC. Moreover, LLR shows promise for liver tumors beyond HCC; although, its use in hilar cholangiocarcinoma (HCCA) remains limited due to high complexity and morbidity rates of up to 40%[43]. Currently, LLR in HCCA is restricted to highly selected cases. In contrast, for colorectal cancer liver metastases, LLR offers benefits; such as fewer complications, shorter hospital stays, earlier chemotherapy initiation and improved quality of life, with long-term outcomes comparable to OLR[44-47]. As techniques improve, LLR could expand its role in liver tumor management.

Authors' contributions

The author contributed solely to the article.

Ethical approval and consent to participate

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Consent for publication

Not applicable

Availability of data and materials

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CONFLICT OF INTEREST

The author declares that there are no conflicts of interest.

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