The current role of laparoscopic resection for HCC: a systematic review of past ten years

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Abstract: The use of laparoscopic liver resection (LLR) has progressively spread in the last 10 years. Several studies have shown the superiority of LLR to open liver resection (OLR) in term of perioperative outcomes. With this review, we aim to systematically assess short-term and long-term major outcomes in patients who underwent LLR for hepatocellular carcinoma (HCC) in order to illustrate the advantages of minimally invasive liver surgery. Through an advanced PubMed research, we selected all retrospective, prospective, and comparative clinical trials reporting short-term and long-term outcomes of any series of patients with diagnosis of HCC who underwent laparoscopic or robotic resection. Reviews, meta-analyses, or case reports were excluded. None of the patients included in this review has received a previous locoregional treatment for the same tumor nor has undergone a laparoscopic-assisted procedure. We considered morbidity and mortality for evaluation of major short-term outcomes, and overall survival (OS) and disease-free survival (DFS) for evaluation of long-term outcomes. A total of 1,501 patients from 17 retrospective studies were included, 15 studies compare LLR with OLR. Propensity-score matching (PSM) analysis was used in 11 studies (975 patients). The majority of the studies included patients with good liver function and a single HCC. Cirrhosis at pathology ranged from 33% to 100%. Overall mortality and morbidity ranges were 0–2.4% and 4.9–44% respectively, with most of the complications being Clavien-Dindo grade I or II (range: 3.9–23.3% *vs.* 0–9.52% for Clavien I–II and ≥ III respectively). The median blood loss ranged from 150 to 389 mL; the range of the median duration of surgery was 134–343 minutes. The maximum rate of conversion was 18.2%. The median duration of hospitalization ranged from 4 to 13 days. The ranges of overall survival rates at 1-, 3- and 5-year were 72.8–100%, 60.7–93.5% and 38–89.7% respectively. The ranges of disease free survival rates at 1-, 3- and 5-year were 45.5–91.5%, 20–72.2% and 19–67.8% respectively. The benefits of LLR in term of complication rate, blood loss, and duration of hospital stay make this procedure an advantageous alternative to OLR, especially for cirrhotic patients in whom the use of LLR reduces the risk of post-hepatectomy liver failure. The limits of LLR can be overcome by robotic surgery, which could therefore be preferred. Further benefits of minimally invasive surgery derive from its ability to reduce the formation of adhesions in view of a salvage liver transplant. In conclusion, the results of this review seem to confirm the safety and feasibility of LLR for HCC as well as its superiority to OLR according to perioperative outcomes.

Keywords: Hepatocellular carcinoma (HCC); laparoscopic liver resection (LLR); review

Introduction

Hepatocellular carcinoma (HCC) is the sixth most frequent primary cancer and the third cause of cancer-related deaths worldwide, with 782 000 diagnoses in 2012 and a rising incidence (1). According to Barcelona Clinic Liver Cancer (BCLC) staging system, liver resection represents the first choice for treatment of patients with very early and early HCC (BCLC stage 0–A) (2). About 80–90% of HCCs arise in a cirrhotic liver (1), therefore any surgical procedure in these patients implies higher risks of complications, both intra-operative (e.g., bleeding) and post-operative (e.g., post hepatectomy liver failure, PHLF) (3). Before 1991, when first laparoscopic liver resection (LLR) was described (4), open approach was the only choice for liver surgery. Since then, LLR spread exponentially: initially only non-anatomical wedge resections were considered as a safe procedure; later on, anatomical resections were introduced and today specialized centres perform also major hepatectomies. At present, more than 9,000 LLRs are described in literature (5), but most of them are minor resections of subcapsular lesions or lesions located in the left lobe. For these lesions, laparoscopy is now considered a standard practice. Major hepatectomies and resections of posterosuperior segments, instead, are still regarded as innovative procedures that need to be fully developed (6). Since open liver resection (OLR) represents the standard technique, it is crucial to determine advantages and disadvantages of LLR versus OLR. Unfortunately, no randomized controlled trial has been published up to now, therefore the quality of evidence in this field is low, mainly based on case series and case-matched analyses. In order to define the current role of LLR and to establish guidelines, the Second International Consensus Conference on LLR was held in 2014, in Morioka (7). According to Morioka's statements, LLR does not show inferior results considering mortality, overall survival (OS), negativity of margins, and costs, while seems to be superior in term of length of hospitalization and number of intra-operative blood transfusions. Morbidity rates in LLR are inferior when major resections only are considered. Minimally invasive surgery reduces the rate of decompensation in cirrhotic patients and adherence formation, the latter being a desirable goal in view of an eventual salvage liver transplantation (6). Further advantages are given by image magnification allowed by the endoscope and better aesthetical results. On the other side, LLR requires higher skills (e.g., suturing skills) and shows some technical limitations such as lack of tactile feedback, restriction of movements, and presence of physiologic tremors. Furthermore, resections of lesions located in posterosuperior segments (I, IVa, VII and VIII) still constitute a big challenge even for expert surgeons. Finally, difficult haemorrhage control is the main reason of conversions to laparotomic approach (6). However, some of these limitations might be overcome by the introduction of robotic surgery. In fact, this new minimally invasive technique guarantees stability, increases freedom of movement thanks to instrument flexibility and introduces a three-dimensional vision with depth perception (8).

The aim of this review is to systematically assess short-term (morbidity and mortality) and long-term (OS and disease-free survivals) major outcomes in patients who underwent LLR for HCC.

Materials and methods

We conducted an advanced PubMed research to select articles of interest. The following keywords were used to search in titles or abstracts: "HCC" or "hepatocellular carcinoma" and "liver resection" or "surgery" or "hepatectomy" and "laparoscopic" or "minimally invasive" or "robotic". Our enquiry was restricted to English articles, published from January 2007 to December 2017 and for which full text was available. We applied the "article types" filter to select "clinical trial", "comparative study", "multicenter study" and "validation study". A total of 86 remaining articles were considered for revision. We included all retrospective, prospective, and comparative clinical trials reporting short-term major outcomes and long-term outcomes of any series of patients with diagnosis of HCC who underwent laparoscopic or robotic resection. Morbidity and mortality were considered for evaluation of short-term outcomes, while long-term outcomes were expressed in terms of overall survival (OS) and disease-free survival (DFS). Data related to intra-operative outcomes (blood loss, total operation time and duration of surgery) and post-operative outcomes (duration of hospitalization) were collected, although not being the main object of this review. Among comparative studies, we included only those comparing different surgical techniques (e.g., laparoscopic versus robotic), while we excluded those comparing laparoscopies to all other curative options for HCC (e.g., ablative treatments). Studies were excluded if they: (I) were reviews, meta-analyses or case reports; (II) included patients resected after receiving locoregional treatments for

Citations identified
for screening n=86

Rejected (met exclusion criteria)
n=38

Studies retrieved
n=48

Rejected (did not meet inclusion
criteria) n=31

Studies retrieved
n=17
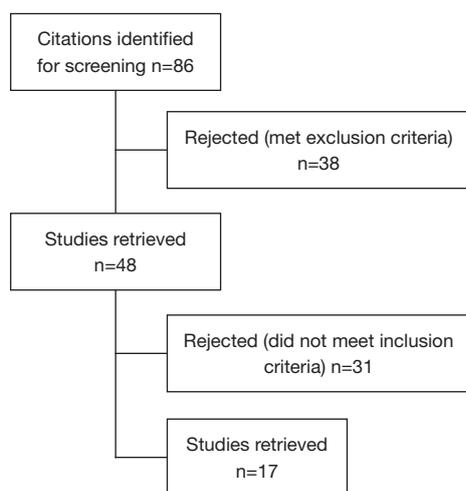
Figure 1 Flow chart illustrating selection process.

the same tumor; (III) included patients resected for lesions other than HCC (e.g., metastatic tumors); (IV) included laparoscopic-assisted procedures; (V) considered series of highly selected patients (e.g., obese patients or elderly patients); (VI) did not report any of the outcome considered in this review; (VII) full text was not available.

When more than one article was reported by the same institution and/or authors, we selected either the one with the largest series or the most recent, with the exception of multicenter studies. We considered patients after propensity-score matching (PSM) whenever it was performed.

Laparoscopic resections were included when performed with pure laparoscopic or hand-assisted techniques. Pure laparoscopic resection's essential features are pneumoperitoneum induction, generally through a periumbilical incision, and ports placing (usually three or four ports from 5 to 12 mm), followed by intra-abdominal parenchymal transection; at the end of the resection a larger incision is performed in order to retrieve the specimen from abdominal cavity, most frequently through an enlarged port site or a new incision, such as Pfannenstiel incision. For hand-assisted technique, besides ports for laparoscopic instruments, a further incision is performed through the abdominal wall for the placement of a hand port, allowing the introduction of the operator's hand in the abdomen for manual palpation of the various structures and for parenchyma retraction during transection. Laparoscopic-assisted liver resections were not considered as "laparoscopic" procedures in this review.

Pre-operative diagnosis of HCC was based on invasive (i.e., biopsy) or non-invasive European Association for the Study of the Liver (EASL) criteria (9). The percentage of patients with liver cirrhosis at pathology was reported for each study whenever available. Mortality is considered at 30- or 90-day postsurgery or intra-hospital. We reported the overall complication rate for each study and, whenever available, we also reported complication rates classified according to type (surgical *vs.* non-surgical) and severity [grade I–II or ≥ III according to Clavien-Dindo classification (10)]. Wound infections, biliary fistula, liver failure, portal thrombosis, abscesses and other conditions were considered as surgical complications. General postoperative complications such as pulmonary complications, renal failure, and ileus or cardiac arrhythmia were considered as non-surgical complications.

Results

Study and patients characteristics

A total of 1,501 patients from 17 studies were included. The selection process is shown in *Figure 1*. *Table 1* illustrates the main characteristics of the studies. Among the studies selected, all are retrospective and 15 out of 17 compare LLR with OLR; one compares robotic and laparoscopic techniques and one compares recent and early experience of LLR. PSM analysis was used in 11 studies to compare cohorts of patients who underwent LLR *vs.* OLR; variables used for the PSM and PSM ratio are reported in *Table 1*. A total of 975 patients were included after PSM.

The majority of patients underwent pure laparoscopic resection, while robotic and hand-assisted techniques were less represented. Presence of cirrhosis at pathology ranged from 33% to 100%; in 3 studies cirrhosis was an inclusion criteria (142 patients). All the patients included had a good liver function, resulting in Child-Pugh class A or normal liver function without portal hypertension for most of them. Among the studies included, 6 were conducted on patients with single nodule of HCC and in the other series the majority of patients had only one nodule of HCC. The mean diameter of the major nodule or of the single nodule ranged from 2.5 to 6.7 cm (*Table 1*).

The extension of resections ranged from subsegmentectomies to major hepatectomies. The tumours were located in any part of the liver; thus, resections involved every segment including the posterosuperior ones.

Table 1 Main characteristics of the studies included

Study [year]	Cirrhosis at pathology (%)	Mean diameter (cm)[a]	Nodules number[b]	Type of minimally invasive surgery	Group of comparison	PSM	Variables for PSM	Ratio PSM
Chen et al. [2017]	45.7%	–	–	Robotic	OLR	Yes	Age, sex, hepatitis profile, underlying hepatopathy (e.g., liver dysfunction, cirrhosis), and tumor size.	1:1
Cheung et al. [2016]	70.9%	2.6 (0.6–10)	90.9% single	Pure laparoscopic	OLR	Yes	Age, sex, liver function, tumor size, tumor number, tumor stage, hepatitis serology, and comorbidity	1:3
Lai et al. [2016]—robotic	80%	3.3±1.9	1 [1–4]	Robotic	R vs. L	No	–	–
Lai et al. [2016]—laparoscopic	33%	2.7±1.3	1 [1–2]	23 hand assisted, 12 pure laparoscopic	R vs. L	No	–	–
Sposito et al. [2016]	100%	2.6 (1.0–6.5)	1 [1–4]	Pure laparoscopic	OLR	Yes	Age, ECOG performance status, liver cirrhosis, CTP grade, MELD score, portal hypertension, number of nodules, maximum tumour diameter, BCLC stage, tumour location and type of resection	1:1
Han DH et al. [2016]	53.5%	2.51±1.14	92.9% single	83 pure laparoscopic and 16 robotic	OLR	Yes	–	1:2
Takahara et al. [2015]	61.7%	2.88±1.51	1.17±0.52	–	OLR	Yes	Sex, age, underlying liver disease, tumor size and number, AFP and des-gamma-carboxy pro- thrombin levels, indocyanine green retention rate at 15 min (ICGR 15 min), extent of liver damage, Child–Pugh score, tumor location, and distant metastasis	1:1
Xiao et al. [2015]	33%	4.22±2.05	1 [1–1]	Pure laparoscopic	OLR	No	–	–
Martin et al. [2015]	40%	6.7 (2.5)	1.2 [1–2]	65 pure laparoscopic and 35 hand-assisted	OLR	No	–	–
Yoon et al. [2014]	–	2.87 (0.7–4.9)	1 [1–1]	Pure laparoscopic	OLR	Yes	–	1:3
Lee et al. [2015]	41.8%	5.4 [2–16]	95.3% single	Pure laparoscopic	OLR	Yes	Age at operation, maximal tumour size and tumour number	1:2
Memeo et al. [2014]	100%	3.2 (0.9–11)	1 [1–3]	Pure laparoscopic	OLR	Yes	Cause of cirrhosis, Child-Pugh class, surgical resection type, tumor number, tumor size, a-fetoprotein (AFP) value, and pathological characteristics	1:1

Table 1 (*continued*)

Table 1 *(continued)*

Study [year]	Cirrhosis at pathology (%)	Mean diameter (cm)[a]	Nodules number[b]	Type of minimally invasive surgery	Group of comparison	PSM	Variables for PSM	Ratio PSM
Ahn *et al.* [2014]	68.6%	2.6–1.5	100% single	Pure laparoscopic	OLR	Yes	Baseline characteristics, including age, sex, BMI, underlying liver disease, presence of liver cirrhosis, ICG-R15, extent of resection and location and size of the tumor	1:1
Lee *et al.* [2011]	84.8%	2.5 (1.5–9)	93.9% single	Pure laparoscopic	OLR	No	–	–
Dagher *et al.* [2010]	73.6%	3.6 [1–20]	1 [1–1]	95.1% pure laparoscopic, otherwise hand-assisted	Recent *vs.* early experience	No	–	–
Aldrighetti *et al.* [2010]	56.2%	4±2.2	1 [1–1]	Pure laparoscopic	OLR	Yes	Type of resection, tumor size, and the presence/degree of cirrhosis	1:1
Tranchart *et al.* [2009]	73.8%	3.58±1.75	1 [1–1]	Pure laparoscopic	OLR	Yes	Sex, age, ASA score, severity of liver disease, tumor size, and type of resection	1:1
Belli *et al.* [2009]	100%	3.8±1.3	81% single51 pure laparoscopic and 3 hand-assisted	Pure laparoscopic	OLR	No	–	–

[a], mean diameter of the nodule (cm) ± standard deviation or (range); [b], nodules number (cm) ± standard deviation or [range] or rate%. OLR, open liver resection; R, robotic; L, laparoscopic.

Short-term outcomes

Table 2 shows short-term major outcomes for each study. Mortality rates ranged from 0% to 2.4% with 13 series out of 17 reporting 0% mortality. Considering all the studies, 5 patients died in the perioperative period: two of them for acute respiratory distress syndrome, one for liver failure and one for tumour progression. For one patient the cause of death was not reported.

Overall morbidity rates ranged from a minimum of 4.9% to a maximum of 44%. Classification according to Clavien-Dindo was available for 11 studies and in these series most of the post-operative complications fell in Clavien grade I and II (range: 3.9–23.3%), while grades III to V were a minority (range: 0–9.52%). A total of 15 studies reported also surgical *vs.* non-surgical complications; the maximum rate of non-surgical complications was 15.55%, while the maximum rate of surgical complication was 25.16%.

Considering intra-operative and post-operative outcomes of morbidity, the median blood loss ranged from 150 to 389 mL, while the maximum rate of conversion reported was 18.2%, with one study excluding patients for whom conversion was needed and two studies not reporting conversion rates. The median duration of surgery ranged from 134 to 343 minutes and the median duration of hospitalization ranged from 4 to 13 days (*Table 3*).

Long-term outcomes

Table 4 shows long-term outcomes in the selected publications. The ranges of overall survival rates at 1-, 3- and 5-year were 72.8–100%, 60.7–93.5% and 38–89.7% respectively. The ranges of disease free survival rates at 1-, 3- and 5-year were 45.5–91.5%, 20–72.2% and 19–67.8% respectively. One study reported survivals in term of mean months, with 40.2 and 23.3 months for OS and DFS respectively.

Discussion

The progressive spread of minimally invasive liver surgery and the development of new dedicated technologies have led to the need for redefining the role of laparoscopy in the field of liver resection. In this review we focused on short term and long-term major outcomes of LLR for HCC in order to illustrate the feasibility and the advantages of minimally invasive liver surgery.

Although randomized controlled trials (RCT) would be

Table 2 Morbidity and mortality rates in the different studies

Study [year]	No. of patients	Study type	Morbidity	Mortality	Clavien I–II	Clavien III–IV–V	Non-surgical complications	Surgical complications
Chen *et al.* [2017]	81	PSM	4 (4.9%)	0 (0%)	4 (4.9%)	0 (0%)	4 (4.9%)	0 (0%)
Cheung *et al.* [2016]	110	PSM	10 (9.1%)	0 (0%)	8 (7.3%)	2 (1.8%)	7 (6.4%)	4 (3.6%)
Lai *et al.* [2016]—robotic	100	RC	14 (14%)	0 (0%)	–	–	6 (6%)	13 (13%)
Lai *et al.* [2016]—laparoscopic	35	RC	7 (20%)	0 (0%)	–	–	2 (5.7%)	5 (14.28%)
Sposito *et al.* [2016]	43	PSM	8 (19%)	0 (0%)	7 (16%)	1 (2%)	–	–
Han *et al.* [2016]	99	PSM	13 (13.1%)	0 (0%)	10 (10.1%)	3 (3%)	2 (2.02%)	11 (11.11%)
Takahara *et al.* [2015]	387	PSM	26 (6.72%)	0 (0%)	–	–	6 (1.55%)	20 (25.16%)
Xiao *et al.* [2015]	41	RC	7 (17.1%)	0 (0%)	5 (12.2%)	2 (5%)	3 (7.31%)	4 (9.75%)
Martin *et al.* [2015]	100	RC	44 (44%)	0 (0%)	–	–	–	–
Yoon *et al.* [2015]	58	PSM	5 (8.62%)	0 (0%)	4 (6.9%)	1 (1.7%)	0 (0%)	5 (8.6%)
Lee *et al.* [2015]	43	PSM	10 (23.3%)	0 (0%)	10 (23.3%)	0 (0%)	–	–
Memeo *et al.* [2014]	45	PSM	9 (20%)	1 (2%)	–	–	7 (15.55%)	3 (6.66%)
Ahn *et al.* [2014]	51	PSM	3 (5.88%)	0 (0%)	2 (3.9%)	1 (2%)	0 (0%)	3 (5.88%)
Lee *et al.* [2011]	33	RC	2 (6.1%)	0 (0%)	–	–	2 (6.1%)	0 (0%)
Dagher *et al.* [2010]	163	RC	17 (10.4%)	2 (1.2%)	30 (18.4%)	8 (4.9%)	9 (5.52%)	27 (15.56%)
Aldrighetti *et al.* [2010]	16	PSM	4 (25%)	0 (0%)	3 (18.75)	1 (6.25%)	0% (0%)	4 (25%)
Tranchart *et al.* [2009]	42	PSM	4 (9.5%)	1 (2.4%)	3 (7.14%)	4 (9.52%)	4 (9.5%)	5 (11.9%)
Belli *et al.* [2009]	54	RC	10 (19%)	1 (2%)	–	–	0% (0%)	10 (19%)

PSM, propensity-score matching; RC, retrospective comparative.

the gold standard to obtain the highest quality of evidence, ethical and practical aspects make it difficult to set them up. Therefore, no randomized prospective clinical trial has been published yet and all the available data derive mainly from retrospective case-control studies, reviews or meta-analysis.

In view of the selected publications, that include large series of matched patients [e.g., Takahara *et al.* (11), 387 patients], laparoscopy shows comparable results to OLR for what concerns long-term oncologic outcomes (OS and DFS) and mortality, but superior results in term of morbidity and intra-operative outcomes.

The mortality rates are very low, with 13 series having 0% mortality and only 5 unfavourable events among 1,501 patients. Overall morbidity does not exceed 25%, with the exception of the study by Martin *et al.* (12) in which the morbidity rate amounts to 44% in LLR, anyway it was not found to be significantly different from the morbidity rate in OLR. This difference may be attributed to the time interval during which LLRs were performed; in fact,

even if the study was published in 2015, patients included were resected from 2004 to 2009. For what concerns complications' severity, only Tranchart *et al.* (13) reported a rate of complication classified as Clavien grade ≥ III higher than those classified as Clavien I–II; in all other study, the rate of complications classified as Clavien I–II is higher. Considering intra-operative outcomes, no substantial difference was found in blood loss; while for what concerns median operation time the longest duration, reported by Chen *et al.* (14) (343 min), might be mostly attributable to the need for extra time for the robot docking. In two studies the conversion rates exceeded 10% [Lee *et al.* (15) and Lee *et al.* (16), respectively 14% and 18.2%] and were due to uncontrolled bleeding. Finally, the study by Takahara *et al.* (11) reported the longest duration of hospitalization with a median of 13 days, but it resulted significantly shorter (P<0.001) than for the OLR patients anyway.

Overall, our results are in line with recent meta-analysis (6,17-19) which have demonstrated that LLR has shorter

Table 3 Intra- and post-operative outcomes in different studies

Study [year]	Total operation time (min)[a]	Blood loss (mL)[b]	Conversion (%)	Duration of hospitalization (days)[c]
Chen *et al.* [2017]	343 [140–715]	282 [50–2,200]	0 (0%)	7.5 [3–26]
Cheung *et al.* [2016]	185 [50–756]	150 [1–15]	6 (5.45%)	4 [2–41]
Lai *et al.* [2016]—robotic	207.4±77.1	334.6 [5–3,500]	5 (5%)	7.3±5.3
Lai *et al.* [2016]—laparoscopic	134.2±41.7	336.0 [5–2,000]	2 (5.7%)	7.1±2.6
Sposito *et al.* [2016]	199 [110–448]	67% <100 mL, 28% 100–500 mL, 2% 500–1,000 mL	2 (5%)	5 [1–31]
Han *et al.* [2016]	285.11±173.92	389.55±655.10	8 (8.08%)	8.39±4.96
Takahara *et al.* [2015]	294.4±158.8	158 [79–711]	25 (0.4%)	13 [9–18]
Xiao *et al.* [2015]	242.41±73.69	272.20±170.86	(7.32%)	9.44±2.72
Martin *et al.* [2015]	–	336±237	–	6.2±3.7
Yoon *et al.* [2014]	207 [146–251]	–	0 (0%)	9.2 [6–14]
Lee *et al.* [2015]	170 [88–536]	330 [0–6,500]	6 (14%)	5 [3–51]
Memeo *et al.* [2014]	140 [45–360]	200 [0–1,500]	–	7 [0–69]
Ahn *et al.* [2014]	210.7±131.3	350.0±432.5	Excluded from the study	8.2±4.6
Lee *et al.* [2011]	225 [100–420]	150 [10–1,610]	6 (18.2%)	5 [2–15]
Dagher *et al.* [2010]	180 [60–655]	250 [30–2,000]	15 (9.2%)	7 [2–76]
Aldrighetti *et al.* [2010]	150±57	258±186	1 (6.25%)	6.3±1.7
Tranchart *et al.* [2009]	233.1±92.7	364.3±435.7	2 (4.76%)	6.7±5.9
Belli *et al.* [2009]	167 [80–240]	297 [100–750]	4 (7%)	8.4 [3–15]

[a], median total operation time (min) ± standard deviation or (range); [b], median blood loss (mL) ± standard deviation or (range); [c], median duration of hospitalization ± standard deviation or (range). PSM, propensity score matching; RC, retrospective comparative.

operation time, lower complications' rates, reduced blood loss, reduced need for transfusions, and, consequently, a shorter hospital stay. Furthermore, other benefits can derive from minimally invasive surgery. Of note, all three comparative studies conducted solely on patients with proven cirrhosis found that morbidity was significantly lower in the LLR group than in OLR group. In fact, patients with liver cirrhosis represent a fragile category and they could take huge advantage from LLR, since it is associated to a lower incidence of postoperative ascites and liver failure (20-23). Indeed, cirrhotic patients are exposed to a higher risk of decompensation also attributable to surgery-induced injury. The risk of decompensation can be appreciably minimized when choosing a minimally invasive approach, in which round ligament and venous collateral circulation are preserved and a smaller abdominal incision is performed. Based on these considerations, LLR should be the first choice in patients with liver cirrhosis with resectable HCC.

LLR also allows the reduction of the adhesions due to previous liver resection, that may be responsible for a remarkable increase of the surgical difficulty of a salvage liver transplantation (LT) in case of recurrence. A study by Laurent *et al.* (24) comparing intra-operative LT after ORL and LLR, showed that the latter was associated with a reduced blood loss, a reduced need for transfusions and a shorter duration of the hepatectomy phase and whole LT. Consequently, LLR should be preferred in patients listed for LT or in patients for whom LT is a possible option in case of recurrence (25,26).

Robotic liver resection (RLR) is emerging as a valid alternative to laparoscopic and OLR, a strong point being its ability to overcome some evident limits of the other techniques. Still, robotic surgery encounters operators' resistance mainly due to the lack of evidence of comparable

Table 4 Overall survival and disease-free survival in the different studies

Study [year]	No. of patients	Study type	1-yr OS	3-yr OS	5-yr OS	1-yr DFS	3-yr DFS	5-yr DFS
Chen *et al.* [2017]	81	PSM	100%	92.6%	–	91.5%	72.2%	–
Cheung *et al.* [2016]	110	PSM	98.9%	89.8%	83.7%	87.7%	65.8%	52.2%
Lai *et al.* [2016]—robotic	100	RC	–	–	65%	–	–	42%
Lai *et al.* [2016]—laparoscopic	35	RC	–	–	48%	–	–	38%
Sposito *et al.* [2016]	43	PSM	–	75%	38%	–	41%	25%
Han *et al.* [2016]	99	PSM	100%	93.5%	89.6%	86.1%	57.4%	40.2%
Takahara *et al.* [2015]	387	PSM	95.8%	86.2%	76.8%	83.7%	58.3%	40.7%
Xiao *et al.* [2015]	41	RC	95.1%	78%	–	87.8%	70.7%	–
Martin *et al.* [2015]	100	RC	72.8%	60.7%	–	45.5%	20%	–
Yoon *et al.* [2015]	58	PSM	95.0%	–	86.0%	82.0%	–	56.0%
Lee *et al.* [2015]	43	PSM	95.3%	89.7%	89.7%	60.5%	53.5%	53.5%
Memeo *et al.* [2014]	45	PSM	88%	–	59%	80%	–	19%
Ahn *et al.* [2014]	51	PSM	–	–	80.1%	–	–	67.8%
Lee *et al.* [2011]	33	RC	86.9%	81.8%	76%	78.8%	51%	45.3%
Dagher *et al.* [2010]	163	RC	92.6%	68.7%	64.9%	77.5%	47.1%	32.2%
Aldrighetti *et al.* [2010]	16	PSM	40.2 months	–	–	23.3 months	–	–
Tranchart *et al.* [2009]	42	PSM	93.1%	74.4%	59.5%	81.6%	60.9%	45.6%
Belli *et al.* [2009]	54	RC	94%	67%	–	78%	52%	–

PSM, propensity-score matching; RC, retrospective comparative.

oncologic outcomes. Our review includes two of the largest series of RLR for HCC, none of which found any difference in OS and DFS between RLR and ORL and between RLR and LLR. Even if literature in this field is scarce, RLR seems to be at least not inferior to other approaches, but brings the advantages of robotic surgery such as a three-dimensional vision, tremor filtration and the possibility of intra-corporeal suturing. This consideration seem to be applicable also to patients with liver cirrhosis, as Di Sandro *et al.* (27) found that totally RLR for single HCC on cirrhosis had shorter operative time if console time only is considered, reduced blood loss and less need of packed RBC and FFP transfusions.

The study conducted by Dagher *et al.* (28) included an analysis of results separating the first 25 resections from each centre (early experience) versus the latter resections (recent experience), showing a significant improvement of surgical and postoperative results in the recent experience group. These study underlines the importance of minimally invasive surgery being performed in experienced centres, specially for lesions located in posterosuperior segments and for major resections (29,30). In this regard, a recent analysis demonstrated robotic surgery to have a shorter learning curve if compared to laparoscopy (31), with only 16 procedures required to significantly increase difficulty index of robotic procedures; thus, the implementation of robotic surgery can be useful in order to rapidly and safely expand indications for complex liver resections.

In conclusion, our review confirms the superiority of LLR compared to ORL regarding perioperative outcomes without compromising long-term outcomes, especially for cirrhotic patients. Robotic surgery overcomes some weaknesses of laparoscopy and its use should be encouraged in order to perform difficult procedures.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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