

Laparoscopic resection for hepatocellular carcinoma: comparison between Middle Eastern and Western experience

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Background: Laparoscopic liver resection (LLR) is growing in popularity, but the short- and long-term outcome of patients undergoing LLR for hepatocellular carcinoma (HCC) has not yet been established.

Methods: A literature search was performed using PubMed, Scopus, and Web of Science (WoS) from cited English and Chinese publications. Clinical and survival parameters were extracted. The search was last conducted in October 2013. After application of selective criteria, 24 remaining original studies with more than 15 patients were analyzed.

Results: In the Western experience, mean operative time was between 150 to 300 minutes, and mean blood loss ranged from 55 to 452 mL. Transfusion was required in all series, ranging from 2.8% to 50%. The conversion rate ranged from 5% to 19.4%. Three cases of death were reported. General morbidity rate ranged from 1.5% to 25%. Specific complications were divided into hemorrhage (2.4% to 25%), ascites (3.7% to 15.3%), and biliary collection (0.6% to 5%). Liver insufficiency was reported in two cases. Mean hospital stay ranged from 5.4 to 15 days. In all case-matched studies, LLR was statistically associated with a shorter hospital stay. The 5-year overall survival rate ranged from 55% to 70%. No trocar-site recurrence was observed. The recurrence rate ranged from 21.4% to 50%. Comparative studies did not demonstrate any significant difference in terms of recurrence between LLR and open liver resection (OLR). In the Middle Eastern experience, mean operative time ranged from 147 to 325 minutes, and mean blood loss ranged from 88 to 808 mL. Transfusion was required, ranging from 1.8% to 19.2%. The conversion rate ranged from 1.8% to 18.6%, and four series reported no conversion. There was no mortality. The main specific complication was ascites (1.7% to 26.6%). A biliary collection was reported in only two series (10.7% and 13.3%), and only one case of postoperative liver insufficiency was reported. Mean hospital stay ranged from 4 to 11.5 days. Statistically, three comparative studies reported a shorter postoperative hospital stay following LLR versus OLR. The 5-year overall survival rate ranged from 50% to 76.6%. Comparative studies did not demonstrate any significant difference in terms of overall survival and recurrence rate between LLR and OLR. No trocar-site recurrence was reported. The recurrence rate ranged from 26.9% to 45.5%, and two series reported no recurrence.

Conclusions: Laparoscopic surgery should be considered an acceptable alternative for the treatment of HCC.

Keywords: Laparoscopic liver resection (LLR); hepatocellular carcinoma (HCC); outcome; survival; morbidity; review

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Introduction

Hepatocellular carcinoma (HCC) is the most common primary liver cancer. Currently, the treatment of HCC is multidisciplinary but surgery remains the gold standard. HCC can be treated by either liver resection or liver transplantation (LT). Resection can precede LT according to different strategies such as primary therapy, patient selection for LT based on tumor histology or as a bridge treatment before LT (1). In this context, the development of minimally invasive surgery has led to an increase in laparoscopic liver resection (LLR) for HCC in which the possibility of repeat surgery is normally accepted.

The LLR technique could be divided into three main categories based on the Louisville statement, i.e., pure laparoscopy, hand-assisted laparoscopy, and the hybrid technique (2). Pure laparoscopy involves the performance of the entire liver resection using laparoscopic ports only. The hand-assisted approach is defined as laparoscopy with the addition of a hand-port placed to facilitate the procedure, and the hybrid technique is when the operation is started laparoscopically to mobilize the liver, followed by a mini-laparotomy to complete parenchymal transection. Today, in patients with a solitary HCC <5 cm in the anterior segment, with no evidence of an extrahepatic tumor burden, in case of compensated liver disease with absence of significant portal hypertension, LLR is considered a safe and feasible treatment option (2,3). In addition, due to improved laparoscopic instruments and increasing surgical experience, the technical difficulty of LLR is slowly being overcome. Henceforth, series have reported LLR of lesions located in posterior superior segments with good results (4,5). A number of advantages have been recognized when comparing LLR to open liver resection (OLR) from case-matched analyses, including reductions in postoperative pain, less operative morbidity, and shorter length of hospital stay (6-10).

The purpose of this review is to provide a thoroughly detailed description of reported studies about LLR for HCC in the literature in recent years. Specific emphasis will be placed on the comparison between Middle Eastern and Western experience with regards to resection types, technical approaches, postoperative course, and outcomes.

Methods

A literature search was performed using PubMed, Scopus, and Web of Science (WoS) from cited English and Chinese

publications. Data collection was performed until October 2013. Search phrases were “laparoscopy”, “liver resection”, and “HCC”. Manual cross-referencing was performed for all titles and abstracts, and relevant references from selected papers were reviewed. Publications with fewer than 15 cases, case reports, abstracts, letters, editorials and expert opinions were not considered for the drafting of the study. Review articles and meta-analyses were considered for the study. When there was more than one publication from the same team and/or authors, only the last publication in chronological order was considered for the study. Should a publication be written in Chinese, a translation was carried out, as faithful as possible, with the help of translators as native speakers.

Tables have been drawn up based on the geographical origins of authors and divided into Middle Eastern and Western experience. The results of the meta-analysis were not included in the tables.

Three reviewers (TP, DS, PP) independently considered the eligibility of potential publications and archived the following parameters from each study, namely first author, study design, number of patients, laparoscopic liver technique (pure laparoscopic, laparoscopic hand-assisted, laparoscopic assisted open), patient characteristics (age, gender, presence of cirrhosis, Child-Pugh score), size and number of tumors, location of tumor, type of resection (i.e., minor resection: ≤ 2 segments, major resection: ≥ 3 segments), associated resections, conversion rate, operative outcomes (operative time, blood loss, number of patients requiring transfusion, number of units of packed red blood cells (PRBCs), use and duration of portal clamping), postoperative outcomes (hospital stay, mortality and morbidity [general and specific: hemorrhage, ascites, biliary collection, liver failure]), and oncologic results [surgical margins, overall survival (1-3-5 years) and percentage of recurrence].

Results

Studies included in the analysis

There were 593 relevant papers in the initial search. After eliminating case reports, abstracts, letters, duplicates and studies where it was impossible to recover the data of HCC only, 24 remaining original studies with more than 15 patients were analyzed. There were 11 studies from the Western world (11-21) including two multicenter series (12,18), and 13 studies from the Middle Eastern world (4,22-33), and 4 meta-analyses from Chinese institutions (6-9).

Table 1 Study design

Authors	Period of inclusion	Number of patients	Pure laparoscopy	Laparoscopic Hand-assisted	Hybrid technique
Truant S <i>et al.</i> (11)	2002-2009	36	36	0	0
Dagher I <i>et al.</i> * (12)	1998-2008	163	155 [95%]	8 [4.9%]	0
Tranchart H <i>et al.</i> (13)	February 1999-August 2008	42	42	0	0
Sarpel U <i>et al.</i> (14)	2004-2007	24	24	0	0
Belli G <i>et al.</i> (15)	2000-2008	65	60 [92.3%]	5 [7.6%]	0
Casaccia M <i>et al.</i> (16)	June 2005-February 2009	20	20	0	0
Aldrighetti L <i>et al.</i> (17)	September 2005-June 2009	16	16	0	0
Soubrane O <i>et al.</i> * (18)	1998-2010	351	351	0	0
Santanbrogio R <i>et al.</i> (19)	January 2007	22	22	0	0
Cherqui D <i>et al.</i> (20)	May 1998-December 2003	27	27	0	0
Vibert E <i>et al.</i> (21)	January 1995-December 2004	16	16	0	0

*, Multicentre experience.

Table 2 Study design

Authors	Period of inclusion	Number of patients	Pure laparoscopy	Laparoscopic Hand-assisted	Hybrid technique
Lai EC <i>et al.</i> (22)	January 1998-december 2007	25	3	21	0
Lee KF <i>et al.</i> (23)	June 2004-march 2010	33	33	0	0
Kobayashi S <i>et al.</i> (24)	1997-2011	56	24	3	29
Kaneko H <i>et al.</i> (25)	15 years	39	33	2	4
Shimada M <i>et al.</i> (26)	1994-2000	17	17	0	0
Teramoto K <i>et al.</i> (27)	May 1997-April 2003	33*	15	0	0
Cheung TT <i>et al.</i> (28)	October 2002-september 2009	32	26	6	0
Hu BS <i>et al.</i> (29)	January 2006-January 2011	30	30	0	0
Yoon YS <i>et al.</i> (4)	September 2003- November 2008	69	69	0	0
Chen HY <i>et al.</i> (30)**	1998-2006	116	116	0	0
Sasaki A <i>et al.</i> (31)	May 2007-April 2008	37	37	0	0
Kim HH <i>et al.</i> (32)	July 2005-December2009	26	26	0	0
Kanazawa A <i>et al.</i> (33)	2006-2010	28	23	2	5

*, including 18 thermal ablation; **, group I (G1) (≤ 2 segments) and group II (G2) (> 2 segments).

Western experience (Table 1)

All 11 publications were retrospective analyses: four retrospective case-matched studies comparing LLR *vs.* OLR (11,13,14,17), two multicenter series from the French experience performed between 1998 and 2010 (18), and a European experience which included the databases of three European academic liver surgical centers (12). The other five series originated from a monocentric experience with minimally invasive approaches of LR: one series reported LLR

in benign conditions and malignant tumors (21), and four series reported the feasibility of LLR in HCC (15,16,19,20).

Middle Eastern experience (Table 2)

All 13 publications were retrospective analyses: only four studies were designed to compare the results of LLR versus OLR (28,29) including two retrospective case-matched analyses (23,32). The other 9 publications were monocentric experiences.

Selection criteria and type of laparoscopic approaches

Western experience

In three studies (12,13,15), selection criteria for LLR were well-compensated Child-Pugh Class A/B cirrhosis, esophageal varices \leq grade 2, platelet count $\geq 80 \times 10^9/L$, small tumors less than 10 cm, without major vascular invasion, and ASA score not exceeding 3. Casaccia *et al.* (16) and Truant *et al.* (11) selected patients with platelet count $\geq 40 \times 10^9/L$, solitary lesion of ≤ 5 cm, and treatable via limited resection (< 3 segments). In contrast, Vibert *et al.* (21) considered a disease with fewer than three nodules and no invasion of the portal convergence irrespective of the lesion's diameter eligible for LLR. Aldrighetti *et al.* (17) and Santambrogio *et al.* (19) advocated the absence of previous major upper abdominal surgery as well as cardiac or respiratory failure.

In the Western surgical experience, only two series (12,15) reported the use of hand-assisted laparoscopy, with a percentage of total LLR of 92.3% and 95.1% respectively. No series reported any experience with the hybrid technique. All other experiences reported in the literature proposed a total laparoscopic approach associated with an incision to remove the surgical specimen.

Middle Eastern experience

In major series, lesions were ≤ 5 cm without any vascular invasion. For pure laparoscopic resection, Kobayashi *et al.* (24) reported a sufficient distance from major vascular branches, small tumors peripheral to the liver; for hand-assisted LLR, tumors located in the right posterior sector; and for hybrid resection, cancers not fulfilling any of the aforementioned criteria.

There were selective biological liver function tests such as albumin levels above 3.5 g/dL, bilirubin levels below 1.5 mg/dL, indocyanine green (ICG) retention at 15 min lower than 40%, and prothrombin time (PT) greater than 60% (26,33).

Five publications (38.4%) reported different techniques of LLR. In particular, Kobayashi *et al.* (24) compared hybrid with pure laparoscopic procedures as well as with open surgery. The hybrid procedure was applied to enlarge indications to minimally invasive surgery and represented about half of the cases in Kobayashi's series. The percentage of laparoscopic hand-assisted procedures ranged from 5.1% to 84%.

Patients and tumors' characteristics

Western experience (Table 3)

In all series, mean age was between 60 to 66 years with a

predominance of male patients. The ASA score was > 2 only in 30% of patients.

Fifty to one hundred percent of patients with cirrhosis presented a well-compensated chronic liver disease (Child-Pugh Class A). However, seven series reported patients with Child-Pugh Class B with a rate ranging from 3.2% to 22.7% (13,19). Only two series (12,18) reported their experience with Child-Pugh Class C patients.

LLR was recommended for lesions within 5 cm and with a mean size ranging from 2.7 to 6.5 cm. Vibert *et al.* (21) and Soubrane *et al.* (18) reported maximal tumor sizes of 18 and 17 cm respectively. The lesions were located only in anterior lateral segments more or less associated with segments VII and VIII in four studies (11,17,19,20). The most common type of LLR was a wedge resection or segmentectomy and left lateral sectionectomy. However, without considering multicenter studies, 13 major LLRs were performed (6%) (13,15,20). Radiofrequency ablation was associated for the treatment of intrahepatic lesions in three series (12,16,19).

Middle Eastern experience (Table 4)

Only five studies (38.4%) reported an ASA score which was > 2 in only 12.8% of cases.

Cirrhosis was present also from 50% to 100% of patients. Only two series did not describe the Child-Pugh status of the patients. Eight publications reported patients with Child-Pugh Class B cirrhosis ranging from 8.7% to 66.7%. In fact, Teramoto *et al.* (27) included 66.7% of Child-Pugh Class B patients with ICG retention rate at 15 minutes of $22.1 \pm 12.0\%$. Three series (4,25,30) reported their experience with Child-Pugh Class C patients. Chen *et al.* (30) reported patients with Child-Pugh Class B/C without distinguishing between the two different statuses.

Mean size of the tumor was less than 5 cm except for Hu *et al.* (29) who reported a mean tumor size greater than 6 cm. However, tumor size ranged from 0.6 to 9 cm. The lesions were located in all segments. Teramoto *et al.* (27) reported a thoracoscopic approach for posterior segments in five cases (S8=4, S7=1). Most of the resections were minor but 27 major LLRs (10.8%) were reported. The most common major liver resection was right hepatectomy. Only one central hepatectomy was performed by Yoon *et al.* (4).

Intraoperative and immediate postoperative outcomes

Western experience (Table 5)

Mean operative time was between 150 to 300 minutes. In the four case-matched studies (11,13,14,17), there was no

Table 3 Patients and tumors descriptions

Authors	Mean age years	Gender [M/F]	ASA >2 n [%]	Child-Pugh A-B-C n [%]	Cirrhosis n [%]	Mean size of the tumor cm [range]	Location of the tumor	Number of tumours	Type of resection n	Associated resections	Surgical margin mm [range]
Truant S <i>et al.</i> (11)	60.6±10.2	31/5	11 [30.6]	A: 32		2.9±1.2	Ant.segments	1.1±0.3	Minor	4 LC	9.5±2.8
Dagher I <i>et al.</i> * (12)	65 [24-84]	112/51	45 [27.6]	A: 111 B: 8 C: 1	120 [73.6]	3.6 [1-20]	All segments	NR	Minor: 147; major: 16	40 LC 14 other 12 RFA	12 [0-58]
Tranchart H <i>et al.</i> (13)	63.7±13.1	27/15	12 [28.5]	A: 30 B: 1	31 [73.8]	NR	NR	NR	Minor: 37; major: 5	NR	10.4±8.0
Sarpel U <i>et al.</i> (14)	63.8±10.3	15/9	NR	NR	9 [45]	4.2±2.1	NR	NR	NR	NR	NR
Belli G <i>et al.</i> (15)	63±6.8	38/27	13 [20]	A: 58 [89] B: 7	65 [100]	3.8±1.4	All segments	Single: 53; multiple: 12	Minor: 6; major: 59	NR	<10: 9 >10: 56
Casaccia M <i>et al.</i> (16)	66 [47-76]	12/8	NR	A: 17 B: 3	20 [100]	3.1 [0.9-5]	All.segments	>1	Minor: 19; major: 1	5 LC 3 other	15 [0-40]
Aldrighetti L <i>et al.</i> (17)	65±10	11/5	2 [12.9]	A: 9	9 [56]	4±2.2	Ant.segments + VII	NR	Minor: 16	5 LC	11±7.4
Soubrane O <i>et al.</i> * (18)	63 [30-90]	260/91	91 [31.4]	A: 275 B: 8 C: 1	NR	3.5 [0.5-17]	All segments	Single: 302; multiple: 49	Minor: 315; major: 36	NR	10 [0-78]
Santambrogio R <i>et al.</i> (19)	61.4±8.3	13/9	NR	A: 17 B: 5	22 [100]	2.7±1.2	Ant.segments	NR	Minor: 22	3 RFA 1 alchoolic ablation	11.1±7.4
Cherqui D <i>et al.</i> (20)	63±9	22/5	NR	A: 20	20 [74]	3.3 [2-5]	Ant.segments + VIII	1	Minor: 26; major: 1	NR	11 [1-47]
Vibert E <i>et al.</i> (21)	NR	NR	NR	A: 7 B: 1	8 [50]	6.5 [0.8-18]	NR	Single: 15; multiple: 1	NR	NR	10 [1-50]

*, Multicentre experience; Ant. segments, II, III, IVb, V, VI; LC, laparoscopic cholecystectomy; RFA, radiofrequency ablation; NR, no reported.

Table 4 Patients and tumors descriptions

Authors	Mean age years	Gender [M/F]	ASA >2 n	Child-Pugh A-B-C n [%]	Cirrhosis n [%]	Mean size of the tumor cm [range]	Location of the tumor* segments	Number of tumours n [%]	Type of resection	Associated resections	Surgical margin cm [range]
Lai EC <i>et al.</i> (22)	59 [35-79]	18/7	1	A: 23 [92]	23 [92]	2.5 [1-7]	Ant. segments	NR	Minor: 24 Major: 1	NR	0.5 to 4
Lee KF <i>et al.</i> (23)	59 [36-85]	24/9	6	A: 33 [100]	28 [84.8]	2.5 [1.5-9]	Ant. segments	Single: 31; multiple: 2	Minor	NR	1.8 [0-4]
Kobayashi S <i>et al.</i> (24)	70 [37-86]	41/15	9	A: 48 [85.7] B: 8 [14.3]	NR	2 [1-9]	All segments	1 [1-3]	Minor	NR	NR
Kaneko H <i>et al.</i> (25)	59±8	NR	NR	A: 30 [76.9] B: 8 [21] C: 1 [2.5]	39 [50.6]	<4	All segments	NR	Minor: 38 Major: 1	NR	NR
Shimada M <i>et al.</i> (26)	62±9	15/2	NR	NR	76.5	2.6±0.9	Ant. segments	NR	Minor	3 splenectomy	0.8±0.7
Teramoto K <i>et al.</i> (27)	64±10	9/6	NR	A: 5 [33.3] B: 10 [66.7]	NR	1.9±0.6	All segments	NR	NR	NR	NR
Cheung TT <i>et al.</i> (28)	59.5 [39-79]	22/10	NR	A: 32 [100]	28 [87.5]	2.5 [1-10]	All segments	NR	Minor	NR	0.95 [0-3]
Hu BS <i>et al.</i> (29)	46±12	19/11	NR	A: 24 [80] B: 6 [20]	25 [83.3]	6.7±3.1	Ant. segments	NR	NR	NR	NR
Yoon YS <i>et al.</i> (4)	56.5±11.7	50/19	NR	A: 62 [89.8] B: 6 [8.7] C: 1 [1.5]	38 [55]	3.1±1.5	All segments	Single: 56 [81.5]; multiple: 12 [17.3]	Minor: 60 Major: 9	NR	1.5±1.6
Chen HY <i>et al.</i> (30)**	G1: 57±12.6 G2: 61.6±13.1	G1: 78/19 G2: 14:5	G1: 13 G2: 1	G1: A: 79 B/C: 18 G2: A: 19	NR	G1: 2.1±0.8 G2: 3.2±1.9	All segments	NR	Minor: 104 Major: 12	NR	≤1
Sasaki A <i>et al.</i> (31)				A: 23 [86] B: 4 [14]	27 [100]	2.5 [1.5-6]	All segments	NR	Minor	NR	0.7 [0-2.5]
Kim HH <i>et al.</i> (32)	57.84±9.66	18/8	3	NR	24 [92.3]	3.15 [1-8]	All segments	NR	Minor: 22 Major: 4	NR	NR
Kanazawa A <i>et al.</i> (33)	69 [40-85]	16/12	NR	A: 20 [71.4] B: 8 [28.5]	28 [100]	2 [0.6-2.7]	All segments	Single: 18 [64.2]; multiple: 10 [35.7]	NR	NR	0.5 [0-1.8]

* , Ant. segments (I,III,IVb,V,VI); ** , group I (G1) (≤2 segments) and group II (G2) (>2 segments); NR, no reported.

Table 5 Surgical results

Authors	Conversion n [%]	Mean operative time min [range]	Mean blood loss mL [range]	Transfusion n [%] n [range]	PRBC units n [range]	Use of portal clamping n [%]	Mortality n [%]	Morbidity n [%]	Specific morbidity: n
Truant S <i>et al.</i> (11)	7 [19.4]	193±104	452±442	1 [2.8]	-	13 [36]	0	4 [11.7]	Ascites: 5
Dagher I <i>et al.</i> * (12)	15 [9.2]	180 [60-655]	250 [30-2,000]	16 [9.8]	2.5 [1-5]	43 [26.4]	2 [1.2]	17 [10.4]	Hemorrhage: 4; ascites: 14; biliary collection: 1
Tranchart H <i>et al.</i> (13)	2 [4.7]	233.1±92.7	364.3±435.7	4 [9.5]	3±0.7	0	1 [2.4]	4 [9.5]	Hemorrhage: 1; ascites: 3; biliary collection: 1
Sarpel U <i>et al.</i> (14)	4 [17]	161±37	NR	NR	NR	0	NR	NR	NR
Belli G <i>et al.</i> (15)	7 [10.7]	169±46	311±180	7 [10.7]	NR	2 [3]	1 [1.5]	1 [1.5]	Hemorrhage: 2; ascites: 10
Casaccia M <i>et al.</i> (16)	1 [5]	300 [120-560]	55 [20-1,400]	10 [50]°	1 [1-4]	1 [5]	0	0	Ascites: 2; biliary collection: 1
Aldrighetti L <i>et al.</i> (17)	1 [6.25]	150±57	258±186	4 [25]	NR	0	0	0	Hemorrhage: 4
Soubrane O <i>et al.</i> * (18)	45 [13]	180 [15-655]	NR	12 [3]	NR	85 [24]	7 [2]°	52 [14.8]	Ascites: 16; biliary collection: 7; hepatic failure: 5
Santanbrogio R <i>et al.</i> (19)	3 [13.6]	199±69	183±72	1 [4.5]	2	NR	0	0	Hemorrhage: 2
Cherqui D <i>et al.</i> (20)	7 [26]	240±75	338±182 [6 patients ≥1,000 mL]	3 [15]	2-5	27 [100]	0	7 [25]	Ascites: 1; hepatic failure: 1
Vibert E <i>et al.</i> (21)	NR	NR	NR	NR	NR	NR	1 [6.25]	NR	NR

* , Multicentre experience; PRBC, packed red blood cell units; ° , 30-days mortality; NR, no reported.

difference between LLR and OLR. In the series with major hepatectomy, maximal operative time ranged from 325.7 to 655 minutes.

Mean blood loss ranged from 55 to 452 mL. In two series, blood loss >1,000 mL was reported (12,16). Transfusion was required in all series, ranging from 2.8% to 50%. In case-matched studies, one study (17) reported a lower blood loss in the LLR group as compared to the OLR group (258±186 versus 617±433 mL; P=0.008). In contrast, the two other studies did not determine any difference between LLR and OLR (11,14). More than 50% of the series reported the use of a Pringle maneuver during resection. Cherqui *et al.* (20) reported 100% of intermittent portal triad clamping.

The conversion rate ranged from 5% to 19.4%. The most frequent reasons for conversion were bleeding during parenchymal transection, technical difficulties in exposure, and adhesions. In the four case-matched series (11,13,14,17), there was no difference in terms of surgical margins between LLR and OLR. Three cases of death were reported: one liver failure (13), one severe respiratory distress syndrome (15), and one cerebral infarction (21). The global morbidity rate ranged from 1.5% to 25%. Specific complications were divided into hemorrhage (2.4% to 25%), ascites (3.7% to 15.3%), and biliary collection (0.6% to 5%). A liver insufficiency was reported in two cases (18,20). Mean hospital stay ranged from 5.4 to 15 days. In all case-matched studies, LLR was statistically associated with a shorter hospital stay.

Middle Eastern experience (Table 6)

Mean operative time ranged from 147 to 325 minutes. In the two case-matched studies, there was no difference between LLR and OLR. In the five series with major hepatectomy, maximal operative time ranged from 210 to 500 minutes.

Mean blood loss ranged from 88 to 808 mL. In six series, blood loss >1,000 mL was reported (12,16). Save from two studies (28,33), transfusion was required, ranging from 1.8% to 19.2%. The two case-matched studies did not report any difference between LLR and OLR (23,32). Only three series reported the use of a Pringle maneuver during parenchymal transection (22,26,33).

The conversion rate ranged from 1.8% to 18.6%, and no conversion was reported in four series (7,8,31,33). The most frequent reasons for conversion were uncontrolled bleeding, and inadequate margin or poor localization (4,27,30). In five series (38.5%), the surgical margin was not reported. There

was no mortality. There was no specific morbidity in five series (22,23,27,28,32). The main specific complication was ascites (1.7% to 26.6%). A biliary collection was reported in only two series (4,29) (10.7% and 13.3% respectively), and only one case of postoperative liver insufficiency was reported (26). Mean hospital stay ranged from 4 to 11.5 days. Three comparative studies statistically reported a shorter postoperative hospital stay following LLR versus OLR (23,28,32).

Long-term results: survival and recurrence

Western experience (Table 7)

The 5-year overall survival rate was reported in five studies and ranged from 55% to 70%. Trancart *et al.* (13) reported no difference between LLR and OLR with a 1-, 3-, and 5-year overall survival rate of 93.1%, 74.4%, and 59.5% versus 81.8%, 73%, and 47.4% (P=0.25) respectively. No trocar-site recurrence was observed. The recurrence rate ranged from 21.4% to 50%. Comparative studies did not demonstrate any significant difference in terms of recurrence between LLR and OLR (11,13,14,17).

Middle Eastern experience (Table 8)

The 5-year overall survival rate was reported in six studies and ranged from 50% to 76.6%. Comparative studies did not demonstrate any significant difference in terms of overall survival and recurrence rate between LLR and OLR. Chen *et al.* (30) differentiated two groups of patients according to the type of resection (minor or major): the 1, 3 and 5 years were 85.4%, 66.4%, and 59.4% in the minor resection group, and 94.7%, 74.2%, and 61.7% in the major resection group respectively, without significant difference. No trocar-site recurrence was reported. The recurrence rate ranged from 26.9% to 45.5%, and two series (26,29) reported no recurrence.

Discussion

LLR for HCC is safe and feasible. Additionally, using a progressive approach, excellent outcomes can be obtained in the setting of underlying cirrhosis. Since the first reported case (34), an increasing number of series was published, and especially so since year 2000. Eight studies (four Middle Eastern and four Western ones) compared the benefits of the LLR versus the OLR approach but, to the best of our knowledge, a prospective randomized study has not been published yet (Table 9). In these different

Table 6 Surgical results

Authors	Conversion n [%]	Mean operative time min [range]	Mean blood loss mL [range]	Transfusion n [%]	PRBC *units n [range]	Use of portal clamping n [%]	Mortality [%]	Morbidity n [%]	Specific morbidity: n [%]
Lai EC et al. (22)	1 [4]	150 [75-210]	200 [5-2,000]	2 [8]	NR	16 [58.8]	0	4 [16]	0
Lee KF et al. (23)	6 [18.2]	225 [100-120]	150 [10-1,610]	2 [6.1]	NR	0	0	2 [6.1]	0
Kobayashi S et al. (24)	1 [1.8]	202 [45-512]	150 [0-1,180]	1 [1.8]	NR	NR	NR	0	Ascites: 1
Kaneko H et al. (25)	2 [2.6]	182±38	380±210	NR	NR	NR	NR	0	Ascites: 2
Shimada M et al. (26)	NR	325 [214-430]	400 [188-1,050]	5.9	NR	Yes	0	0	Hepatic failure: 1
Teramoto K et al. (27)	2 [13.3]	214±63	296±341	NR	NR	NR	NR	4/15 [26.6]	0
Cheung TT et al. (28)	0	235.5 [70-450]	150 [100-1,460]	0	0	0	0	2 [6.3]	0
Hu BS et al. (29)	0	180±45	520±30	NR	NR	NR	0	0	Biliary collection: 4
Yoon YS et al. (4)	5 [7.2]	280.9±128.2	808.3±1011.7	23 [33.3]	NR	0	0	15 [21.7]**	Ascites: 4 [26.6]; biliary collection: 2
Chen HY et al. (30)**	6 [5.2]	G1: 152.4±336.3 G2: 175.8±57.4	G1: 101.6±324.4 G2: 329.2±338.0	G1: 5 [5.2] G2: 3 [15.8]	G1: 36.1±148.7 G2: 105.3±267.7	NR	G1: 0 G2: 0	G1: 6.2 G2: 5.2	Ascites: 2
Sasaki A et al. (31)	0	195 [91-355]	103 [1-917]	NR	NR	0	0	1 [2.7]	Ascites: 1
Kim HH et al. (32)	3 [10.3]	147.5 [45-500]	NR	5 [19.2]	0.35±0.75	0	0	1 [3.8]	0
Kanazawa A et al. (33)	0	228 [69-515]	88 [0-900]	0	0	Yes	0	3 [10.7]	Ascites: 3

PRBC, packed red blood cell units; †, blood transfused in mL; **, group I (G1) (≤2 segments) and group II (G2) (>2 segments).

Table 7 Outcomes

Authors	Mean hospital stay days [range]	1-year survival [%]	3-years survival [%]	5-years survival [%]	Recurrence n [%]	Mean follow-up months
Truant S <i>et al.</i> (11)	6.5±2.7	NR	NR	70	16 [44.4]	35.7±27
Dagher I <i>et al.</i> * (12)	7 [2-76]	92.6	68.7	64.9	64 [39]	30.4
Tranchart H <i>et al.</i> (13)	6.7±5.9	93.1	74.4	59.5	10 [23.8]	29.7
Sarpel U <i>et al.</i> (14)	NR	NR	NR	NR	NR	NR
Belli G <i>et al.</i> (15)	8.2±2.6	95	70	55	31 [48]	29
Casaccia M <i>et al.</i> (16)	8 [5-16]	NR	NR	NR	10 [50]	26
Aldrighetti L <i>et al.</i> (17)	6.3±1.7	NR	NR	NR	6 [37.5]	22
Soubrane O <i>et al.</i> * (18)	7 [1-90]	NR	NR	65.7		21
Santanbrogio R <i>et al.</i> (19)	5.4±1	NR	NR	50, 4 years	5 [26.3]	11.5
Cherqui D <i>et al.</i> (20)	15±17.5	NR	93	NR	8 [30]	24
Vibert E <i>et al.</i> (21)	NR	85	66	NR	3 [21.4]	40

*, Multicentre experience; NR, no reported,

Table 8 Outcomes

Authors	Mean hospital stay days [range]	1-years survival [%]	3-years survival [%]	5-years survival [%]	Recurrence n [%]	Mean follow-up months
Lai EC <i>et al.</i> (22)	7 [4-11]	NR	60	NR	25 [36]	29
Lee KF <i>et al.</i> (23)	5 [2-15]	87.5	87.5	75	15 [45.5]	35.4
Kobayashi S <i>et al.</i> (24)	11.5 [7-28]	NR	100	NR	NR	19.2
Kaneko H <i>et al.</i> (25)	NR	NR	NR	NR	NR	NR
Shimada M <i>et al.</i> (26)	12±5	85	75	50	0	16.6
Teramoto K <i>et al.</i> (27)	12±7.2	100	80	–	6 [40]	23±21
Cheung TT <i>et al.</i> (28)	4 [2-16]	96.6	87.5	76.6	NR	NR
Hu BS <i>et al.</i> (29)	13±2.1	NR	NR	50	0	NR
Yoon YS <i>et al.</i> (4)	9.9±5.6	NR	90.4	NR	21 [30.4]	21.3
Chen HY <i>et al.</i> (30)**	NR	G1: 85.4 G2: 94.7	G1: 66.4 G2: 74.2	G1: 59.4 G2: 61.7	NR	94
Sasaki A <i>et al.</i> (31)	10 [6-37]	NR	73	53	13 [35]	36
Kim HH <i>et al.</i> (32)	11.08±4.96	NR	NR	NR	7 [26.9]	21.75
Kanazawa A <i>et al.</i> (33)	10 [6-25]	NR	NR	NR	NR	NR

**, group I (G1) (≤2 segments) and group II (G2) (>2 segments); NR, no reported.

Table 9 Summary of trends comparing data of Middle Eastern and Western experiences (no statistical analysis)

	Middle Eastern	Western
Technique	Hybrid technique	No hybrid technique; more pure laparoscopic approach
Patients	Severity of the cirrhosis (more Child B and C)	More patient with cirrhosis
Tumor		Slightly larger size
Procedure		More conversion; more portal clamping

comparative studies, LLR can achieve survival equal to open hepatectomy in patients with HCC but with the benefit of less blood loss, less transfusion requirement, and a shorter hospital stay.

Selection criteria included tumor size and location as well as the severity of the underlying disease. It appears that the selection of patients is quite uniform in the Western experience. The Western most centers are French or Italian, and as reported in the multicenter study of Dagher *et al.* (12), centers use the same selection of patients and surgical techniques. On the opposite, in the Middle Eastern experience, selection criteria were less clear and authors reported that these criteria were similar to the ones of open surgery. In the Middle Eastern experience, for surgical evaluation, the ICG retention rate at 15 minutes represented the most reliable and faithful index of hepatic reserve. More Child-Pugh Class B and/or Class C patients were operated on in Middle Eastern series. No series used the Model for End-Stage Liver Disease (MELD) score for the selection of patients, currently used as a disease severity index of cirrhotic patients awaiting LT. However, the MELD score related with mortality and liver-related morbidities in HCC patients who underwent hepatic resection. A MELD score >8 represented the trigger for intensive treatment to improve patient outcome (35). In the Mayo clinic experience (36), a MELD score >9 was an independent predictor of perioperative mortality and long-term survival after multivariate analysis.

For some Middle Eastern surgeons, tumor location does not seem to be a selection criterion but the type of approach was different from pure laparoscopy. The Middle Eastern experience reported more hand-assisted or hybrid techniques. Huang *et al.* (37) reported a series of LLR with or without the hand-assisted approach and concluded that surgical results between hand-assisted and non-hand-assisted approaches were similar except for higher blood losses with the hand-assisted technique. The authors found that there was a higher use of hand-assisted LLR when liver cirrhosis was present, and less likelihood of using hand-assisted LLR when there was a superficial location of the tumor or lesion. In a comparative study (24), pure LLR was associated with lesser blood loss, and shorter skin incisions than in hybrid and open hepatectomy. Hybrid hepatectomy was associated with a longer operative time. It is probably for these few advantages and mainly for blood loss that Western surgeons prefer to use a pure laparoscopic approach. The hybrid technique in the Western experience was particularly described in cases of living donor right hepatectomies (38).

The laparoscopic approach could be used in cases of HCC recurrence: a previous surgery and the grade of adhesions have not been subject to contraindications (39,40). Fewer adhesions represent an additional benefit of laparoscopic hepatectomy. This could well facilitate an easy reoperation for either a subsequent laparoscopic surgery or an open abdominal surgery to treat HCC recurrence or metastasis. LLR could be proposed as a bridge treatment before LT: LLR facilitated the LT procedure as compared to OLR in terms of reduced operative time, blood loss, and transfusion requirements (41).

With the benefit of experience, pure laparoscopy could be proposed for all tumor locations (42). Regarding the type of resection, the learning curve inherent to LLR reflects the attitude of the different teams for which the more accessible lesions are approached first prior to undertaking more difficult resections. LLR requires expertise in OLR, minimally invasive surgery, and laparoscopic ultrasonography. Resections in posterior and superior segments of the liver and major liver resections should be reserved for centers with a significant experience in laparoscopic liver surgery (42). In all groups, wedge resection and minor resection were more commonly performed. However, major hepatectomies such as right hepatectomies are increasingly proposed nowadays (43,44).

The resection margin is another factor that could well influence survival. A positive margin may have a profound influence on disease-free survival and long-term survival. The incidence of surgical margins <1 cm was reported in 62.5% of Middle Eastern articles. This result was set in contrast with “the dogma” in which a gross resection margin aiming at 2 cm provided better survival outcome than a narrow resection margin at 1 cm (45) for macroscopically solitary HCCs. However, in all case-matched control studies, survival rates, resection margins, and local recurrence rates following LLR were comparable to OLR. Laparoscopic intraoperative ultrasonography can be used to locate the tumor, making it possible to keep the intended margin. Another concern about laparoscopic resection of malignancies is the potential risk of tumor seeding. However, neither peritoneal carcinomatosis nor port-site recurrence were observed following HCC resection by laparoscopy. The use of a plastic bag to remove the specimen could help prevent this complication. The meta-analyses (6,8) have shown that LLR is comparable to OLR for HCC at 1-, 3- and 5-year overall survival. Consequently, LLR should be considered an acceptable alternative for the treatment of malignant liver tumors.

The results of the literature should be construed with caution due to several limitations. First, all data stem from non-randomized trials, and the overall level of clinical evidence is low. However, results have shown that LLR for HCC is superior to OLR in terms of perioperative results and does not compromise oncological outcomes. Consequently, LLR may be an alternative choice in the treatment of HCC.

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