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REVIEW ARTICLE

Laparoscopic Parenchymal-Sparing Hepatectomy: the New Maximally Minimal Invasive Surgery of the Liver—a Systematic Review and Meta-Analysis

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Abstract

Background Parenchymal-sparing hepatectomies (PSH) are liver resections with preservation of as much liver parenchyma as possible. PSH can be performed laparoscopically (LPSH), but access to the posterosuperior segments is difficult and they are challenging when there are multiple bilobar lesions; the procedure may require repositioning and may be long and cumbersome. The objective of this systematic review is to analyze the feasibility and limitations of laparoscopic PSH in the literature.

Methods A systematic review of the literature was performed by searching Medline/PubMed, Scopus, and Cochrane databases. Resections were categorized by segment(s), and data regarding operative time, blood loss, length of hospital stay, complications, and R0 resection were analyzed.

Results Of 351 studies screened for relevance, 48 studies were reviewed. Ten publications fulfilled inclusion criteria, reporting data from 579 patients undergoing LPSH. The most common indication was CRLM (58%) followed by hepatocellular carcinoma (16%). Only 92 patients were reported to have resections of more than one tumor; the maximum number of lesions resected was seven. Of resected lesions, 21.5% were located in the cranial segments. Mean operating time was 335.2 min, estimated blood loss was 462 cc, and hospital stay was 7.6 days. Conversion rate was 9.7%, and complications occurred in 19.4% of cases. No perioperative mortality was reported. R0 resections were achieved in 87.7% of cases.

Conclusion Laparoscopic PSH is performed and reported, but the data quality is low so far. The main limitation of LPSH is the low number of lesions resected, especially for bilobar, metastatic disease. Prospective reports with tumor-specific oncological data are desirable.

Keywords Laparoscopic parenchymal-sparing hepatectomy · Parenchymal-sparing liver surgery · Colorectal liver metastasis

Introduction

Techniques and strategies of liver resection have changed over time.[1] Between 1954 and 2000, the increased understanding of hepatic anatomy and intraoperative ultrasound allowed anatomic liver resections (AR) and brought morbidity and mortality into an acceptable range.[1, 2] Due to improvement in multimodality treatment, colorectal liver metastases (CRLM) became the most common indication for liver surgery in the Western world, and the challenge to resect multiple, sometimes bilobar lesions, unmasked the limitations of the anatomical approach to resection. As long as the anatomic paradigm was followed, bilobar metastases remained difficult to resect without maneuvers to increase the future liver remnant, resulting in increased morbidity and mortality. Leaving the path of anatomic resections and predominantly performing non-anatomic resections by leaving the skeleton of the Glissonian system and the hepatic veins intact opened the field of parenchymal-sparing liver surgery.[3–5] The morbidity after liver surgery is known to correlate with the amount of liver resected either by anatomic segments[2] or by volumetric

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assessment,[6] which supports the parenchymal-sparing approach. Additionally, parenchymal-sparing liver surgery allows for future re-resections in cases of colorectal liver metastasis recurrence, which may lead to improved overall survival in patients undergoing non-anatomical resections.[7]

Due to the inferocaudal perspective, laparoscopic liver resections are easier for lesions located in segments 3, 4b, 5, and 6[8] while laparoscopic resections of lesions in the three posterosuperior segments (4a, 7, and 8) and in segment 1 are technically challenging and remain easier to resect in continuity with a large anatomic liver resection like a right hepatectomy.[4,9,10] However, several studies have shown the safety and feasibility of selective laparoscopic resections in these difficult-to-reach segments.[10–14] This review aims to survey the published literature on laparoscopic resections of liver segments which are performed with a parenchymal-sparing approach to better understand the strengths and limitations of this novel approach, determine which resections are reported and feasible, and to give the first meta-analysis of outcomes.

Materials and Methods

Review Protocol and Registration

A systematic review of the literature on laparoscopic parenchymal-sparing hepatectomy was performed. The review protocol was made available online on the international PROSPERO database (CRD42017074435).

Information Sources

A search of PubMed/MEDLINE, Cochrane, and Scopus databases was performed containing the following medical subject headings (MeSH): "neoplasm metastasis" or "neoplasm micrometastasis," "margins of excision," "parenchymal tissue," "laparoscopy," "neoplasm recurrence, local" or "outcome assessment" or "treatment outcome." Other keywords used to complete the literature search included "parenchyma," "liver/hepatic," "hepatectomy," "parenchymal sparing/preserving," "neoplasm," "non-anatomic," "resection margin," "laparoscopic," "recurrence," "mortality," "complication," and "survival." The literature search included articles up to August 29, 2017, as well as a search of relevant information from references of identified articles. Two reviewers (J.K. and E.S.) performed the literature review, study selection, and data extraction.

Study Selection and Data Collection Process

The review was conducted according to the Preferred Reporting Items for Systematic Review (PRISMA) guidelines. Figure 1 gives the flow chart for the selection of articles. After all searched articles were identified, duplicates were removed. Only series reporting outcomes of patients undergoing laparoscopic PSH were included. Titles and abstracts were screened for relevance. Exclusion criteria included papers on laparoscopic liver resections with a lack of differentiation of results between parenchymal-sparing and non-parenchymal-sparing surgery, single case reports, editorials and opinion pieces, and non-English articles. The remaining articles were screened at full-text level to identify those which reported outcome data. Primary outcomes considered essential for inclusion were feasibility (rate of conversion), number of lesions, type of resection (i.e., anatomic and non-anatomic), and safety (operating time, estimated blood loss, length of hospital stay, morbidity, mortality). Secondary parameters were oncologic efficacy (R0 resection, overall survival (OS), disease-free survival (DFS) and incidence of recurrence) were included when available, but their absence was not an exclusion criterion.

Statistics

Data were extracted from all ten papers and given the number of studies available for each analysis; fixed effects meta-analyses were performed. When the original publications reported only medians, medians of medians and ranges were reported without meta-analysis. Meta-analysis and Forest plots were made using R 3.3.2 (Vienna, Austria, 2016).

Results

Study Selection

Initial screening criteria resulted in 351 studies. After screening, 48 publications remained for full-text evaluation. Thirty-eight studies were excluded for interventions not of interest for this study (i.e., robotic resections and ablation), lack of granularity in outcomes (i.e., subgroup analyses were not performed), not being in English, or because they represented an editorial and opinion pieces. Ten studies were included in the final analysis, and of these, a quantitative meta-analysis could be performed on between 5 and 10 studies, depending on the parameters reported.

Clinicopathologic Characteristics

Across 10 studies, there were a total of 579 patients (341 male, 238 female) with a mean (weighted) age of 61.5 (median 64.6).[10–19] Individual cohort size ranged from 23 to 114 patients.[10–19] Most patients underwent resection for a solitary tumor with a mean (weighted) tumor number of 1.6 (range 1–7)[11,14,15,18,19] and mean (weighted) size of 38.9 mm.[11–13,19] Of the 579 patients, 92 were reported to have

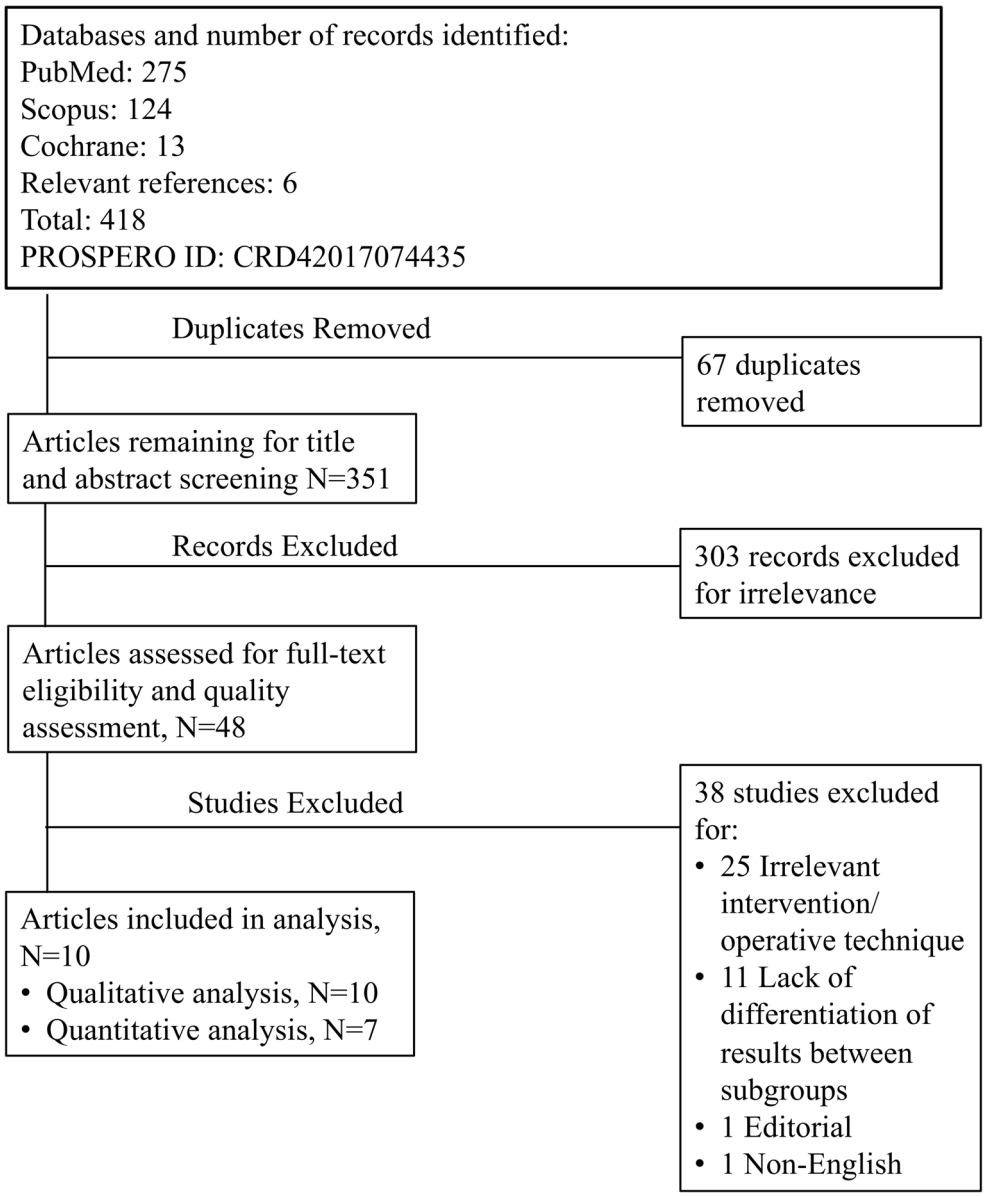


Fig. 1 PRISMA flowchart of databases and exclusions. There were a total of 418 abstracts that met the screening criteria of patients undergoing laparoscopic parenchymal-sparing hepatectomy. After screening, 10 studies met inclusion criteria and were included in the analysis

undergone parenchymal-sparing resection for more than one tumor.[11,12,14–17,19] Additionally, only two papers reported patients with bilobar disease.[17,19] The highest number of tumor resection in one procedure was seven. The most common indication for resection was for colorectal liver metastasis (58%) followed by hepatocellular carcinoma (16%). Other less common indications for resection included metastatic neuroendocrine tumors (3.8%),[15–17] liver adenoma (2.2%),[11,14,16] and intrahepatic cholangiocarcinoma (1.5%).[10,13,15]

Resected Segments

Lesions were resected by either an anatomic segmental approach or a non-anatomic approach.[11,12,14,15,17] Parenchymal transection was performed with cavitron ultrasonic surgical aspirator (CUSA)[11,16,18,19] and bipolar forceps[11–14,17,19] in almost all cases, while one study used a monopolar coagulation device in conjunction with the harmonic scalpel without ultrasonic dissection.[15]

There were a total of 676 resections performed and of these, 539 had reports of specific segment locations. The six most commonly reported locations of lesions resected by LPSH were segment 8 instead of a right hemihepatectomy (56 resections, 10.4%),[12,13,16,17] segment 6 instead of a right hemihepatectomy (42 resections, 7.8%),[12,13,15,17,18] segment 7 instead of a right posterior sectionectomy (37 resections, 6.9%),[12,13,16,17] segment 4a instead of a left hemihepatectomy (32 resections, 5.9%),[16,17] and segment 3 instead of a left lateral sectionectomy (25 resections, 4.6%).[13,15,16,18] The most commonly reported bisegmentectomy was the

posterior sectionectomy of segment 6/7 instead of a right hemihepatectomy with 15 resections (2.8%).[12,13,15] These resections in order of common occurrence are illustrated in Fig. 2. This pattern of occurrence of parenchymal-sparing resections reflects the great temptation in laparoscopic liver surgery to use major anatomical resection which is standardized and technically predictable. Specifically, in variants 2, 5, and 6, a large amount of unaffected liver tissue can be preserved.

A few studies analyzed resections based on *regions* using the categories posterosuperior (segments 1, 7, 8, and 4a) and anterolateral (segments 2, 3, 5, 6, and 4b) without specifying how many resections were done in the specific segments of these regions. For example, Montalti et al. reported outcomes from 72 patients undergoing LPSH for lesions in the posterosuperior region but did not separate the data according to segments.[11] In a different study, Montalti et al. reported outcomes on 114 patients undergoing LPSH for lesions in either the posterosuperior or the anterolateral region, but did not separate the data into specific segments.[19] Ogiso et al. compared resection outcomes between different surgical approaches—combined lateral and abdominal approach versus abdominal approach—only for lesions in segments 7 and 8. Specific segments were not specified.[14] Due to the categorization of data by *region* rather than by *segment*, the most commonly performed resections reported in this review may differ from those reported elsewhere.

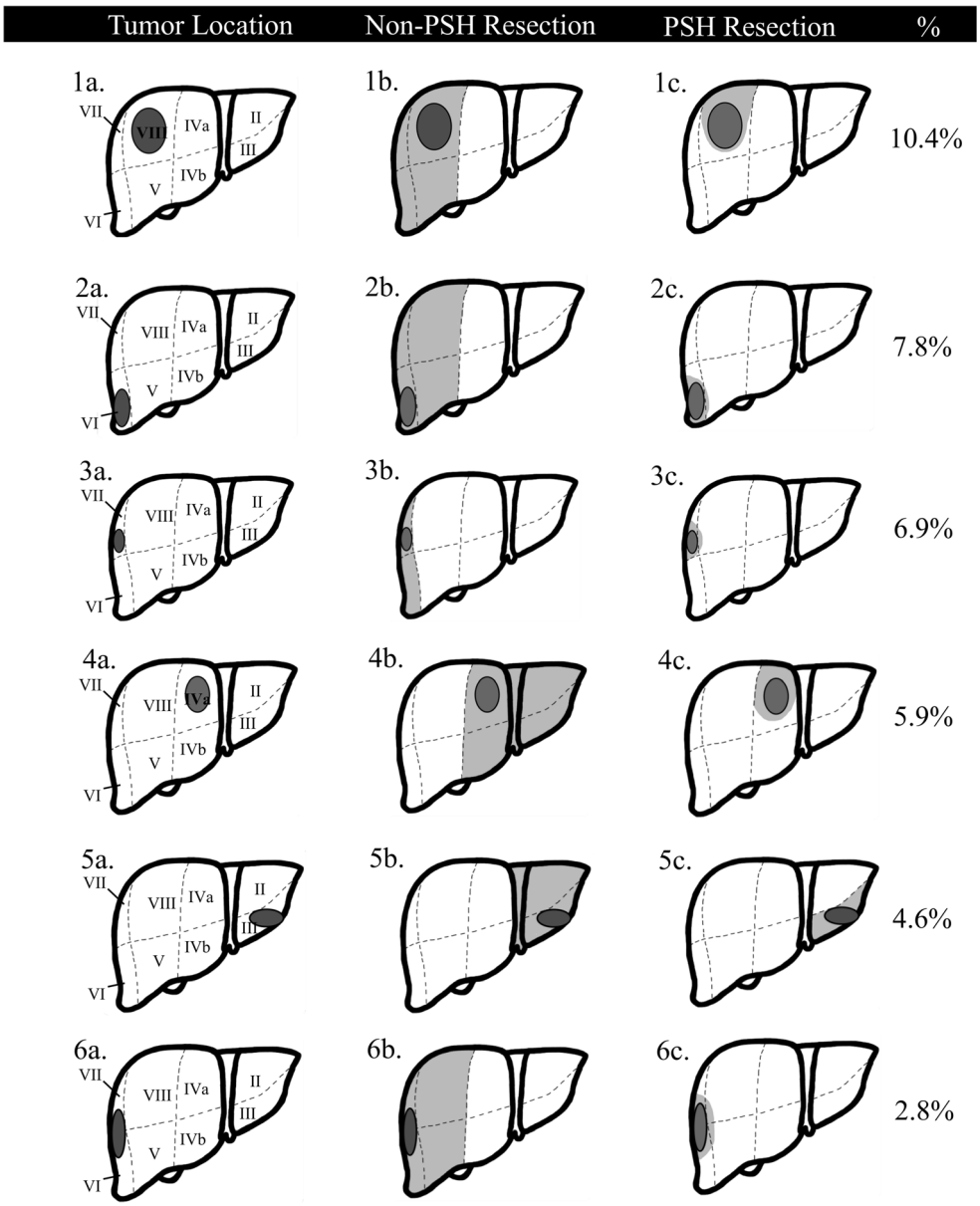


Fig. 2 Diagram of top six LPSH found in the literature and percent reported. **1a.** Tumor in segment 8; **1b.** Right hepatectomy; **1c.** Non-segment-oriented PSH segment 8; **2a.** Tumor in segment 6; **2b.** Right hepatectomy; **2c.** Non-segment-oriented PSH segment 6; **3a.** Tumor in segment 7; **3b.** Bisegmentectomy 6 and 7; **3c.** Non-segment-oriented PSH segment 7; **4a.** Tumor in segment 4a; **4b.** Left hepatectomy; **4c.** Non-segment-oriented PSH segment 4a; **5a.** Tumor in segment 3; **5b.** Left lateral sectionectomy; **5c.** Segmentectomy 3; **6a.** Tumor in segments 6 and 7; **6b.** Right hepatectomy; **6c.** Non-segment-oriented PSH segments 6 and 7

Perioperative Outcomes of LPSH

Quantitative meta-analysis using weighted means resulted in a mean operating time of 335.2 min, EBL of 462 cc, and hospital stay of 7.6 days.[11,15,17,19] For the studies that did not report means, the median operating time was 189.8 min (range 125–369), median EBL was 200 cc (range 100–450), and median length of hospital stay was 6 days (range 2–7).[10,12–16,18,19] The meta-analysis conversion to open rate was 9.7%, the post-operative complication rate 19.4%, and the R0 resection rate 87.7% (Fig. 3).[10–19] The reasons for conversion included intra-abdominal adhesions, bleeding, prolonged operative time, oncologic reasons (inability to assess tumor extent, unclear anatomic relationships), and injury to major vascular structures.[11,13–17,19] These are listed in no particular order, since the number of conversions due to each reason was not specified.[11,13–17,19] Six studies used the Clavien-Dindo classification for reporting post-operative complications,[10–12,14,17,19,20] one study used the Accordion severity grading system,[16,21] and three studies did not report a standard classification system at all.[13,15,18] Not a single perioperative mortality was reported across studies.[10–19] Differences between subgroups and the clinicopathologic characteristics of the patients undergoing LPSH within studies are displayed in Table 1. Table 2 summarizes the perioperative outcomes from LPSH.

However, individual studies selected very specific subgroups, which are therefore spelled out in the following paragraph:

1. Chen et al. compared outcomes between anatomic and non-anatomic parenchymal-sparing resections and found a significantly longer operating time (364 min vs 252 min, $p < 0.001$) and higher EBL (623.5 cc vs 389.9 cc, $p = 0.072$) in the patients undergoing anatomic resections.[15] There was no difference in the number of post-operative complications ($p = 0.468$) between the groups.[15]
2. Ogiso et al. assessed differences between resections of segments 7 and/or 8 using a combined lateral and abdominal approach (left lateral decubitus position) versus an abdominal approach. Operating time was longer in the lateral approach (217.5 min vs 165 min, $p = 0.046$), while there were no differences between EBL or post-operative complications between the two groups ($p = 0.163$ and $p = 0.723$, respectively).[14]
3. Montalti et al. assessed the differences between robotic versus laparoscopic resection of posterosuperior segments. There were no differences noted between the two groups in operating time, EBL, or post-operative complications ($p = 0.65$, $p = 0.85$, and $p = 1$, respectively).[11]
4. Lee et al. compared outcomes between left lateral sectionectomies and wedge resections of the left lateral segments and found no difference between operating time ($p = 0.972$), EBL ($p = 0.435$), or post-operative complications ($p = 0.489$).[18]
5. D'Hondt et al. compared the outcomes of left lateral sectionectomies to resections in the posterosuperior segments. Both longer operating time and higher EBL were observed in the posterosuperior segment resections (160 min vs 100 min, $p = 0.002$; 150 cc vs 50 cc, $p = 0.01$, respectively), while there was no difference in post-operative complications ($p = 0.682$).[12]
6. Two studies compared the outcomes between resections for posterosuperior versus anterolateral segments.[10,13] Kazaryan et al. found no difference in operating time ($p = 0.891$), EBL ($p = 0.849$), or post-operative complications ($p = 0.626$) between the two groups, while Ishizawa et al. observed a significantly longer operating time (240 min vs 155 min, $p < 0.01$) and higher EBL (350 cc vs 100 cc, $p = 0.02$) in the posterosuperior segment resections.[10,13]

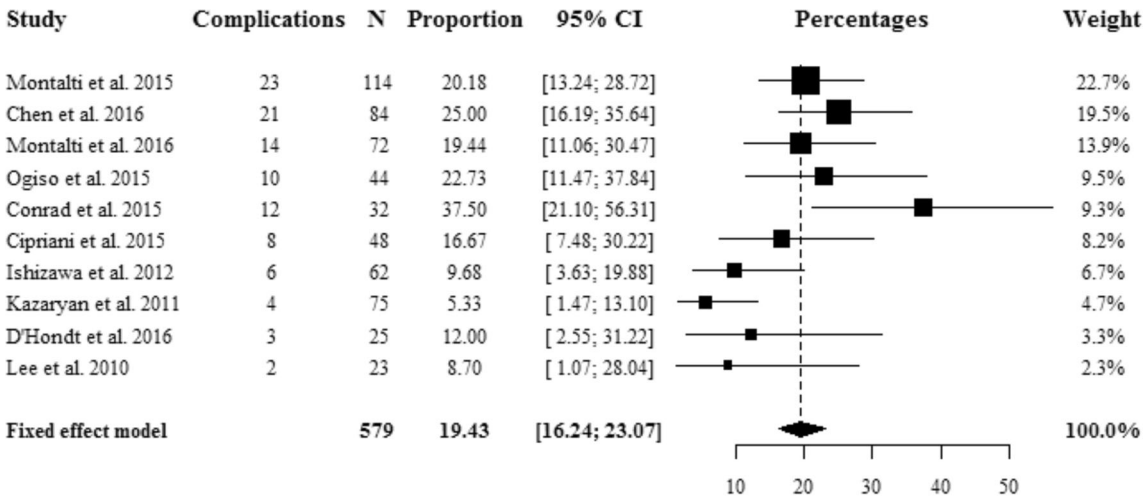
Oncologic Efficacy of LPSH

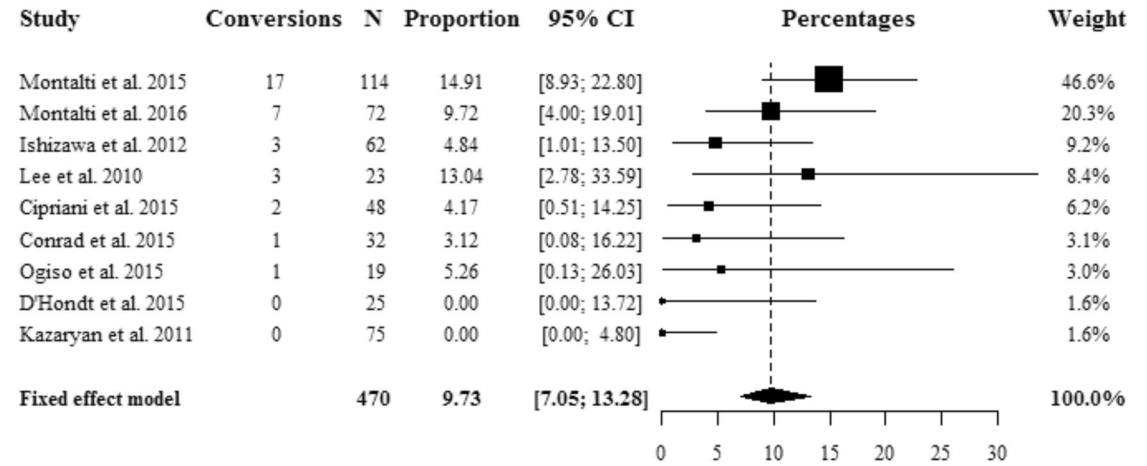
Completeness of resection (R0) was achieved in 91% of all patients for which margins were reported. Three studies analyzed OS and DFS only for the subgroup of colorectal liver metastasis.[11,16,19] Two studies compared OS and DFS between patients who underwent anatomic resection and those with non-anatomic resection, but these studies included patients with different tumor types, which were not separated in the analysis. Those data are therefore difficult to interpret.[15,18]

Discussion

This first systematic review of the laparoscopic approach to parenchymal-sparing liver surgery has identified 10 studies with over 500 patients and demonstrates that this new maximally minimally invasive approach is gaining considerable traction among liver surgeons in experienced centers and has an acceptable safety and feasibility profile.[10–19] While randomized studies show that laparoscopic hepatectomy is as safe as an open resection while allowing lower EBL, shorter length of stay, faster recovery, and less pain,[8,22–24] the combination of the parenchymal-sparing and the laparoscopic approach renders the surgical approach to these lesions even less invasive and may very well convey an improved overall survival in the subgroup of patients with CRLM, who have a high recurrence rate and frequently require re-resections.[7,25]

This summary of outcomes includes only retrospective studies and they report no mortality, a post-operative complication rate of 17%, and a conversion rate of 7%. Mean operative time, EBL, and length of stay are similar to those observed in laparoscopic hemi-hepatectomies.[26]





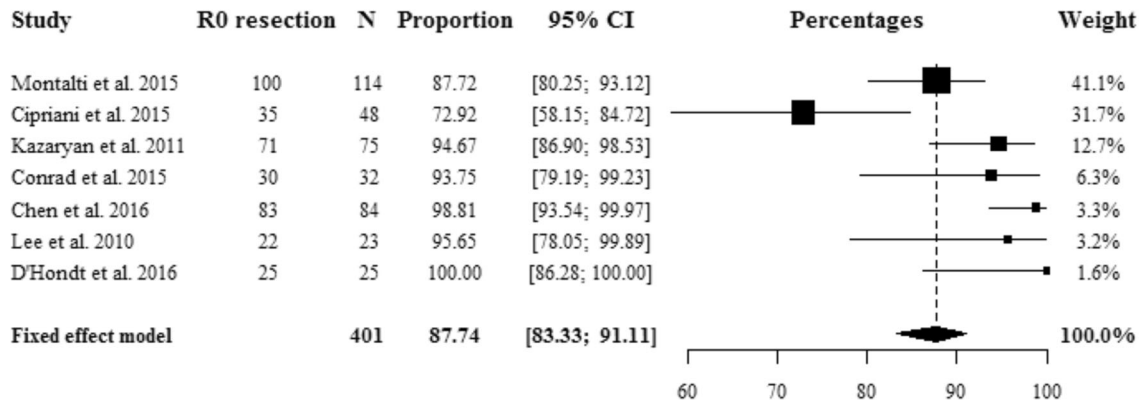


Fig. 3 Meta-analysis of complication, conversion, and R0 resection. Forest plots demonstrate adjusted event rates and 95% CI's for each study with relative weight of the study in the meta-analysis

Table 1 Demographics and clinicopathologic characteristics of patients undergoing LPSH

Study	Group	Patients (*n*)	Age (years)		Male (%)	Number of tumors		Tumor size (mm)	
			Mean (Range)	Median (Range)		Mean (Range)	Median (Range)	Mean (Range)	Median (Range)
Chen et al. 2016[15]	Anatomic	34	58.8	59 (30–78)	62	1.7	1 (1–5)	47.7*	38 (10–130)
	Non-anatomic	50	58.5	58.5 (33–83)	62	1.6	1 (1–6)	28.7*	25 (5–120)
Cipriani et al. 2015[16]	NA	48	NR	64.6 (32–84)	60	NR	NR	NR	25 (8–75)
Conrad et al. 2015[17]	NA	32	61	NR	59	NR	NR	NR	NR
D'Hondt et al. 2016[12]	LLS[a]	20	NR	64.5 (27–85)	35	NR	NR	22.6	NR
	Posterosuperior	25	NR	66 (23–82)	32	NR	NR	20.2	NR
Ishizawa et al. 2012[13]	Posterosuperior	26	NR	66 (62–89)	63	NR	NR	NR	31 (4–160)
	Anterolateral	36							
Lee et al. 2010[18]	LLS[a]	21	NR	58 (34–80)	62	NR	1 (1–2)	NR	27 (15–90)*
	Wedge resection	23	NR	58 (25–76)	61	NR	1 (1–3)	NR	20 (8–40)*
Montalti et al. 2015[19]	NA	114	66.4	NR	68	1.7 (1–7)	NR	40.8 (3.5–145)	NR
Montalti et al. 2016[11]	Robotic, posterosuperior	36	62 (32–84)	NR	58	1.81 (1–6)	NR	44.4 (2–110)	NR
	Laparoscopic, posterosuperior	72	56.8 (17–79)	NR	54	1.5 (1–5)	NR	49.5 (6–140)	NR
Ogiso et al. 2015[14]	Combined lateral abdominal	25	60 (22–85)	NR	64	NR	1 (1–4)	NR	24.5 (8–49)
	Abdominal only	19	66 (48–79)	NR	47	NR	1 (1–4)	NR	15 (8–40)
Kazaryan et al. 2011[10]	Posterosuperior	28	NR	68 (43–82)	43	NR	NR	NR	24 (6–80)
	Anterolateral	47	NR	62 (35–88)	57	NR	NR	NR	25 (7–75)

NR indicates not reported in study

*$p < 0.05$

[a] Left lateral sectionectomy

The data summarized here are similar to the data published on open PSH. In a recent systematic review with 2505 patients across 12 studies that compared the open PSH approach with open anatomic liver resections for CRLM, there were no differences between groups in EBL (PSH 100–896 cc, AR 200–1489 cc), length of stay (PSH 6–17 days, AR 7–15 days), mortality (PSH 0–3.7%, AR 0–3.2%), and post-operative complications (PSH 3.2–27.8%, AR 6.3–29.3%).[27]

While open or laparoscopic PSH appears comparable in outcomes to their respective non-parenchymal-sparing counterparts, the critical difference is in the number of tumors resected. In the above systematic review, the studies included reported *median* number of tumors resected as high as 7, while the highest *median* number of tumors resected in this review was only 1 (Table 1).[28] Patients with a higher number of tumors are more likely to undergo an open parenchymal-sparing resection than a laparoscopic one. The key limitation of the LPSH when compared with the open PSH appears to be that only 16% of patients in this series underwent resections of more than one tumor. One important reason may well be that the laparoscopic approach requires different positioning for the right and left side, which requires repositioning during the case for bilobar multifocal lesions. A unique position which allows laparoscopic resections in all parts of the liver or the robotic approach may solve these limitations in the future.

This review has significant limitations. All 10 studies were retrospective with the expected concerns about reporting and selection bias. No mortalities were reported in 579 patients undergoing liver resections, which is quite unlikely. A further concern is the heterogeneity of patients included. Although CRLM were the most common indication for resection, other tumor types were reported resulting in low numbers of each tumor types resulting in a lack of oncologic data about survival and disease-free survival. Studies about the open PSH approach for CRLM demonstrated that the oncologic outcome is not

Table 2 Perioperative outcomes of LPSH

Study	Group	OR time (min)		EBL (ml)		R0 n (%)	Length of Stay (days)		Complications, *n* (%)	Conversions (*n*)
		Mean (Range)	Median (Range)	Mean (Range)	Median (Range)		Mean (Range)	Median (Range)		
Chen et al. 2016[15]	Anatomic	364*	369.5 (185–787)	623.5	450 (50–2500)	34 (100)	7.5	6.5 (3–19)	10 (29)	NR
	Non-anatomic	252*	199.5 (62–742)	389	100 (5–3000)	49 (98)	5.9	6 (2–14)	11 (22)	NR
Cipriani et al. 2015[16]	NA	NR	215 (22–360)	NR	225 (0–2000)	35 (73)	NR	3 (0–12)	8 (17)	2 (4)
Conrad et al. 2015[17]	NA	183	NR	403	NR	30 (94)	10.4	NR	12 (38)	1 (3)
D'Hondt et al. 2016[12]	LLS[a]	NR	100 (60–260)*	NR	50 (0–550)*	20 (100)	NR	6 (3–16)	4 (20)	0 (0)
	Posterosuperior	NR	160 (95–270)*	NR	150 (50–700)*	25 (100)	NR	6 (4–11)	3 (12)	0 (0)
Ishizawa et al. 2012[13]	Posterosuperior	NR	240 (132–390)*	NR	350 (20–1500)*	NR	NR	7 (4–25)	4 (15)	2 (8)
	Anterolateral	NR	155 (90–360)*	NR	100 (10–1100)*	NR	NR		2 (6)	1 (3)
Lee et al. 2010[18]	LLS[a]	NR	215 (125–305)	NR	100 (10–1610)	21 (100)	NR	4 (2–11)	0 (0)	2 (10)
	Wedge resection	NR	225 (90–420)	NR	150 (5–1500)	22 (96)	NR	4 (2–15)	2 (9)	3 (13)
Montalti et al. 2015[19]	NA	276	NR	250 (0–2800)	NR	100 (88)	NR	6 (2–17)	23 (20)	17 (15)
Montalti et al. 2016[11]	Robotic, posterosuperior	306 (53–790)	NR	415 (0–1500)	NR	NR	6 (2–91)	NR	7 (19)	5 (14)
	Laparoscopic, posterosuperior	295 (75–590)	NR	437 (0–2200)	NR	NR	4.9 (2–20)	NR	14 (19)	7 (10)
Ogiso et al. 2015[14]	Combined lateral abdominal	NR	217.5 (90–390)*	NR	200 (20–2900)	NR	NR	7 (4–22)	5 (20)	0 (0)
	Abdominal only	NR	165 (75–570)*	NR	100 (0–1800)	NR	NR	6 (3–49)	5 (26)	1 (5)
Kazaryan et al. 2011[10]	Posterosuperior	NR	125 (50–336)	NR	200 (< 50–1700)	26 (93)	NR	2 (1–9)	2 (7)	0 (0)
	Anterolateral	NR	130 (50–315)	NR	200 (< 50–2500)	45 (96)	NR	2 (1–7)	2 (4)	0 (0)

NR indicates not reported in study

*$p < 0.05$

[a] Left lateral sectionectomy

compromised as long as a negative margin is achieved.[7,19,29] The topic of PSH versus anatomic hepatectomy has been highly debated in HCC, where it has been argued that local liver recurrence of HCC is higher after a limited or non-anatomic resection, but the data on OS and DFS are mixed.[30–32] This controversy will likely be revived in the field of laparoscopy, but the data basis is so far marginal.

There is also high heterogeneity in the collected studies on outcome reporting. Due to low numbers and distribution of data, some studies only report medians. Additionally, three studies assessed the feasibility of LPSH of only the posterosuperior segments, making these segments more commonly reported in this series and did not allow conclusions on localization.[11,12,14]

Overall, the number of studies and patients remains small, but the summary gives a direction for the future: collaborative prospective multicenter report stratified by tumor types with standardized oncological outcome variables and diseased based reporting of all patients, operative and non-operative; monitoring of databases to avoid reporting and selection bias; and standardized reporting of resections by segments to avoid heterogeneity. The most important insight of this review is that the frontier of PSH is the number of tumors resected, especially in bilobar tumors, where repositioning may become necessary.

Conclusion

Laparoscopic PSH is being performed and reported, but the data quality is low so far. The main limitation of LPSH is that there is little experience with the resection of multiple lesions in differing locations in the liver, especially for bilobar metastatic disease. Randomized prospective reports of tumor-specific oncological data would be desirable for the future.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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