Surgical Oncology 28 (2019) 140–144

Contents lists available at ScienceDirect

Surgical Oncology

journal homepage: www.elsevier.com/locate/suronc

Laparoscopic liver surgery in cirrhosis – Addressing lesions in posterosuperior segments

Philipp Konstantin Haber[a], Simon Wabitsch[a], Felix Krenzien[a,b], Christian Benzing[a], Andreas Andreou[a,c], Wenzel Schöning[a], Robert Öllinger[a], Johann Pratschke[a], Moritz Schmelzle[a,*]

[a] Department of Surgery, Campus Charité Mitte and Campus Virchow-Klinikum, Charité - Universitätsmedizin, Berlin, Germany
[b] Berlin Institute of Health (BIH), Berlin, Germany
[c] Berlin School of Integrative Oncology (BSIO), Berlin, Germany

ARTICLE INFO

Keywords:
Laparoscopic liver surgery
Liver cirrhosis
Hepatocellular carcinoma

ABSTRACT

Background: Minimal-invasive liver resection has gained considerable attention in recent years, assuming a weighty position in the field of HPB surgery. Even lesions in posterosuperior segments, the technically most challenging localization, have been resected while achieving comparable outcomes to laparotomy. The objective of this study is to evaluate whether the similar beneficial results can be conveyed through minimal-invasive techniques for patients with liver cirrhosis.

Materials and methods: We retrospectively analyzed all consecutive patients undergoing laparoscopic liver resection with at least one lesion in the posterosuperior liver segments (IVa, VII, VIII) at our center between January 2012 and July 2018. Patients were separated in two groups based on the presence (n = 43) or absence (n = 115) of liver cirrhosis.

Results: Preoperative patient characteristics showed that patients with cirrhosis were older ($p < 0.001$), had more frequently diabetes ($p < 0.005$) and a history of alcohol consumption ($p < 0.0005$). Preoperative liver function, as assessed by LiMAx score was markedly decreased in patients with liver cirrhosis ($p < 0.005$).

While a similar percentage in both groups had anatomical resection, significantly more major resections were performed in patients without cirrhosis (cirrhosis: 23.3% vs. no cirrhosis 55.7%; $p < 0.0005$). Consequently, surgeries were markedly longer in the no cirrhosis group ($p < 0.0005$). There was no difference with regard to the need for perioperative transfusion or conversion to laparotomy.

There was no differences found between both groups with regard to the postoperative course showing similar ICU- and hospital stays. Complication rate, both with regard to minor and major complications, as well as rate of clear resection margins were similar between the two groups as well.

Conclusion: Patients with liver cirrhosis and a lesion in the posterosuperior liver segments are amenable to the minimal-invasive approaches as no significant differences can be observed with regard to safety and oncologic sufficiency. As these procedures are from a technical perspective challenging, they should be performed in specialized centers.

1. Introduction

Minimal-invasive approaches have assumed an important position in the treatment of various hepatobiliary diseases. Through minimization of the surgical trauma, the different minimal invasive techniques have been able to elicit rapid recovery and reduced morbidity while achieving high-quality oncologic outcomes when compared to traditional open surgery [1–5]. Consequently, laparoscopic liver surgery (LLS) has gained marked interest as a viable option to treat a vast array of hepatic lesions.

In this context, identifying patients that are particularly amenable to the laparoscopic approach remains a crucial unmet need in the field of hepatobiliary surgery. In terms of feasibility, several studies have identified lesion size and location as the pivotal factors determining whether laparoscopy is conducive or not. Initially, procedures were widely restricted to left lateral sectionectomy and wedge resections. Recently, however, indications have been extended markedly, allowing for complex resections such as hemihepatectomies and at specialized

* Corresponding author. Department of Surgery, Campus Charité Mitte and Campus Virchow-Klinikum, Charité Universitätsmedizin Berlin, Augustenburger Platz 1, 13353, Berlin, Germany.
E-mail address: moritz.schmelzle@charite.de (M. Schmelzle).

https://doi.org/10.1016/j.suronc.2018.12.001
Received 12 November 2018; Accepted 14 December 2018
0960-7404/

centers even living donor-hepatectomy.

Considerable efforts have been made to provide objective criteria defining the difficulty of different resections. Consequently, various scores have been introduced to characterize factors determining resection difficulty [6–9]. The Iwate criteria have emerged through external validation as the most commonly applied score [7,10]. Of note, resections in the posterosuperior segments (VII, VIII, IVa) have been described consistently as the most difficult resection types [9,11]. The available studies have for the most part focused on comparing laparoscopy with open surgery showing similar overall outcomes from both a safety as well as an oncologic perspective for patients with colorectal liver metastasis (CRLM) [12,13].

The aim of this study was to evaluate whether patients with pre-existing liver impairment might profit disproportionally from minimal-invasive liver surgery. We therefore compared patients with underlying liver cirrhosis undergoing minimal-invasive surgery for lesions in the posterosuperior segments with patients without liver cirrhosis.

2. Methods

2.1. Patients characteristics

All consecutive patients from January 2012 until July 2018 who were operated minimal invasively for at least one lesion in the posterosuperior segments VII, VIII and IVa at the Department of Surgery – Charité Universitätsmedizin Berlin, Germany were included in this study. Analysis was performed retrospectively with regard to patients' characteristics, intra- and postoperative course. Exclusion criteria were multivisceral resections as well as patients undergoing 2-stage hepatectomy.

Major hepatectomy was defined as liver resections comprising at least 3 segments. Postoperative complications occurring within 90 days postoperatively were classified using the Clavien-Dindo classification [14].

2.2. Preoperative assessment

Patient workup prior to surgery included medical history, physical status and routine biochemistry lab. As staging diagnostics either computed tomography (CT) and/or magnetic resonance imaging (MRI) were performed. Multidisciplinary tumor board approval was required preoperatively for malignant lesions in order to assess whether surgery was indeed indicated. Liver function was vetted preoperatively using LiMAx (maximum liver function capacity) as well as the biochemistry lab workup. A Child-Pugh score of 5–6 equaling a class A cirrhosis was deemed sufficient for surgery. The utilization of Child-Pugh system was applied as proposed in the revised system by Pugh et al. based on encephalopathy (1, none; 2, minimal; 3, coma), ascites (1, absent; 2, controlled; 3, refractory), bilirubin (1, < 34 μmol/L; 2, 34–51 μmol/L; 3, > 51 μmol/L), albumin (ALB) (1, > 35 g/L; 2, 28–35 g/L; 3, < 28 g/L) and INR (1, < 1,7; 2, 1,71-2,2; 3, > 2,2). Diagnosis of liver cirrhosis was confirmed by an expert pathologist postoperatively by using the Desmet-Scheuer score [15].

2.3. Surgical approaches

Indication for the particular minimal-invasive procedure was given at the operating surgeon's discretion. Surgery was performed under general anesthesia. Patients were placed in the French position. Different surgical techniques were applied: Standard multiport laparoscopy (MILL) was carried out using 3–8 trocars in various different position constellations. Alternatively, an epigastric median mini-incision was performed in order to insert a handport as previously described [16]. Need-based additional trocars were placed. Laparoscopic ultrasound was performed in order to define the resection margin and rule out further intrahepatic tumors/lesions. Parenchymal dissection was performed using shears (Thunderbeat®, Olympus or Harmonic Ace®, Ethicon or UltraCision®, Ethicon Inc. Somerville, NJ, USA), CUSA or ERBEJET®, (Tübingen, Germany) and/or vascular staplers (Echelon, Ethicon, Somerville, New Jersey, USA).

At our center an anterior approach in the French position is generally preferred, even for lesions in the posterosuperior lesions. Intercostal trocar placement is rarely performed as even very challenging lesions can be addressed by arranging trocars along the lines of the L-shape which is used for laparotomy.

Exposure of the posterosuperior liver segments is pivotal for the success of the resection. Particularly in the case of non-cirrhotic livers with increased size, the diligent mobilization of the right liver lobe by cleaving the falciform, triangular and right coronary ligament might be critical. This essentially allows for superior exposure of the segments VII and VIII by putting them in an anterior position. In recent years the diamond technique evolved as our method of choice in most cases: Prior to resection a square-shaped transection area was outlined with varying distance to the tumor depending on the depth of the lesion. Transection planes are then created from the square area. Ultrasound is repeatedly performed in order to inspect resection margins. This technique has been described by Cipriani et al. as the “diamond technique” since the resected specimen bears similarity to the shape of a diamond [17]. The main advantage of this technique is that through the perpendicular transection planes lesions in the deep parenchyma can be resected with reduced risk of incising tumor tissue.

In order to decrease intraoperative hemorrhage we have recently increasingly performed inflow control intermittently during transection phase. In our experience, postoperative liver function is not affected by this maneuver which is in line with other reports [18]. Recovery of the resected specimen was performed through either the handport incision, or a suprapubic Pfannenstiel incision. Alternatively, extension of the umbilical incision was performed. Need based, abdominal drains were inserted.

2.4. Postoperative management

Postoperatively patients were either transferred to a specialized surgical intensive care unit for postoperative observation or directly transferred to a general surgical ward depending on preoperative condition as well as intraoperative course. Fluid and food intake was permitted generally on the day of the operation. Abdominal drains were removed if wound secretion was inconspicuous. Pending an unremarkable clinical course without clinical or paraclinical indices of complications, patents were discharged.

2.5. Statistical analysis

Statistical analysis was performed using the GraphPad Prism software package, version 6 (Software, Inc., La Jolla, CA USA). Chi-square test as well as Mann-Whitney *t*-test were applied for comparison. Quantitative variables are expressed as the median, while categorical variables are expressed through percentages. P values < 0.05 were considered statistically significant.

3. Results

3.1. Patients characteristics

Between January 2012 and July 2017 148 surgeries were performed for lesions in the posterosuperior segments that fulfilled the inclusion criteria. Preoperative conditions are summarized in Table 1. Forty-three patients (26.7%) had underlying liver cirrhosis. Of these patients, 39 (91%) were operated due to hepatocellular carcinoma (HCC). The remaining 4 patients were operated due to intrahepatic cholangiocarcinoma (iCC) (9%). With regard to patients without liver cirrhosis indications were colorectal liver metastasis (CRLM; 44%), non-colorectal

Table 1
Demographics.

Variable	Cirrhosis (n = 43)	No Cirrhosis (n = 115)	p value
Age	68 (19–80)	59 (13–85)	**0,0008**
Gender (M/F)	29/14	68/47	0,3649
BMI	26 (18–40)	26 (17–44)	0,9589
ASA score ≥ 3	20 (46.5%)	51 (44.3%)	0,7106
Diabetes	14 (32.6%)	14 (12.2%)	**0,0047**
Alcohol	13 (30.2%)	8 (7.0%)	**0,0002**
Smoking	9 (20.9%)	12 (10.4%)	0,1126
Viral Hepatitis			
HBV	6 (14.0)	5 (4.4%)	0,071
HCV	16 (37.2%)	2 (1.74%)	**0,0001**
HDV	0	1 (0.9%)	1
Previous abdominal surgery	11 (25.6%)	61 (53.0%)	**0,0041**
LiMAX score (ug/h/kg)	302 (78–611)	384 (134–668)	**0,003**
preoperative MELD score	8 (6–14)		
Indications			
	HCC (n = 39)		
	iCC (n = 4)	CRLM (n = 51)	
		Other Metastasis (n = 15)	
		HCC (n = 14)	
		Hepatocellular Adenoma (n = 7)	
		iCC (n = 5)	
		FNH (n = 4)	
		Dysplastic nodules (n = 4)	
		NET (n = 3)	
		Abscess (n = 3)	
		Hemangioma (n = 3)	
		Caroli's syndrome (n = 3)	
		Haematoma (n = 1)	
		Cystic echinococcosis (n = 1)	
		Mixed HCC/iCC (n = 1)	

liver metastasis (13%), HCC without cirrhosis (12%), hepatocellular adenoma (6%), iCC (4%), focal nodular hyperplasia (FNH; 3%), dysplastic nodules (3%), NET (3%), liver abscess (3%), hemangioma (3%), Caroli's syndrome (3%), haematoma (1%), cystic echinococcosis (1%) and mixed HCC/iCC (1%).

Patients with cirrhosis were significantly older as compared to patients without underlying liver cirrhosis (cirrhosis: 68 vs. no cirrhosis: 59; $p < 0.001$). While gender ratios as well as preoperative body-mass index (BMI) and ASA score, as assessed by the anesthesiology staff, were similar between the two groups, patients with cirrhosis had significantly more often a history of regular alcohol intake (cirrhosis: 30.2% vs. no cirrhosis: 7.0%; $p < 0.0005$). Moreover, patients with liver cirrhosis had significantly more often diabetes as a preoperative condition (cirrhosis: 32.6% vs. no cirrhosis: 12.2%; $p < 0.005$). With regard to preoperative liver conditions, patients with cirrhosis were markedly more often affected by Hepatitis C virus (HCV) infection (cirrhosis: 37.2% vs. no cirrhosis 1.7%; $p < 0.0005$). Of note, a trend towards higher prevalence of HBV was observed although this was short of statistical significance (cirrhosis 14.0% vs. no cirrhosis 4.4%; $p = 0.071$). LiMAx score was significantly decreased in the cirrhosis group as compared to patients without cirrhosis (cirrhosis: 302 μg/h/kg vs. no cirrhosis: 384 μg/h/kg; $p < 0.005$; reference > 315 μg/h/kg).

3.2. Details of surgical procedures

As depicted in Table 2, operative course was comparable between the groups with the exception of a markedly decreased time of surgery in the cirrhosis group (cirrhosis 223min vs. no cirrhosis: 328min; $p < 0.0005$). The proportion of anatomical resections between the two groups was not significantly different (cirrhosis: 48.8% vs. no cirrhosis 49.6%; $p = 1$); however significantly more major resections were performed in patients without cirrhosis (cirrhosis: 23.3% vs. no cirrhosis 55.7%; $p < 0.0005$). Conversion to open surgery was required in 1 case in the cirrhosis group vs. 7 cases in the non-cirrhosis group (2.3% vs. 6.1%; $p = 0.45$).

Table 2
Operative procedures.

Variables	Cirrhosis (n = 43)	No Cirrhosis (n = 115)	p value
Hemihepatectomy	10 (23.3%)	60 (52.7%)	**0,0012**
Right Hemihepatectomy	6 (14.0%)	37 (32.2%)	**0,0267**
Left Hemihepatectomy	3 (7.0%)	11 (9.6%)	0,7598
Extended right Hemihepatectomy	1 (2.3%)	9 (7.8%)	0,2882
Extended left Hemihepatectomy	0	3 (2.6%)	0,5630
Bigsegmentectomy	3 (7.0%)	13 (11.3%)	0,5600
Segmentectomy	13 (30.2%)	21 (18.3%)	0,1281
Subsegmentectomy	17 (39.5%)	21 (18.3%)	**0,0111**
Major resection	10 (23.3%)	64 (55.7%)	**0,0003**
Operative time (min)	223 (49–461)	328 (52–758)	**0,0001**
Perioperative transfusion	5 (11.6%)	16 (13.9%)	0,7981
Conversion to open surgery	1 (2.3%)	7 (6.1%)	0,4487
Lymphadenectomy	3 (7.0%)	7 (6.1%)	1

3.3. Postoperative outcomes

Between the two groups no significant difference was found when comparing ICU stay (cirrhosis: 1 day vs. no cirrhosis: 1 day; $p = 0.658$). There was a slight trend towards a shorter hospitalization time in the cirrhosis group, although that did not reach statistical significance (cirrhosis: 8 days vs. no cirrhosis: 9 days; $p = 0.098$).

Tumor free resection margins were achieved in 83.8% of the patients in the cirrhosis group vs. 86.1% in patients without cirrhosis ($p = 0.8$).

Postoperative morbidity, as summarized in Table 3, was not significantly different between the two groups neither with regard to general complications nor if only complications ≥ grade III according to the Dindo-Clavien classification are taken into consideration. There was a trend towards more major complications in the no cirrhosis group, likely ascribable to the more extensive resection extend. This

Table 3
Postoperative outcomes.

Variables	Cirrhosis (n = 43)	No Cirrhosis (n = 115)	p value
ICU stay (days)	1 (0–43)	1 (0–41)	0,6583
Hospital stay (days)	8 (5–43)	9 (3–59)	0,0965
R1 Status	7 (16.2%)	16 (13.9%)	0,8004
Mortality	1 (2.3%)	2 (1.7%)	1
Morbidity	12 (27.9%)	28 (24.3%)	0,6832
liver failure	1	2	1
Biliary leakage	1	11	0,1823
Ascites	3	1	0,0617
Postoperative bleeding	1	–	0,2722
Abdominal collection	2	2	0,2986
Pulmonary complications	2	7	1
Kidney injury	1	1	0,4715
Urinary tract infection	1	–	0,2722
cardiac complications	1	3	1
deep tissue wound infection	–	3	0,563
Post-ERC bleeding	–	1	1
Morbidity ≥ Grade III	4 (9.3%)	22 (19.1%)	0,1567
Complication treatment ≥ Grade III			
Reoperation	–	4	0,5752
Interventional endoscopy	1	9	0,2903
percutaneous drainage	2	8	0,7294
Medical	1	1	0,4715

trend however, was short of statistical significance.

The obtained data prompted us to limit the scope in our patient collective subsequently on patients undergoing local resection only, i.e. segmentectomy, subsegmentectomy and enucleation to allow for superior commensurability between the two groups. In doing so, we identified 30 patients in the cirrhosis group and 42 patients in the no cirrhosis group. Major complication rate was comparable between the two groups (cirrhosis: 10.0% vs. no cirrhosis: 9.5%; $p = 1$). In keeping with this, both ICU stay (cirrhosis: 1 day (0–43) vs. no cirrhosis: 1 day (0–5); $p = 0.8$) and total hospital stay were similar as well (cirrhosis: 8 days (5–43) vs. 8 days (4–17); $p = 1$).

4. Discussion

Through the substantial experience with laparoscopic liver surgeries, it is well established that lesions in the posterosuperior liver segments are the most difficultly attainable from a technical perspective. With limited exposure and close proximity to the hepato-caval junction addressing these lesions using a minimal-invasive approach entails challenging steps even for the experienced laparoscopically-adept liver surgeon.

At our center, we have performed a steadily increasing number of laparoscopic procedures within recent years. In 2017, out of the 383 conducted hepatectomies at our center, 94 (24.5%) were performed minimal-invasively. Of note, some patients were scheduled for open surgery not due to the difficulty of the liver resection, but for other reasons, e.g. liver resection in combination with peritonectomy or multi-visceral resections. Consequently, the proportion of laparoscopic procedures for isolated liver resections is considerably higher. Out of the laparoscopic procedures in 2017, 59 (62.8%) were performed in patients with at least one lesion in the posterosuperior segments. As patients with liver cirrhosis and hepatocellular carcinoma are increasingly considered for resection in the setting of scarce donor organs for transplantation, evaluating the option of safe minimal invasive resection in challenging localizations is of great interest to us.

Previous studies have shown resection of lesions located in the posterosuperior segments of the liver to achieve similar outcomes when compared to open surgery [12,19,20]. One study reported a marked decrease in postoperative complications while retaining high-quality oncologic outcomes [21]. The limited number of studies investigating lesions aside from CRLM focus on whether patients with HCC benefit from laparoscopy instead of laparotomy showing comparable results [22–24].

Therefore, the available evidence, hints at least at a non-inferiority of minimal-invasive resection for patients with lesions in the posterosuperior segments. The aim of this study was to evaluate whether the presence or absence of liver cirrhosis affects the outcome of patients after resection of lesions in the posterosuperior segments.

In our cohort, preoperative conditions between the two groups were similar, although patients in the cirrhosis group were markedly older as well as more often diabetic and had a higher prevalence of regular alcohol intake. Expectedly, patients with cirrhosis had a markedly impaired liver function as evidenced by the reduced LiMAX score. The significantly higher rate of previous abdominal surgeries is in context of the high number of CRLM cases in the non-cirrhosis group.

In evaluating the operative course, operative time was markedly increased in the no-cirrhosis group, potentially attributable to the markedly higher proportion of major resections in this group. Of note, both groups had a similar proportion of anatomical resections. Moreover, patients in the no-cirrhosis group had more frequently conducted previously abdominal surgeries and subsequent need for adhesiolysis. Interestingly, patients in the cirrhosis group did not have a higher need for perioperative transfusion nor was conversion more frequently required. Typically, limited exposure in terms of a poor operative field is perceived as an impediment towards achieving sufficient resection margins and control in case of intraoperative hemorrhage. Several techniques such as intercostal trocar placement [25], a transdiaphragmatic approach [26] as well as modified patient position [27] have been introduced to improve exposure of the transection plane; however, are not routinely used at our center.

Despite the limitations of minimal-invasive techniques our results indicate a similar intra- and postoperative course independent of whether a patient had liver cirrhosis. Even for challenging enucleations or monosegmentectomies in the segments 7 or 8, which are included in this study, similar results can be achieved even if the patient is cirrhotic. Neither ICU stay nor hospital stay were significantly different. Postoperative morbidity was similar between the two groups with regard to overall complications as well as complications ≥ Grade III according to the Dindo-Clavien Classification [14]. In fact, a trend towards less morbidity in the cirrhosis group was observed, which, however, did not reach statistical significance. Likely, the markedly reduced resection extend in the cirrhosis group is causative for this trend. This observation compelled us to improve comparability between the two groups. We addressed this via a subanalysis of all patients receiving local resections for lesions in the posterosuperior lesions, i.e. segmentectomy, subsegmentectomy and enucleation. Comparison between the two groups showed similar postoperative outcomes with regard to ICU stay, hospital stay and morbidity. Likewise, oncologic results in terms of tumor-free resections margins were similar as well.

The obtained data revealed that the occurrence of complications in the cirrhosis group did not correlate with preoperative MELD score, revealing inconspicuous postoperative courses even in patients with a MELD score > 10 preoperatively.

Laparoscopy has in hepatobiliary surgery initially encountered a certain wariness particularly with regard to oncologic sufficiency. As considerable resources have been dedicated to establish minimal-invasive techniques for hepatic resections, these concerns have been refuted by various case matched series [22,28–30] and one randomized controlled trial, which limited the scope on CRLM [1]. Consequently, minimal-invasive techniques have been applied to treat lesions even in the posterosuperior segments. In our cohort, no difference was observed in terms of clear resection margins between the two groups. Pathology workup of the resected specimens confirmed the presence of liver cirrhosis in all patients in the cirrhosis group. Cirrhosis was defined through the Desmet-Scheuer scoring system [31]. Accordingly, all patients with liver cirrhosis had a score of 4.

The most obvious limitation of this study is the division of patients based on the presence or absence of liver cirrhosis and the according bias this division entails since most patients in the cirrhosis group have HCC as the indication while most patients in the no-cirrhosis group had liver metastasis as indication. Certainly, by design of the study, this key difference in preoperative condition and therefore operative risk poses the central point of investigation. Indeed, establishing that, despite unfavorable preoperative characteristics, minimal invasive resection can elicit similar results in patients with cirrhosis compared to patients without was the aim of this study. The entity of the lesions is from this perspective secondary to the presence of cirrhosis as a potentially complicating factor. As of now, the available studies have only investigated whether minimal invasive resection is comparable to open surgery or whether resections in the posterosuperior segments can be performed without jeopardizing safety and oncologic results. In this context the considerable population of patients with liver cirrhosis and their operative risk is hardly accounted for in the available reports. Further limitations of this study include its retrospective design as well as its lack of long-term oncologic data, which are not meaningful to observe due to different entities in both groups.

In conclusion, our study shows that patients with liver cirrhosis and lesions in the technically demanding posterosuperior segments (IVa, VII, VIII) are amenable to minimal-invasive procedures without compromising intraoperative safety and oncologic outcomes. Certainly, critical individual features determining the indication for a specific procedure interfere with coherent analysis. As such, preoperative liver

function and estimated remnant function, detailed location with regard to tissue depth and relative adjacency to major structures determining resection extent pose persisting impediments towards a 1:1 case matched analysis. Further efforts are needed to develop objective criteria guiding a surgeon in indication setting for such lesions.

Declarations of interests

None.

Disclosures

The authors have no conflicts of interest to disclose.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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