Analysis of open and laparoscopic liver resections in a German high-volume liver tumor center

Dissertation
zur Erlangung des akademischen Grades

Dr. med.

an der Medizinischen Fakultät
der Universität Leipzig

eingereicht von Hanna Guice, geboren am 07.11.1993 in Burglengenfeld

angefertigt am Universitätsklinikum Leipzig in der Klinik und Poliklinik für Viszeral-, Transplantations-, Thorax- und Gefäßchirurgie

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Beschluss über die Verleihung des Doktorgrades vom: 19.07.2022

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Vorbemerkung

Für diese Dissertationsschrift wurde die Form der Publikationspromotion gewählt. In der Originalpublikation werden die Methodik und Ergebnisse detailliert erläutert sowie ausführlich diskutiert.

Bibliographische Beschreibung:

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Analysis of open and laparoscopic liver resections in a German high-volume liver tumor center. *Laparosc Surg* 2021;5:3 doi: 10.21037/ls-20-93

Seiten: 11, Literaturquellen: 49, Abbildungen: 3, Tabellen: 3

Abkürzungsverzeichnis

CCA	Cholangiocarcinoma
CRLM	Colorectal liver metastase
CT	Computertomography
CUSA	Caviton Ultrasonic Surgical Aspirator
FNH	Focal nodular hyperplasia
GI-tract	Gastrointestinal tract
HALS	Hand-assisted laparoscopic surgery
HCC	Hepatocellular carcinoma
iCCA	Intrahepatic cholangiocarcinoma
ICG	Indocyanine green
LiMax-test	Liver Maximum Capacity test
LLR	Laparoscopic liver resection
LPMH	Laparoscopic posterosuperior major hepatectomy
LTMH	Laparoscopic traditional major hepatectomy
MRI	Magnetic resonance imaging
OLR	Open laparoscopic resection
pCCA	Perihilar Cholangiocarcinoma
TACE	Transaterial chemo embolization

Einführung

1. Development of minimal invasive liver surgery:

Laparoscopic liver resection (LLR) reached an irreversible significant standing in hepatic surgery today. Over the last two decades, it has processed from an experimental procedure to a routine approach in the surgical treatment of many liver lesions. Despite of that, minimally invasive treatment modalities of liver tumors still remain a matter of development and further research is required.
Due to its positive short- and long-term benefits that skilled surgeons could already demonstrate, it slowly underwent a gradual expansion. In comparison with the traditional open liver resections (OLR) it is considered a feasible, efficient[1] and valid alternative compared to the traditional open liver resections (OLR)[2,3].

Historically the first LLR was reported by Gagner[4] et al. in 1992 for a 6cm focal nodular hyperplasia (FNH). The first successful laparoscopic anatomical hepatectomy was performed by Azagra[5] et al. He described a laparoscopic left lateral segmentectomy in a patient with benign liver adenoma.

Over the last two decades, the incidence of minimal invasive liver surgery has increased exponentially[6]. Nowadays LLRs are performed for benign and various malign indications like HCC, CRLM and many other pathologic entities worldwide with promising results[7]. The acceptance of LLR for minor liver resection developed quite quickly, however the incidence of large numbers of laparoscopic major hepatectomies was limited at first[8].

Some retrospective studies and case reports addressing the theme of LLR have been published by now, thus slightly more comparison with respect to long-term outcomes like recurrence rates and survival can only be drawn by now.

Another milestone in the development of laparoscopic liver surgery was the founding of the International Laparoscopic Liver Society[9] (ILLS) in 2016, which constantly aims to present and validate guidelines for laparoscopic liver surgery. Since its first meeting in Paris 2017, an unification of indications, applied techniques, and strategic approaches in laparoscopic liver surgery can be identified.

2. Prior concerns of LLR

It has been very hard to popularize LLR in the generation of laparoscopic surgery and its development of was accompanied by reservations and concerns. So the expansion of the laparoscopic approach in liver surgery has been delayed due to a number of prior concerns[2]. It was argued that mobilization of the liver and parenchymal transection is very demanding applying laparoscopic techniques, especially regarding loss of manual palpation. Also control of perioperative hemorrhages and obtaining haemostasis is a quite challenging factor[10,11]. It may not only lead to obscured views and the need to convert to open surgery but also the requirement for blood transfusion is associated with an increased risk of postoperative morbidity and mortality[12]. Under pneumoperitoneum, the risk of gas embolism has been described, when dividing hepatic veins or if major bleeding from hepatic veins occurs[13]. Another uncertainty is the adequate long-term oncological outcome with LLR due to its technical inapplicability, where maintaining adequate tumor margins is a difficulty. Also "the possibility of port-site tumor cell implantation during removal of instruments or tissue"[12] as well as tumor cell-seeding is an addressed problem. Concerns regarding insufficient exploration possibilities, e.g. in patients after undergoing downsizing chemotherapy, were mentioned[14].
All these listed issues combined contributed to the slow gain of popularity of LLR compared to other laparoscopic procedures[14]. With time already many these initial concerns could have been scientifically disproved and outperfomed by invincible benefits[15], which are discussed in the following.

3. Benefits of laparoscopic surgery

3.1. General advantages of minimal invasive surgery

Minimal invasive techniques revolutionize the common surgical procedures of the GI-tract. If Laparoscopic treatment is even considered as the approach of choice for most indications if practicable. Proven advantages of laparoscopic surgery in general include reduced postoperative pain thus reduced analgesic requirement, less bleeding, shorter delay to oral intake, lower morbidity, shortened duration of hospitalization and an improved cosmetic outcome.[2,14,16]

3.2. Specific benefits of applying LLR

Regarding direct advantages of LLR, encouraging results in terms of safety, feasibility and efficiency were demonstrated[17]. The oncological outcome has been reported to be equal to open surgery treatment[15]. Also a quicker improvement of the serum transaminase levels has been shown postoperatively[14]. Improved recovery after undergoing LLR may also be associated with an earlier access to adjuvant radiation- or chemotherapy options.
The very rare risk of gas embolism might be prevented by options like abdominal-wall-lifting and the effectiveness of gasless laparoscopy is reported quite well[18].
Even repeated resections or salvage liver transplantation can predominantly be facilitated in patients after LLR when compared to open liver surgery[10]. It appeared that repeated LLR are considered safe, feasible and can also be performed with minimal morbidity and without higher complications rates when compared to a primary LLR[19].
Improvements in terms of visualization like the use of ultrasonography, novel intraoperative staining techniques and hyperspectral imaging can refute concerns about insufficient exploration[20,21].

4. Indications for LLR

Localization of lesions is an important landmark when indicating laparoscopic resection. Small, focal, and localized tumors on antero-lateral segments are favored for laparoscopic approach. Also partial resection of the peripheral liver or left-lateral segment resection is very suitable for LLR, since the periphery of the liver is lacking large venous vessels so bleeding is more controllable[3]. For major and massive resections you have to consider the balance between postoperative organ reserve and surgical curability, e.g. liver cirrhosis is considered a limiting factor[22].

20-50 percent of all liver resections seem to be feasible in a laparoscopic manner[14]. When performing oncologic LLR, treatment norms should be followed the same as in OLR, e.g. radical resection with 1 cm free surgical margin[23].

4.1 Benign liver lesions

It is reported that, benign liver disease makes up 35 percent of LLRs[24], taking in consideration benign liver tumors are quite frequent incidental findings. Benign diagnoses for LLR comprise hemangiomas, FNH, liver adenomas, regenerate nodes, abscesses, cysts or intrahepatic stones. Their indication for resection is justified by presence of symptoms, risk of rupture and amount of affected liver tissue or size. Symptoms in patients with benign lesions usually appear through rupture or enlargement. The laparoscopic approach can be defined as the standard of care for benign liver lesions based on today's available data.

4.2 Malignant liver lesions

The worldwide most common indication for LLR is represented by hepatocellular carcinoma (HCC)[14,25], known as the most common malignant liver tumor and commonly associated with liver cirrhosis. Although only 15-30 percent of HCC patients have potentially resectable lesion, curative surgical resection is the treatment of choice[26].
Liver metastases constitute another big group of malignant liver resection indication, as the liver is the site for gastrointestinal malignancies to spread via hematogenic portal drainage. Thereof most frequently found are colorectal liver metastases (CRLM). For patients having one to three liver metastases, surgical excision is the desired therapy. Also systematic reviews and meta-analysis have shown favorable short-term outcomes after laparoscopic liver surgery for CRLM[27].

Other malignant findings that can indicate LLR are cholangiocarcinomas (CCA) (intra- and perihilar) or gallbladder carcinomas. Initial reservations with applying LLR in CCA were due to its complexity regarding bile duct reconstruction and lymphadenectomy that held back broader acceptance[28]. Recent meta-analysis demonstrated that LLR for intrahepatic CCA appears to provide short-term benefits without negatively affecting oncologic adequacy regarding microscopically tumor-free margins and tumor recurrence[29,30].

The high number of different and complex liver entities that can nowadays be treated minimally invasive resembles the global attitude that LLRs are not reserved for selected tumor entities.

4.3. LLR in liver transplantation

Regarding liver transplantation, while full left or right laparoscopic donor hepatectomy is performed rarely and still remaining developmental, laparoscopic left lateral donor hepatectomy from adult to child is achieving broader acceptance[31]. The significance of major liver resection in living donor living transplantation still needs further clarification[32].

5. Technical supplement

The implementation of the laparoscopic approach in the field of liver surgery was only possible by technical innovations and strategic modifications of open surgery.
LLRs are commonly known as quite challenging procedures that demand expertise in liver surgery as well as plenty experience in laparoscopy. Accomplishing LLR requires the surgeon an acquisition of new skills to ensure safe and efficient performance[33]. D. Cherqui states, that "complex dissection and suturing techniques must be combined with mastery of various novel technologies, including enhanced video equipment, laparoscopic ultrasonography, energy devices, laparoscopic ultrasonic aspirators and staplers"[14].
Intraoperative ultrasonography (IOUS) is frequently used. With its sensitivity comparable to CT or MRT, it improves resectability by being able to visualize hepatic lesions <1 cm[34] thus having enormous impact on surgical decision-making. IOUS allows a superior tumor clearance, helps sparing of functional liver tissue and enables anatomical resections and precise vessel mapping by color dopplering[35].

Special laparoscopic instruments comprise the Cavitron Ultrasonic Surgical Aspirator (CUSA), which provides selective fragmentation and aspiration of collagen-sparse tissue as the liver parenchyma, while blood vessels and bile ducts remain safe.
Ultrasonic shear can effectively seal small vessels and bile ducts with minimal fogging of the camera lens. Compared to conventional electrocautery, it rarely sticks to the liver parenchyma and has only limited heat and smoke generation. It is used for tissue dissection, coagulation, and preparation.

Novel intraoperative visualization techniques like hyperspectral imaging[36] (HSI) and indocyanine green (ICG) staining increases todays laparoscopic capabilities. ICG can be used directly for intraoperative tumor demarcation or as an counter perfusion for anatomic resections as visualization method and can guide difficult parenchymal dissecctioning[20]. HSI is applied to identify the exact resection planes for anatomic liver resection based on the optically determined perfusion and oxygenation status of liver segments, thereby being "non- contact, non-ionizing and non-invasive"[36].
3D-laparoscopy represents another example of supportive visual techniques. Research on the application of virtual realities is progressing[37].
Another maturing area in liver surgery is the robotic-assisted surgery. This technique is still in its infancy and first experience does not yet allow final evaluation[38].

Applying Pneumoperitoneum, the insufflation pressure should be adjusted as low as possible (<10 mmHg) to reduce danger of air embolism. For gasless laparoscopy, as mentioned earlier, alternatively abdominal-wall-lifting with special devices can be considered. Anesthesiological monitoring the endexpiratory CO_2-level is important because of gas diffusion into pulmonary tissue. In high-risk patients a pulmonary artery catheter can be useful. Also hemodynamic parameters should be recorded before applying CO_2 insufflation, as well as recording time of cross clamping the hepatic pedicles[39].

5.1 Hybrid and hand-assisted techniques

Hybrid and hand-assisted techniques (HALS) allow a semi-laparoscopic approach and enable even challenging and more complex resections that would otherwise not be possible to

conduct. These techniques are in particular useful in the learning curve and represent valid alternative to a full laparoscopic surgery in regard to postoperative outcomes.[40]
The insertion of a handport can be associated with higher incidence of hernias, still the postoperative outcome does not seem to be negatively affected compared with fully laparoscopic treatment[41].

6. Classification systems

The need for organizing LLRs into classification systems is justified by the fact that there exist no consistent applicable tools that can help to categorize different kinds and extends of LLRs uniformly.
To provide a universal terminology the Brisbane 2000 nomenclature was introduced in liver surgery, depending on the amount of liver segments resected [42]. In our study we applied this nomenclature to divide all cases in minor and major hepatic resections.

6.1 Difficulty Scoring

The grading of difficulty degrees is needed for LLR as expansion from minor to major and complex hepatectomies is happening. It can serve as a guiding stepping up to more advancing LLR procedures. Ban et al. developed a difficulty scoring index that assesses tumor location, extent of resection, tumor size, proximity to major vessels and liver function[43], so the difficulty level can be determined universally. However, a validation of this scoring system needs to be carried out.
As complex LLR procedures gain more popularity, especially in high-volume hepatobiliary centers such as the University hospital in Leipzig, the demand for classifying major hepatectomy is rising. Di Fabio et al. distinguished major hepatectomies according to the Louisville statement[44] in laparoscopic traditional major hepatectomy (LTMH) (include: hemi-, and trisectorectomies) and laparoscopic posterosuperior major hepatectomy (include segments 4a, 7 and 8)[16].
Both rankings were applied on all LLR-cases in our study.

6.2 Clavien-Dindo Classification

For quality assessment in aspect to postoperative surgical complications, we used the Clavien-Dindo Classification in our study. It "represents a compelling tool for quality assessment in surgery in all parts of the world"[45] and is used for morbidity assessment with grading I (=any deviation from normal course) to V (=death). Occuring postoperative complications in LLR were impairment of wound healing, infectious/inflammatory processes, abscess formation at the resection margin and bile leakage with biliom formation.

7 Limitations in LLR

Although the laparoscopic technique is on the rise, compromises regarding intraoperative safety and adherence to oncological principles remains inacceptable. Therefore, the decision whether to operate in a laparoscopic manner or rather conventionally open should be based on the own learning curve, personal experiences and weighed against the benefit for patients outcome. Limitations of minimally invasive liver surgery need to be taken in consideration.

Patients that underwent prior open surgery may have extensive abdominal adhesions, that can be a limiting factor for the laparoscopic approach, especially when evident in the upper abdomen[46].

Concerning tumor size, tumors larger than 3 cm are classified with an increase in difficulty[47]. These giant tumors in particular are very challenging to operate on, where technically feasibility cannot always be achieved. Placing trocars, mobilization of liver tissue, longer operation times or incidental tumor perforation are risks that come along. Similar limitations can be found with multiple liver metastases, that might be extremely technically challenging and time consuming.

Resection of tumor lesion in the posterosuperior segments of the liver, 7 and 8, classified as technically major, often represent limitations. LLRs in this region should be reserved for most experienced laparoscopic liver surgeons, who can safely master possible complications and handle upcoming bleedings. That also applies to biliary reconstruction, perihilar lymphadenectomy and trisectorectomies with hepaticojejunostomies, which are considered technically possible but limited for highly specialized liver surgery centers.

Compromises in favor of the laparoscopic technique should always be viewed critically and early conversion in case of suboptimal settings should be preferred.

8 Aims of the study

Even though LLR has gained solid acceptance in liver surgery in recent years, it is still in a maturing process. Consent guidelines are developing and keep being updated and adapted constantly while also the amount of published series is increasing. As the hepatobiliary surgical team of the University hospital of Leipzig was one of the first to adapt to the laparoscopic approach, a support to the development of LLR is made by analyzing our surgical data, publish the progress and draw a learning curve. With increasing experience and capability, more complex LLRs with beneficial outcome were achieved on a regular basis today. In contribution to further progression in LLR, the aim of our study was to evaluate the peri- and short-term postoperative outcomes of our patients requiring liver resection for benign and malignant lesions. We wanted to rule out the conventional concerns about LLR, even in complex cases, and emphasize the laparoscopic approach as a safe treatment of choice compared with open procedures. However, if laparoscopic surgery is capable to replace open surgical procedures needs further investigation. Despite high numbers of complex liver resections, that commonly entail open liver resection, we showed that by laparoscopic handling and the necessary surgical skills you can accomplish excellent surgical outcomes, low morbidity and mortality rates.

Publikation

Titel:	**Analysis of open and laparoscopic liver resections in a German high-volume liver tumor center**
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Journal:	Laparoscopic Surgery
ISSN:	2616-4221
Begutachtung:	peer-reviewed
Publikationsdatum:	25.01.2021
DOI:	10.21037/ls-20-93
Literaturangaben:	49
Sprache:	Englisch

Analysis of open and laparoscopic liver resections in a German high-volume liver tumor center

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Background: Minimally invasive treatment modalities of liver tumors remain a matter of development. This study aims to compare the surgical results and postoperative outcomes of consecutive laparoscopic liver resections (LLR) and open liver resections (OLR) in a German Liver Tumor Center.

Methods: A retrospective data analysis of consecutive patients undergoing LLR and OLR was performed.

Results: A total of n=217 patients were included in the study. Mean patient age was 62±13 years. Forty-three percent (n=93) were treated by minimally invasive surgery. Seventy-seven percent (n=166) of patients were operated for malignant disease and 28% (n=61) had at least one previous upper abdominal surgical intervention. Within the LLR group 61% (n=57) patients received an oncologic tumor resection. With 32% (n=30) hepatocellular carcinoma (HCC) represented the main indication for oncologic LLR, followed by Colorectal Carcinoma Liver Metastases (CRLM) with 13% (n=12) and Cholangiocarcinoma (CCA) with 4% (n=4). Major morbidity (> Clavien Dindo 3b) was 11% (n=23). Morbidity was especially low in the LLR group 5% (n=5) when compared to the OLR 15% (n=18) group. Likewise, overall mortality 6% (n=13) was very low in the LLR group 1% (n=1) when compared to OLR: 10% (n=12) group. In line, mean overall hospital stay was short (14±13 days). With regard to surgical technique, R0 resection in LLR was achieved in 97% (n=90) when compared to OLR 86% (n=107). Overall R0 resection rate was 91% (n=197).

Conclusions: The incidence of complex LLR in our cohort is high. LLR is the preferred surgical strategy for HCC treatment. Satisfactory R0 resection rates, morbidity and mortality rates can be achieved in a high-volume liver tumor center, especially with the application of recently introduced minimally invasive treatment modalities.

Keywords: Open liver resection (OLR); laparoscopic liver resection (LLR); hepatocellular carcinoma (HCC); Colorectal Carcinoma Liver Metastases (CRLM)

Received: 18 May 2020; Accepted: 30 September 2020.

doi: 10.21037/ls-20-93

View this article at: http://dx.doi.org/10.21037/ls-20-93

Introduction

Minimally invasive liver surgery is a maturing field (1). Since the initial report in 1992 by Gagner *et al.* (2) the incidence of laparoscopic liver resections (LLR) has increased exponentially (3). Initial concerns with regard to oncological inferiority and technical inapplicability have been scientifically disproved and even outplayed by reduced morbidity, and mortality in selected groups of patients (4).

"First movers" in this novel field of minimally invasive liver surgery comprised groups in Asia, the United States and Europe. Consensus guidelines have been established (5) and constantly updated (6) and adapted to anticipated new challenges (7). Today, difficulty scoring methodologies help to estimate and rank the complexity of a minimally invasive liver resection (8). However, open and minimally invasive resections cannot be compared one to one. In contrast to open procedures, which are graded in major and minor, depending on the amount of liver segments resected (according to the Brisbane 2000 terminology) (9), minimally invasive resections of posterosuperior segments, which are difficult to access with conventional laparoscopic instruments, justify for a "technical major" designation (10), which would be classified as minor according to the conventional open surgical terminology.

In recent years there has been a significant increase in the number of series published on LLR, that include single center series. In Germany, our team was among the first to adapt to laparoscopic liver surgery. Initially we shared the opinion that LLR was ideally suited for the resection of Hepatocellular carcinoma (HCC) in patients with cirrhosis (11,12). With an increase in experience and the implementation of open surgical strategies into the minimally invasive liver surgical world, more complex procedures were accomplished to the patients benefits owing to our increasing capability (13). Among other things, this included the implementation of novel intraoperative visualization techniques like hyperspectral imaging (14) and indocyanine green (ICG) staining (15,16). Today laparoscopic hemi-hepatectomies are performed on a regular basis for both malignant and benign indications and even extended resections for perihilar cholangiocarcinoma (pCCA) requiring biliary reconstruction are commonly addressed laparoscopically in specialized liver tumor centers (17). In this study, we aimed to analyze perioperative and short-term postoperative outcomes of our patients requiring liver resection for benign and malignant disease. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/ls-20-93).

Methods

Our prospectively maintained Liver Tumor Center database for patients undergoing liver resection was analyzed for the years 2018 and 2019. This study was conducted in congruence with the Declaration of Helsinki (as revised in 2013) and was approved by the ethics committee of the University Clinic of Leipzig (Ref. #: 142/18-ek). Because of the retrospective nature of the research, the requirement for informed consent was waived. The primary outcome measure was short-term surgical outcome. All liver resections were performed or assisted by the same two surgeons.

Before surgery, each case was reviewed in a multidisciplinary tumor-board meeting. In principle every patient was primarily evaluated for LLR. This included patients with resectable liver disease, independent of the liver segment affected, and sufficient functional parenchyma and liver function, which was measured by CT volumetry and the LiMAx test (18). Patients with tumor disease of the liver hilus, involving central vascular structures requiring vascular reconstruction during resection, and patients receiving portal vein embolization for liver augmentation, were not considered for LLR at that time.

Patient demographics, pathologic diagnosis, radiologic findings, and peri- and intraoperative surgical data were reviewed. The extent of OLR was graded according to the Brisbane 2000 terminology of liver anatomy and resections (9). LLRs were classified according to both the Asian (8,19) and European (10) difficulty scoring systems. The Clavien-Dindo classification was used for morbidity assessment, and major morbidity was defined as being Clavien Dindo 3b or greater (20).

Surgical technique

Open liver resections (OLR) were performed as described earlier by our group (14,21,22). For laparoscopic resections we preferred a supine patient position with split legs, with the surgeon standing between the legs and the assistant on the left side of the patient. Intraoperative ICG counter perfusion staining was utilized in anatomic liver resections following inflow control and direct ICG tumor staining was employed for intraoperative tumor demarcation of HCC, CCA and CRLM (15). If appropriate, a laparoscopic liver hanging maneuver was utilized for extensive resections to reduce bleeding during the parenchymal phase and furthermore simplify the procedure (13). A tourniquet around the hepatoduodenal ligament was always placed prior to resection, to facilitate a Pringle Maneuver in case of bleeding.

Special laparoscopic instruments comprised ultrasonic shears (Harmonic, Ethicon®) a laparoscopic CUSA (Caviton Ultrasonic Surgical Aspirator), and bipolar forceps.

Table 1 Demographic data and pathologic diagnosis

Variables	LLR (n=98, 42%)	OLR (n=133, 58%)	Total (n=231)	P values
Demographics				
Mean age at operation in years (SD)	59 (14.3)	65 (11.8)	62 [13]	0.002
	Range 24–68	Range 22–85		
Sex-ratio, female/male (%)	45/53 (45.9/54.1)	53/80 (39.9/60.1)		
Pathologic diagnosis				
Malignant	61 (62.2)	118 (88.7)	179 (77.5)	
Colorectal carcinoma liver metastases, n (%)	13 (13.3)	43 (32.3)	56 (24.2)	
Recurrent, n (%)	0	7 (16.3)	7 (12.5)	
Hepatocellular carcinoma, n (%)	31 (31.6)	18 (13.5)	49 (21.2)	
Recurrent, n (%)	2 (6.5)	7 (38.9)	9 (18.4)	
Cholangiocarcinoma, n (%)	5 (5.1)	46 (34.6)	51 (22.0)	
Intrahepatic cholangiocarcinoma, n (%)	4 (80.0)	19 (41.3)	23 (45.1)	
Intrahepatic cholangiocarcinoma recurrent, n (%)	0	4 (8.7)	4 (7.8)	
Perihiliary cholangiocarcinoma, n (%)	1 (20.0)	19 (41.3)	20 (39.2)	
Extrahepatic cholangiocarcinoma, n (%)	0	1 (2.2)	1 (2.0)	
Gallbladder carcinoma, n (%)	0	3 (6.5)	3 (5.9)	
Benign	37 (37.8)	15 (11.3)	52 (22.5)	
Hemangioma, n (%)	8 (8.2)	3 (2.3)	11 (4.8)	
Focal nodular hyperplasia, n (%)	9 (9.2)	0	9 (3.9)	
Liver adenoma, n (%)	7 (7.1)	1 (0.8)	8 (3.5)	
Previous surgeries, n (%)	31 (31.6)	72 (54.1)	103 (44.6)	

Laparoscopic ultrasound was performed for intraoperative tumor visualization and vascular anatomy mapping in every case. All patients undergoing OLR and LLR received overnight intensive care and were discharged to normal care earliest on postoperative day one.

Statistical analysis

Data was collected retrospectively and a database of previously determined variables was generated. A *t*-test was used to determine statistical significance. A P value <0.05 was considered as statistically relevant. Statistical analyses were performed using Microsoft excel 2018.

Results

In the time period investigated, a total number of n=231 patients received a liver resection in our institution. An early termination of the operation without resection was necessary in n=14 (7%) of cases due to histologically confirmed peritoneal metastasis which was not detected in the staging CT or MRI and therefore subsequently excluded from the final study population (n=217). Patient demographics and most frequent pathologic diagnoses are displayed in *Table 1*.

In short, n=124 (57%) patients received OLR and n=93 (43%) was operated with a minimally invasive approach (LLR). From all minimally invasive treated patients, n=73 (79%) received a totally laparoscopic operation and n=15 (16%) patients were operated in a laparoscopic-hand-assisted manner. This exclusively applied to resections of the posterosuperior segments 7, 8 and 4a. In n=5 cases (5%) a conversion to open surgery was necessary due to laparoscopic hand-assisted inaccessibility n=4 (80%), or

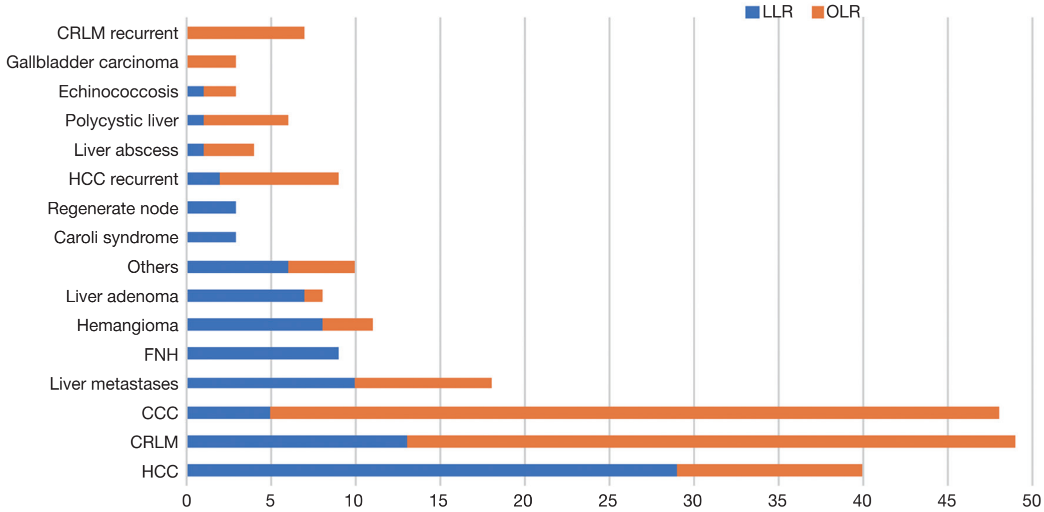


Figure 1 Distribution of LLR and OLR with regard to diagnosis: LLR for HCC n=28 (30.1%), CRLM n=12 (12.9%), Liver metastases n=9 (9.7%), FNH n=9 (9.7%), Hemangioma n=8 (8.6%), Liver adenoma n=7 (7.5%), Others n=6 (6.5%), CCA n= 4 (4.3%), Caroli-syndrome n=3 (3.2%), Regenerate node n=2 (2.2%), HCC recurrent n=2 (2.2%), Liver abscess n=1 (1.1%), Polycystic liver n=1 (1.1%), Echinococcosis n=1 (1.1%). OLR for CCA n=36 (29%), CRLM n=35 (28.2%), HCC n=11 (8.9%), Liver metastases n=8 (6.5%), HCC recurrent n=7 (5.6%), CRLM recurrent n=7 (5.6%), Polycystic liver n=5 (4%), Hemangioma n=3 (2.4%), Others n=4 (3.2%), Gallbladder carcinoma n=2 (1.6%), Liver abscess n=3 (2.4%), Echinococcosis n=2 (1.6%), Liver adenoma n=1 (0.8%).

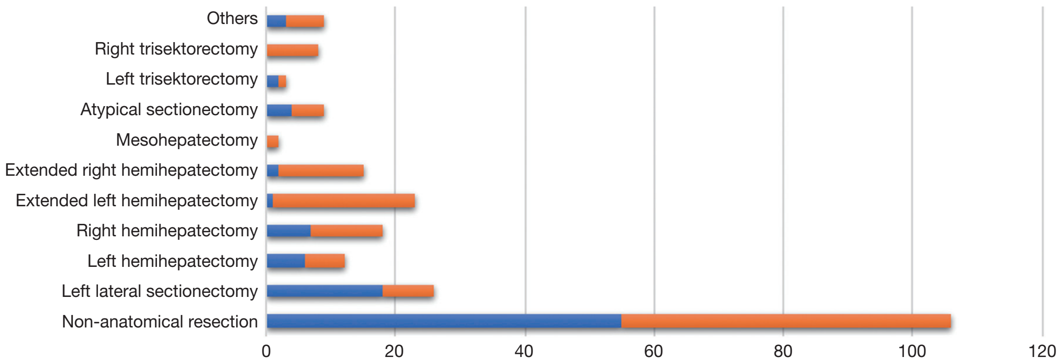
tumor infiltration into other organs (diaphragm, inferior vena cava) in combination with morbid obesity [n=1, (20%)].

Mean patient age was significantly higher in the OLR group (65±12 years), when compared to the LLR group (LLR: 59±14 years; P=0.002), and the sex ratio (female/male) was in favor of men, in both groups [OLR: f:m=54% (n=51):59% (n=73) *vs.* LLR: f:m=41% (n=43):46% (n=50)], respectively.

A total number of n=166 patients (77%) were operated for malignant disease and n=51 patients (24%) were operated for benign indications. This larger number of oncologic operations remained valid for both open [OLR for malignant indication: n=109 (88%) *vs.* OLR for benign indications: n=15 (12%)] and laparoscopic resections [LLR for malignant indication: n=57 (61%) *vs.* LLR for benign indications: n=36 (39%)].

Patients with Cholangiocarcinoma (CCA) and Colorectal Liver Metastases (CRLM) were predominantly treated by OLR [OLR for CCA: n=42 (34%) *vs.* LLR for CCA: n=4 (4%) and OLR for CRLM: n=42 (34%) *vs.* LLR for CRLM: n=12 (13%)], whereas patients with HCC to a greater extent received a LLR [LLR for HCC: n=30 (32%) *vs.* OLR for HCC: n=18 (15%)]. The three major benign indications for liver resection comprised: giant hemangioma [n=11 (5%)], symptomatic focal nodular hyperplasia (FNH) [n=9 (4%)] and liver adenoma [n=8 (4%)]. A total number of n=61 (28%) of patients had previous upper abdominal surgery [OLR with prior abdominal surgery n=45 (36%) and LLR with prior abdominal surgery n=16 (19%)]. This included previous liver resections [n=31 (14%)], cholecystectomies [n=20 (9%)], gastric resections [n=7 (3%)], splenectomies [n=2 (1%)] and prior liver transplantation [n=1 (1%)] etc. A detailed distribution of OLR and LLR with regard to the underlying diagnosis is displayed in *Figure 1*.

With regard to the extent of liver surgery, non-anatomical resections [n=101 (47%)] were the most frequent operations in our cohort with n=51 (55%) performed by LLR, and n=50 (40%) performed by OLR. With a total of n=28 (13%) anatomic right and left hemihepatectomies were the second most common surgical procedures, both commonly performed by LLR [left hemihepatectomy LLR: n=6 (7%), *vs.* left hemihepatectomc OLR: n=6 (5%) and right hemihepatectomy LLR: n=7 (8%), *vs.* right hemihepatectomc OLR: n=9 (7%)]. Left lateral (Segment 1 and 2) resections n=26 (12%), were the third most common resections in our cohort, predominantly performed by LLR [left lateral LLR: n=18 (19%) *vs.* left lateral OLR: n=8 (7%)]. In n=33 (15%) cases an extended resection was necessary,



	Non-anatomical resections	Left lateral sectionectomy	Left hemihepatectomy	Right hemihepatectomy	Extended left hemihepatectomy
LRR	55	18	6	7	1
OLR	51	18	6	11	22

	Extended right hemihepatectomy	Mesohepatectomy	Atypical sectionectomy	Left trisektorectomy	Right trisektorectomy	Others
LRR	2	0	4	2	0	3
OLR	13	2	5	1	8	6

Figure 2 Type of liver resections: LLR: non-anatomical resections n=51 (54.8%), left lateral sectionectomy n=18 (19.4%), left hemihepatectomy n=6 (6.5%), right hemihepatectomy n=7 (7.5%), extended left hemiheptaectomy n=1 (1.1%), extended right hemiheptaectomy n=2 (2.2%), atypical sectionectomy n=4 (4.3%), left trisektorectomy n=2 (2.2%), Others n=3 (3.2%). OLR: non-anatomical resections n=50 (40.3%), left lateral sectionectomy n=8 (6.5%), left hemihepatectomy n=6 (4.8%), right hemihepatectomy n=9 (7.3%), extended left hemiheptaectomy n=18 (14.5%), extended right hemiheptaectomy n=12 (9.7%), Mesohepatectomy n=2 (1.6%), atypical sectionectomy n=4 (3.2%), left trisektorectomy n=1 (0.8%), right trisektorectomy n=8 (6.5%), others n=6 (4.8%).

which was predominantly performed by OLR [LLR: n=3 (3%), OLR: n=30 (24%)]. Two out of 11 trisectionectomies were performed by LLR [Trisectionectomy LLR: 2 (2%) *vs.* Trisectionectomy OLR: 9 (7%)]. Two mesohepatectomies (2%) were performed by open surgery. Laparoscopic lymphadenectomy was performed in patients with CCC and one patient with HCC. A detailed description of types of liver resections performed is given in *Figure 2*.

Surgical data

The mean operative time was longer for OLR with 341 min (range, 141–556 min) when compared to LLR [273 min (range, 44–590 min), (P<0.001)] and intraoperative blood transfusions were necessary in n=7 (3%) cases [intraoperative transfusion LLR: n=3 (3%) *vs.* intraoperative transfusion OLR: n=4 (3%)]. Mean length of hospital stay was 14±13 days (LLR: 9±6 *vs.* OLR: 18±15 days; P<0.001). Abdominal drains were placed in 41% (n=88) of cases [abdominal drain LLR: n=21 (22%) *vs.* abdominal drain OLR n=67 (54%)]. Intraoperative biliary drainages [n=102 (47%)] were predominantly placed in OLR cases [n=95 (77%)] when compared to LLR cases [n=7 (8%)]. Radical Lymphadenectomy was performed in n=74 cases (34%); [radical lymphadenectomy LLR: n=6 (7%) *vs.* radical lymphadenectomy OLR: n=68 (55%)]. R0 resection was achieved in n=197 (91%) of cases [R0 resection LLR: n=90 (98%) *vs.* R0 resection OLR: n=107 (86%)]. R0 resection rates were highest for CRLM resections [LLR: n=12 (100%) *vs.* OLR: n=38 (91%)] followed by HCC resections [LLR: n=27 (90%) *vs.* OLR: n=16 (89%)] and CCA resections [LLR: n=3 (75%) *vs.* OLR: n=31 (74%)]. A detailed description of surgical results is provided in *Table 2*.

Difficulty scoring and morbidity and mortality outcome

A detailed description of classifications and difficulty scoring of liver resections and complications after liver resection for our patient group is given in *Table 3*. In short, according to the Brisbane 2000 terminology of liver anatomy and

Table 2 Surgical data and results

Variables	LLR (n=98)	OLR (n=133)	Total (n=231)	P values
Mean length of hospital stays in days (SD)	8.3 (7.1)	17.4 (15.0)	13.4 (12.9)	<0.0001
Mean operative time in minutes (range)	266 [44–590]	329 [141–556]	302	<0.0001
Received blood transfusion, n (%)	3 (3.1)	4 (3.0)	7 (3.0)	
Drainage				
Intraabdominal drainage, n (%)	22 (22.4)	72 (54.1)	94 (40.7)	
T-drainage, n (%)	7 (7.1)	95 (71.4)	102 (44.2)	
Lymphadenectomy, n (%)	6 (6.1)	72 (54.1)	78 (33.8)	
R0 resections, n (%)	91 (92.9)	107 (80.5)	198 (85.7)	
Colorectal carcinoma liver metastases, n (%)	12 (92.3)	38 (88.4)	50 (89.3)	
Hepatocelullar carcinoma, n (%)	27 (87.1)	16 (88.9)	43 (87.8)	
Cholangiocarcinoma, n (%)	4 (80.0)	31 (67.4)	35 (68.6)	

Table 3 Scoring system and postoperative outcome

Variables	LLR (n=98)	OLR (n=133)	Total (n=231)	P values
Scoring system				
Di Fabio *et al.* major hepatectomy (%)	38 (38.8)			
LTMH (%)	17 (44.7)			
LPMH (%)	21 (55.3)			
Ban *et al.*			11 (11.2)	
Low [1–3]	1 (n=3), 2 (n=0), 3 (n=8)			
Intermediate [4–6]	4 (n=22), 5 (n=3), 6 (n=18)		43 (43.9)	
High [7–10]	7 (n=21), 8 (n=2), 9 (n=14), 10 (n=7)		44 (44.9)	
Brisbane 2000 major (%)		72 (54.1)		
Minor (%)		61 (45.9)		
Clavien-Dindo no complication	68 (96.4)	47 (35.3)	115 (49.8)	
I	12 (12.2)	20 (15.0)	32 (13.9)	
II	6 (6.1)	20 (15.0)	26 (11.3)	
IIIa	6 (6.1)	15 (11.3)	21 (9.1)	
IIIb	4 (4.1)	13 (9.8)	17 (7.4)	
IVa	1 (1.0)	6 (4.5)	7 (3.0)	
IVb	0	0	0	
V	1 (1.0)	12 (9.0)	13 (5.6)	
Morbidity, n (%)	5 (5.1)	19 (14.3)	24 (10.4)	
Mortality, n (%)	1 (1.0)	12 (9.0)	13 (5.6)	

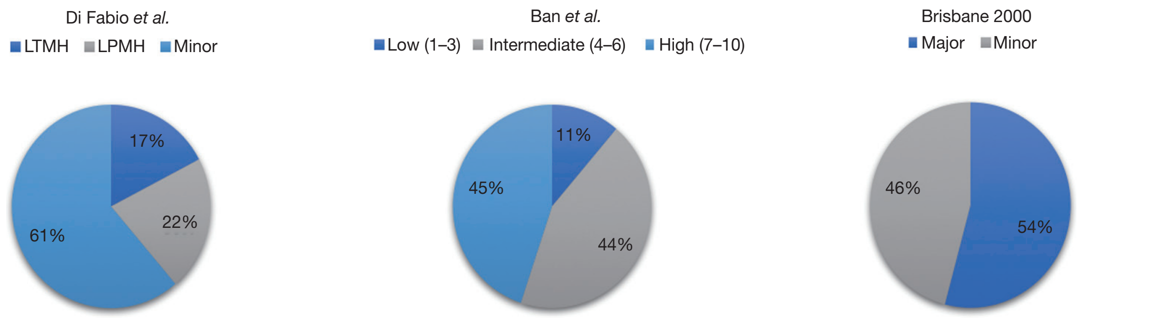


Figure 3 Overview of difficulty scoring and Brisbane 2000 classifications of liver resections: Di Fabio *et al.*: the laparoscopic group got classified based on major hepatectomy in n=16 (17%) LTMH and n=20 (21%) LPMH. Ban *et al.*: the laparoscopic group got classified according to difficulty in n=7 (8%) low difficulty, n=42 (45%) intermediate and n=44 (47%) high. Brisbane 2000: the open group got divided in n=64 (52%) major and n=60 (48%) minor resections.

resections, n=64 (52%) patients were treated by major and n=60 (48%) by minor resections.

According to Di Fabio *et al.* out of n=93 LLRs, n=36 (39%) was classified as laparoscopic major hepatectomies comprising n=16 (44%) traditional major laparoscopic hepatectomies (LTMH) and n=20 (56%) laparoscopic posterosuperior major hepatectomies (LPMH), which were technically challenging as they are considered difficult to approach using straight laparoscopic instruments.

According to Ban *et al.* out of the n=93 minimally invasive operated LLRs, n=7 (8%) was of low, n=42 (45%) was of intermediate and n=44 (47%) was of high difficulty, with regard to performance (*Figure 3*).

Major morbidity, defined as Clavien Dindo 3b or greater was 11% (n=23). Patients with LLR had a significantly lower morbidity [morbidity rate LLR: n=5 (5%)] when compared to the OLR group [morbidity rate OLR: n=18 (15%)]. Likewise, overall in-hospital mortality n=13 (6%) was very low in the LLR group [in hospital mortality LLR: n=1 (1%)] when compared to OLR group [in hospital mortality OLR: n=12 (10%)].

Discussion

Our data demonstrate that despite high numbers of complex liver resections, morbidity and mortality rates were low in our analyzed patient group. The fact that a fraction of more than 42% of all liver resections were performed minimally invasive in the years 2018 and 2019, furthermore reflects our key of propelling minimal invasive surgical techniques for the liver.

The majority (77%) of our patients received an oncologic resection. This was true for both OLR and LLR and resembles the global attitude that minimally invasive techniques are not reserved for selected tumor entities. However, in parallel we would like to strike that the indication for a liver resection must not be loosened especially for benign indications just because of minimal invasive accessibility (23).

Patients with HCC in cirrhosis accounted for the major part of LLRs in our collective. Analysis of the literature confirms that minor liver resections for HCC even in cirrhotic livers should be the approach of first choice (24). This might especially be true for lesions less than 5 cm in diameter (25). A recent propensity score matched analysis demonstrated that in terms of oncologic outcome and surgical outcome, a selected group of patients even might benefit from major LLR for HCC in cirrhosis (26). Decades ago, it has been shown that liver resection prior to transplantation did not increase the morbidity or impair long-term survival following liver transplantation (27). Recent work indicated that salvage liver transplantation after laparoscopic resection for HCC was even more feasible and save, achieving excellent short-term results (28). A recent meta-analysis demonstrated that surgical resection also achieved a better overall-survival when compared to Trans Arterial Chemo Embolization (TACE) in patients with HCC. Therefor laparoscopic resections might be able to partially replace TACE as a bridging therapy to liver transplantation. However, it is clear that efficient bridging strategies for patients with HCC are even more important (29) especially in countries like Germany where waiting time for liver transplantation is long.

Few patients diagnosed with CCA received LLR in our cohort. In this patient collective a minimally invasive approach was predominantly considered for intrahepatic Cholangiocarcinomas (iCCA), which did not require extrahepatic bile duct resection. A recent meta-analysis confirmed that LLR for iCCA achieved excellent surgical outcomes and provided short-term benefits over OLR without negatively affecting oncologic adequacy in terms of R0 resections and disease recurrence (30). Our patient collective only comprised one case with perihilar Cholangiocarcinoma (pCCA) which required Roux – Y laparoscopic bile-duct reconstruction. Similar cases have been published as case reports recently (31). Surgical resection still represents the mainstay of pCCA treatment (32). However, if laparoscopic surgery is capable to replace our initially postulated open surgical resection strategy for pCCA (21) requires further investigations.

Radical lymphadenectomy is mandatory in patients with CCA. Recent data indicate that the laparoscopic technique does not compromise accuracy and outcome of nodal dissection (33,34). From a technical perspective, delicate vascular reconstruction after portal vein resection and biliary reconstruction, represents the "Achilles heel" of a pCCA resection. Performance of vascular and biliary reconstruction with laparoscopic instruments is even more challenging. To overcome the hurdle of restricted visibility and maneuverability we recently introduced a parachute suturing technique for biliary reconstruction in patients receiving a laparoscopic pCCA resection (35). This technique provided a superior view on the anastomosis and facilitated an unrestrained completion of the anastomosis. Although robotic surgery is supposed to deliver substantial benefits over laparoscopic surgery especially when it comes to delicate vascular reconstruction, first data do not support its continued practice on pCCA cases until significant technical and instrumental refinements become available (36).

The liver is the most common site of metastasis in patients with colorectal cancer. In Europe the overall liver metastasis rate from colorectal cancer has been reported to be up to 23% (37). Surgical resection is currently still the only curative treatment modality. The OSLO-COMET randomized controlled trial demonstrated that in patients undergoing parenchyma-sparing liver resection for colorectal metastases, laparoscopic surgery was associated with significantly less postoperative complications when compared to open surgery (38). Patients with CRLM represent the centerpiece of our study population. However, only a fraction of 13% was treated by LLR. High tumor load requiring future liver remnant augmentation strategies (39) were the main reason for the necessity of an OLR strategy. Up to 14% of CRLM may be synchronously detected (40). As described by other groups, in case of synchronous liver metastases, we favored a simultaneous laparoscopic resection (together) rolled into one with primary tumor resection. Provided that the extent of liver resection required was minor (41), including wedge resections, single segmentectomies or left lateral resections. In case of higher tumor loads chemotherapy was administered prior to major liver resection (42).

The basis of a curative liver resection is built on negative resection margins. Overall R0 resection rate was 91%. Our data show that LLR achieved better R0 resection rates than OLR, however this was not a case matched study, and a direct comparison is hence invalid. Nevertheless, our data demonstrate that at least the introduction of LLRs into our program did not impair R0 resection rates. The margin status remains a very important factor in hepatectomies independent of the tumor entity.

Benign liver tumors represent a challenge in clinical management and there is considerable controversy with respect to the indications for surgery as the evidence for surgical treatment is variable (43). Recent data indicate that patients with preoperative symptoms from adenoma and focal nodular hyperplasia (FNH) show a high rate of postoperative symptom relieve (44). From a global perspective, most initial minimally invasive liver resections were typically done for benign lesions in anterior or left lateral segments (45). In our patient group the majority of benign lesions was operated by LLR.

Difficulty scoring and correct taxonomy for liver resections is vital for the establishment and maintenance of an academic liver surgery program. It is not only key for the scientific evaluation of patient data and quality assessment but also helps trainees in their buildup of surgical skills. Especially in the field of minimally invasive surgery difficulty scoring is required to guide surgeons in advancing from simple to difficult resections. We applied the two most common difficulty scoring systems used in Asia and Europe to our patient cohort. Ban *et al.* provided a scoring system based on preoperative parameters which comprise the extent of liver resection, tumor location, tumor size, liver function, and tumor proximity to major vessels (8,19). Accordingly, difficulty of laparoscopic resections can be graded as low, intermediate and high. Di Fabio *et al.* highlighted the fact that liver resections of segments from the posterosuperior segments may be graded as technically major if performed laparoscopically due to the difficult laparoscopic accessibility of these segments. A recent landmark paper by Filmann *et al.* revealed that overall hospital mortality after liver resection is high in Germany (46). With an overall hospital mortality rate of 5.9% for our cohort we were able to achieve good results. Especially the low mortality rate of 1% in the LLR group confirms that our development of a minimally invasive liver resection program should be on the right track.

The learning curve in laparoscopic liver surgery consists of different phases in which hepatobiliary surgeons stepwise edge through more and more complex cases (47). We started our program with smaller resections of left lateral and anteromedial segments predominantly in patients with HCC in liver cirrhosis (12). Little by little we gained more confidence in doing anatomic hemihepatectomies and even extended liver resections (13). We share the opinion that major hepatectomies might have a learning curve of 45–60 cases (48). With a case load of 60–100 LLRs per year we are well aware that it takes time to accomplish individual goals. In our unit all laparoscopic resections were performed by the same surgical team. With an experience of more than 7 years we currently aim to establish a training program for fellows interested in minimally invasive liver surgery. In this context we share the opinion that inter-institutional collaboration and exchange of skills might enable a synergistic development of techniques for safe progression to more complex surgeries (49). The fact that we are still operating on a highly selected patient collective however makes a general comparison to open liver surgery cases difficult.

Acknowledgments

Funding: We acknowledge support from the German Research Foundation (DFG) and Leipzig University within the program of Open Access Publishing.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/ls-20-93

Data Sharing Statement: Available at http://dx.doi.org/10.21037/ls-20-93

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/ls-20-93). Robert Sucher serves as an unpaid editorial board member of *Laparoscopic Surgery*. The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in congruence with the Declaration of Helsinki (as revised in 2013) and was approved by the ethics committee of the University Clinic of Leipzig (Ref. #: 142/18-ek). Because of the retrospective nature of the research, the requirement for informed consent was waived.

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doi: 10.21037/ls-20-93
Cite this article as: Sucher R, Guice H, Recknagel S, Sucher E, Semmling K, Lederer A, Rademacher S, Scheuermann U, Seehofer D. Analysis of open and laparoscopic liver resections in a German high-volume liver tumor center. Laparosc Surg 2020.

Zusammenfassung der Arbeit

Dissertation zur Erlangung des akademischen Grades: Dr. med.

Titel: "Analysis of open and laparoscopic liver resections in a German high-volume liver tumor center"

eingereicht von Hanna Guice, geboren am 07.11.1993

angefertigt am Universitätsklinikum Leipzig in der Klinik und Poliklinik für Viszeral-, Transplantations-, Thorax- und Gefäßchirurgie Liebigstrasse 20, 04103 Leipzig

betreut von Privatdozent Dr. Robert Sucher

Einreichung im Juli 2021

In recent years laparoscopic liver surgery established itself into today's standard of care regarding surgical liver treatment. It was a long way for minimally invasive liver resection to develop and popularize as it was accompanied by initial reservations and concerns. Some of these already had been clarified while other questions still remain and require further investigation in the complex field of laparoscopic liver surgery.

Initial concerns with respect to oncological inferiority and technical inapplicability in contrast to open surgery treatment could have been disproved within the framework of retrospective studies. In contribution to that, the aim of the study was to compare the surgical results and postoperative outcomes of consecutive laparoscopic liver resections (LLR) and open liver resections (OLR) at the high-volume liver tumor center of Leipzig university hospital.

Since common classification systems for open liver surgery cannot be applied for LLR, the introduction of specific difficulty scoring systems for LLR helps to assess and classify the complexity of minimal invasive liver resection. With an increase in experience, modification of hybrid surgery and the application of novel visualization techniques such as indocyanine green (ICG) staining or hyperspectral imaging (HSI), more challenging procedures were accomplished, that initially would have been contraindicated for the laparoscopic approach

(e.g. perihilar cholangiocarcinoma (pCCA) requiring biliary reconstruction). During the years 2018 and 2019 42% of all liver resections were approached laparoscopically at the Leipzig University hospital.

A retrospective data analysis of n=231 patients undergoing LLR or OLR for the years 2018 and 2019 was performed and previously determined variables were collected. As a primary outcome measure, the short-term surgical and postoperative outcome of patients receiving LLR (=LLR group) compared to the patient cohort being treated by open resection (=OLR group) was evaluated. All liver resections were executed or assisted by the same two surgeons. Prior to surgery, every case was reviewed in a multidisciplinary tumor-board meeting and primarily assessed for possible minimal invasive approach. Analysis for patient demographics, pathologic diagnosis, radiologic findings and peri- and intraoperative surgical data was carried out. For LLRs intraoperatively, ICG counter perfusion staining was used in anatomic liver resection and direct ICG tumor staining was employed for tumor demarcation.
With respect to classification, the extent of OLR was graded according to the Brisbane 2000 terminology in minor and major resections, whereas LLRs were categorized by means of difficulty (in accordance with Ban et al. and Di Fabio et al.). For measurement of surgical complication and assessment of morbidity, the Clavien-Dindo classification was applied.

OLR was performed in n=124 (57%) and LLR in n=93 (43%). From all minimally invasive treated patients, 79% were operated totally laparoscopic and 16% were laparoscopic-hand-assisted due to infeasible lesions in the posterosuperior segments 7, 8 and 4a. In 5 cases a conversion to open surgery was necessary because of inaccessibility, tumor infiltration or morbid obesity. 28% of patients had previous upper abdominal surgery, whereof 36% in the OLR group and 19% in the LLR group.
Regarding patient demographics, the mean age was significantly higher in OLR and the sex ratio was in favor of men for both groups.
Malignant tumor lesions comprised 77%, while 24% were benign lesions. In both groups this larger number of malignant oncologic operation remained valid. The most common benign indications comprised focal nodular hyperplasia (FNH) and liver adenomas.

It was shown that patients with CCA and Colorectal liver metastases (CRLM) were predominantly treated by open surgery, while patients with HCC diagnosis received LLR to a greater extent.
Concerning the type of liver resection, non-anatomical resections were the most frequent in the cohort with 47%, thereof 55% LLR and 40% OLR. Followed second most by anatomic right and left hemihepatectomies and third most by left lateral resections, which were predominantly performed in laparoscopic technique. On the other hand, extended resections and trisectionectomies were predominantly operated by OLR. Radical lymphadenectomy was performed to a greater extent during OLR.
Results showed that the mean operative time was longer for OLR (341 minutes in median) compared to LLR (273 minutes in median). Also the mean length of hospital stay was shorter for LLR patients, as well as abdominal drains were placed to lesser extent in LLR compared to OLR. In regard to R0-resection, R0-rates were higher in LLR with 98% vs. 86% in OLR. Thereby being highest for CRLM resections, followed by HCC and CCA.
Putting all liver resections into classification systems, it was found that of all open procedures, 52% had major and 48% underwent minor resection according to Brisbane 2000. From the LLR group, in accordance with Di Fabio et al. 39% were classified as laparoscopic major hepatectomies, comprising 44% laparoscopic traditional major hepatectomies (LTMH) and 56% laparoscopic posterosuperior major hepatectomies (LPMH), which were technically challenging. The difficulty index stated by Ban et al. was classified as low for 8% of all performed LLRs, intermediate for 45% and of high difficulty in even 47%.
Relating to morbidity (=Clavien-Dindo 3b or greater), patients with LLR had significantly lower morbidity compared to OLR. The same applies for in-hospital mortality.

Our data show that despite the high number of complex and high-difficulty-classified liver resections that were performed, morbidity and mortality rates were low. As mentioned before, R0 resection rate in the LLR group was better than in the OLR group, however, this was not a case matched study, so a direct comparison is not valid. But still the study could demonstrate that the high number of LLRs being performed at the Leipzig University hospital, did not impair R0-resection rates. With an overall hospital mortality rate of 5.9% in the cohort, good results were achieved. Particularly the low rate of 1% in the LLR group speaks for itself and confirms that the development of a minimal invasive liver resection program should be on the right track.

The majority of patients in the LLR and OLR group received an oncologic resection, what also resembles the global attitude that minimally invasive techniques are not reserved for selected tumor entities. Still it should be emphasized, the indication for a liver resection should not be loosened just due to minimal invasive accessibility, especially in benign liver lesions. Nevertheless, in the study the majority of benign lesions was operated by LLR.

A few patients diagnosed with CCA received LLR. Thereof predominantly iCCA cases were indicated for a minimal invasive approach without biliary duct reconstruction and satisfying short-term outcomes over OLR could be obtained. However, only one case of pCCA which required Roux-Y bile duct reconstruction was treated with LLR in the study group, so if laparoscopic surgery is capable to replace the open approach in terms of treatment strategies for pCCA remains questionable.

Patients with CRLM represent the centerpiece of our study population, still only 13% received LLR. The main reason of applying OLR was the high tumor load requiring future liver remnant augmentation strategies. As liver resection is confirmed to be the approach of choice for patients with HCC in cirrhosis, it is not surprising that HCC diagnosis accounted for the major part of LLRS in our collective.

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Darstellung des eigenen Beitrags

Erklärung über den Eigenanteil meiner Dissertationsschrift ***„Analysis of open and laparoscopic liver resections in a German high-volume liver tumor center"***, gemäß der Promotionsordnung der Medizinischen Fakultät Leipzig vom 5. Oktober 2017

Maßgebliche Beteiligung an folgenden Arbeitsschritten:

- Literaturrecherche
- Datenerhebung und -aufbereitung
- Datenauswertung und -analyse
- Ergebnisinterpretation
- Teilnahme an der Methodenentwicklung und inhaltliche Konzeption
- Grafische Aufbereitung und Design (Grafiken, Tabellen)
- Teilnahme am Schreiben des Manuskripts, Manuskriptüberarbeitung
- Administrative Unterstützung
- Erstellung des Manuskripts der Promotionsarbeit

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Hiermit versichere ich als Koautor, dass die Promovendin Hanna Guice den wesentlichen Beitrag zur Erstellung und Veröffentlichung der oben genannten Publikation geleistet hat:

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Selbstständigkeitserklärung

<u>Erklärung über die eigenständige Abfassung der Arbeit</u>

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