



Research Article

Benefits of Laparoscopic Liver Resection-A Propensity Score Analysis

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Abstract

Background: The history of laparoscopic surgery portrays a success story of how symbiosis of technical advancements and surgical ingenuity has changed surgery fundamentally. The aim of the study was to investigate the surgical outcome of patients undergoing laparoscopic liver resection compared to open liver resection in a single academic center for hepatobiliary surgery. **Materials and Methods:** We retrospectively analysed patients from our in house database who underwent liver surgery for benign or malignant liver disease from 2000 to 2019. We identified 170 cases, which underwent minimally invasive liver resection and conducted a retrospective matched pair analysis using propensity scores. The final group contained 340 cases (148 female and 192 male, age range 18-86 years). To ensure comparability we carried out a nearest neighbour matching. Surgical statistics, complications, and length of hospital stay were evaluated. **Results:** Eventually 81 major (>3 Segments) and 259 minor resections were included. The extent of resection was equally distributed between the two matched groups ($p=0.703$). We performed more atypical laparoscopic resections than anatomical ($p=0.038$). The conventional approach showed significantly longer operation times ($p<0.001$) and a longer length of hospital stay ($p<0.001$). No difference was found in reported blood transfusions during surgery ($p=0.53$). Overall, complications were significantly more frequent in the open group ($p=0.04$), including bile leakage ($p=0.021$), surgical site infections ($p<0.001$) and postoperative acute kidney injury ($p<0.001$). 20 Patients (11.8%) in the laparoscopic group had to undergo conversion to a conventional approach. **Conclusion:** Laparoscopic surgery proved to be a safe and practical technique. Furthermore, we illustrated the development of indications for laparoscopic liver resections over a period of over ten years. With the data indicating a faster recovery of patients combined with current technical advancements of robotic engineering we see the advancement of laparoscopic surgery ensured.

Introduction

Today laparoscopic surgery is well established and partially replaced open surgery for different medical conditions, i.e. appendectomy or cholecystectomy. Initial concerns about feasibility and safety in general were proven wrong and also improvements of surgical outcomes are clearly displayed [1-3]. In general and visceral surgery several procedures have shown benefits using a minimally invasive approach, such as antireflux surgery [4], colorectal surgery [5,6], hernia repair [7], adrenal gland surgery [8], splenectomy [9,10], bariatric surgery [11] and hepatic cyst fenestration [12]. In the beginning of laparoscopic

liver surgery procedures were limited to cyst fenestration [13], biopsies or limited peripheral resections [14,15]. Owing to growing experience and aspiring intermediate results the portfolio then was expanded to the first laparoscopic anatomical liver resection which were left lateral resections [16,17] followed by left and right hepatectomies [18]. In addition to complete laparoscopic hepatic resection, Hand-Assisted Liver Resections (HALS) [19,20] and hybrid (laparoscopic assisted) liver resections [21] were carried out. Especially in pathologies located in segments 7 and 8 progress was much slower. Primary reservations concerning the feasibility of a laparoscopic approach to those segments have been eliminated in the later years mainly through advances in patient positioning

(semi-prone; left-lateral;) [22,23], altered trocar positioning (i.e. transdiaphragmatic, thoracoscopic approach) [24,25] and a general improvement of surgical skills in this field [26,27]. At present, the complete spectrum of hepatic surgery is offered laparoscopically in specialized, high-volume centers, including Associating Liver Partition with Portal vein Ligation for Staged hepatectomy (ALPPS) [28,29] or concomitant extrahepatic resections (i.e. bile duct resection, lymphadenectomy) [30].

Alongside, laparoscopic surgery had to prove its equality regarding postoperative morbidity, mortality, oncologic safety and other factors [31-34]. Moreover, several distinct benefits of laparoscopic liver surgery came into light. A shorter hospital stay and lower transfusion requirements being among them. Late reports even pointed out a reduced morbidity after laparoscopic liver resection [31,32,35,36]. Especially for elderly [37,38], obese [39,40] or cirrhotic [41,42] patients the laparoscopic approach could yield a better outcome. The aim of the study was to investigate the results of patients undergoing laparoscopic liver resection compared to open resection in a single academic center for hepatobiliary surgery.

Material and Methods

We retrospectively investigated patients of our inhouse database who underwent liver surgery for benign or malignant liver pathologies, dating from 2000 to 2019. We identified 170 cases which underwent minimal invasive liver resection and created a retrospective matched analysis using propensity scores. The final investigation contained 340 cases (148 female and 192 male age range 18-86 years). The propensity score analysis was matched by ASA classification, body mass index, history of liver cirrhosis, extend of resection and malignancy [43]. To ensure comparability we carried out a nearest neighbour matching. Laparoscopic reoperations were allowed as separate cases. In case of conversion or primarily open operations, laparoscopic reoperations were not introduced as separate cases. Cases that were converted to open operations were kept in the laparoscopic group under the intention to treat principle. Hepatic dysfunction was characterized as INR >1.5 and serum bilirubin $\geq 70 \mu\text{mol/l}$ [44,45]. History of renal impairment or preexisting elevated serum creatinine >1.2mg/dl (>105.6 $\mu\text{mol/l}$) were assessed preoperatively, as well as history of ascites preoperative. Postoperative Acute Kidney Injury (AKI) as defined in the KIDGO criteria: Increase of serum creatinine by 50 % within 1-7days after surgery or over 0.3mg/dl ($\geq 26.5 \mu\text{mol/l}$) within 48 hours or oliguria [46]. Furthermore, postoperative ascites was defined as prolonged fluid secretion and or need for forced diuresis. Surgical stats, non-surgical complications, and Length of Hospital Stay (LOHS) were calculated. All complications were

assessed and counted; multiple counts were allowed. Furthermore surgical complications were graded by the most severe using the Dindo classification [47]. All resections were performed by specially trained and qualified hepatobiliary surgeons who regularly perform open and laparoscopic liver resections.

Statistics

All calculations, tables and figures were created with IBM SPSS Statistics 27 (SPSS Inc., Chicago, IL, USA). Continuous variables are shown as median and interquartile range. Categorical variables were investigated with Fisher’s-exact-test and are shown as frequencies and percentages. Comparisons between both groups were performed using the Mann-Whitney U-test, the independent t-test for non-connected samples or the Chi-Q test, depending on the distribution and quality. The distribution was assessed using the Kolmogorov-Smirnov-test. Statistical significance was considered with $P < 0.05$.

Results

The established group of patients underwent surgery between 2000 and 2019 in the university hospital Freiburg, Germany (Table 1). Regarding to the preexisting conditions the laparoscopic group showed a significant higher number of diabetics [36(21.2%) LH vs. 20(11.8%) CH; $p=0.019$]. Whereas the conventional group showed higher numbers of renal impairment [5(2.9%) LH vs. 23(13.5%) CH; $p<0.001$] (Table 2).

	(n=340)
Sex f/m	148 /192 43.5% /56.5%
Age (years)	62.15 y, IQR 19.44y
BMI	26.30kg/m ² IQR 6.31
ASA	3 IQR 1
Benign/malignant	77 /263
	22.6% /77.4%
Cirrhosis (y/n)	81 /259
	23.8% /76.2%
Diabetes mellitus (y/n)	56 /284
	16.5% /83.5%
Renal impairment (y/n)	28 /312
	8.2% /91.8%
Minor/major>3 segments	259 /81
	76.2% /23.8%
Ascites (y/n)	22 /318
	6.5% /93.5%

Table 1: Baseline characteristics. Data is presented as median and interquartile range (25th to 75th percentile) or frequencies and percentages. Sex f/m, Sex female/male; BMI, Body mass index; y/n, yes/no.

	LH (n=170)	CH (n=170)	P value
Sex f/m	77 (45.3%) /93 (54.7 %)	71 (41.8%) /99 (58.2%)	0.512
Age (years)	61.5y (IQR 19.12)	62.85y (IQR 20.23)	0.673
BMI (kg/m ²)	26.67 kg/m ² (IQR 6.19)	25.9 kg/m ² IQR 6.43	0.54
ASA-score	3 (IQR 1)	3 (IQR 1)	0.995
Benign/malignant	41 (24.1%) /129 (75.9%)	36 (21.2%) /134 (78.8%)	0.517
Cirrhosis (y/n)	42 (24.7%) /128 (75.3%)	39 (22.9%) /131 (77.1%)	0.703
Diabetes (y/n)	36 (21.2%) /134 (78.8%)	20 (11.8%) /150 (88.2%)	0.019
Renal impairment (y/n)	5 (2.9%) /165 (97.1%)	23 (13.5%) /147 (86.5%)	<0.001
Tumor mass (mm)	30 (IQR 36)	30 (IQR 36)	0.25
Ascites (y/n)	9(5.3%) /161(94.7%)	13(7.6%) /157(92.4%)	0.378

Table 2: Comparison of matched groups. Data is presented as median and interquartile range (25th to 75th percentile) or frequencies and percentages; p<0.05 is considered as significant marked bold. Sex f/m, Sex female/male; BMI, Body mass index; ASA-score, American society of anaesthesiologists-score; y/n, yes/no.

Surgery

The timeframe displayed in this study shows a rapid increase in laparoscopic liver resections after the year 2010 as displayed in Figure 1. In total 81 major resections (>3 Segments) and 259 minor resections were performed. We found an equal distribution between the groups [minor 131(77.1%) LH vs. 128(75.3%) CH; major 39(22.9%) LH vs. 42(24.7%) CH; p= 0.703]. As a result of matching our conventional cohort consisted of more minor anatomical resections compared to the laparoscopic group, which contained more minor atypical resections [anatomical 84(49.4%) LH vs. 103(60.6%) CH; atypical 86(50.6%) LH vs. 67(39.4%) CH; p= 0.038] (Table 3). The postoperative histopathological grading showed similar negative resection margins in the laparoscopic group [R0 160(94.1%) LH vs. 151(88.8%) CH; R1 10(5.9%) LH vs. 19(11.2%) CH; p=0.08] (Table 3). The median duration of the operation showed significant shorter operation time for laparoscopic surgery (204.5 min. LH; IQR 172 vs. 249 min. CH IQR 127; p<0.001) (Table 3). No difference was found in the number of cases in which blood transfusions were administered during surgery [16(9.4%) LH vs. 19(11.2%) CH; p=0.53] (Table 3) The length of hospital stay was significantly longer for patients with conventional approaches (7d IQR 5 LH vs. 11d IQR 6.25 CH; p<0.001) (Table 3).

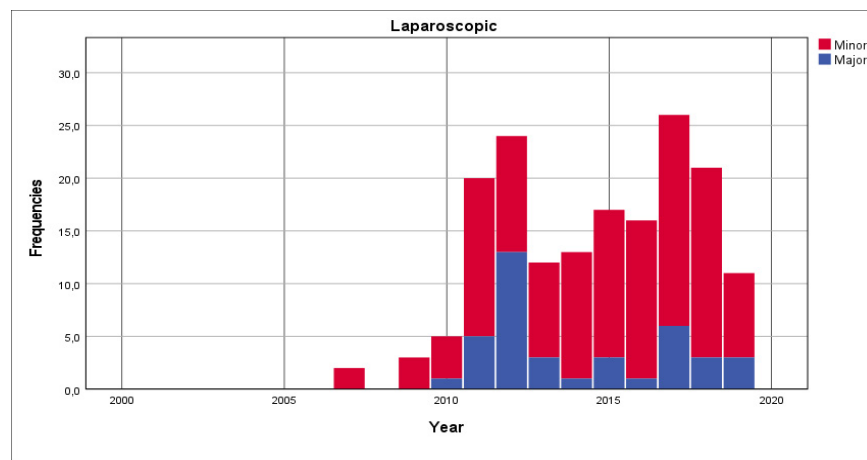


Figure 1: Timeline: Red bar laparoscopic minor liver resections; blue bar laparoscopic major liver resections.

	LH (n=170)	CH (n=170)	P value
Minor/major>3 segment	131(77.1%) /39(22.9%)	128(75.3%) /42(24.7%)	0.703
Anatomical/atypical	84(49.4%) /86(50.6%)	103(60.6%) /67(39.4%)	0.038
R0/R1	160(94.1%) /10(5.9%)	151(88.8%) /19(11.2%)	0.081
Duration (min.)	204.5 IQR 172	249 IQR127	<0.001
Transfusions (y/n)	16(9.4%) /154(90.6%)	19(11.2%) /151(88.8%)	0.53
LOHS	7 IQR 5	11 IQR 6.25	<0.001

Table 3: Operation. Data is presented as median and interquartile range (25th to 75th percentile) or frequencies and percentages; p<0.05 is considered as significant marked bold; min., minute; y/n, yes/no; LHOS, lengths of hospital stay.

Complications

Comparing different degrees of the Dindo classification, the CH group showed a significantly higher amount of I degree complications [9(5.3%) LH vs. 35(21.8%) CH; p<0.001]. The data also shows a significant higher number of IIIa complications [5(2.9%) LH vs. 18(10.6%) CH; p=0.005]. The levels of class IIIb and higher showed no significant differences. Insignificantly more patients died in the conventional group due to septic and cardioembolic complications (Table 4). Overall, the conventional group showed significantly more complications within the DINDO classification [overall 50(29.4%) LH vs. 68(40%) CH (p=0.04)]. Bile leakage occurred in significantly less patients in the laparoscopic group [5(2.9%) LH vs. 15(8.8%) CH; p=0.021] (Table 4). In the conventional group significantly more surgical site infections occurred [6(3.5%) LH vs. 23(13.5%) CH; p< 0.001]. Patients with a conventional approach suffered from postoperative AKI significantly more often (7(4.1%) LH vs. 25(17.7%) CH; p<0.001), of these 32 patients, 18 had a history of renal impairment (Table 2).

20 Patients (11,8%) in the laparoscopic group had to undergo conversion to a conventional approach (Table 4).

	LH (n=170)	CH (n=170)	P value
Complications overall	50(29.4%)	68(40%)	0.040
I	9(5.3%)	35(21.8%)	<0.001
II	19(11.2%)	13(7.6%)	0.265
IIIa	5(2.9%)	18(10.6%)	0.005
IIIb	3(1.8%)	2(1.2%)	0.652
IVa	0	1(0.6%)	0.317
IVb	0	0	1
V	2(1.2%)	4(2.4%)	0.410
Revisions (y/n)	4(2.4%) /166(97.6%)	4(2.4%) /166(97.6%)	1
Bile leakage (y/n)	5(2.9%) /165(97.1%)	15(8.8%) /155(91.2%)	0.021
Bleeding (y/n)	1(0.6%) /169(99.4%)	2(1.2%) /168(98.8%)	0.562
SSI (y/n)	6(3.5%) /164(96.5%)	23(13.5%) /147(86.5%)	<0.001
Abscess (y/n)	0	2(1.2%) /168(98.8%)	0.157
Post OP AKI (y/n)	7(4.1%) /163(95.9%)	25(17.7%) /145(85.3%)	<0.001
Hepatic dysfunction (y/n)	4(2.4%) /166(97.6%)	2(1.2%) /168(98.8%)	0.410

Cholangitis (y/n)	6(3.5%) /164(96.5%)	7(4.1%) /163(95.9%)	0.777
Pneumonia (y/n)	6(3.5%) /164(96.5%)	2(1.2%) /168(98.8%)	0.152
UTI (y/n)	12(7.1%) /158(92.9%)	6(3.5%) /164(96.5%)	0.147
Post OP ascites (y/n)	10(5.9%) /160(94.1%)	14(8.2%) /156(91.8%)	0.397
Conversion (y/n)	20/170 (11.8%)		
Mortality (y/n)	2(1.2%) /168(98.8%)	4(2.4%) /166(97.6%)	0.410

Table 4: Complications. Data is presented as median and interquartile range (25th to 75th percentile) or frequencies and percentages; p<0.05 is considered as significant marked bold; Dindo classification grade I-V; y/n, yes/no; SSI, surgical site infection; Post OP AKI, post OP acute kidney injury; UTI, urinary tract infection.

Discussion

The advance and the technical achievements of laparoscopic surgery made it one of the fastest growing and rapidly developing fields in surgery. In the case of hepatobiliary surgery, laparoscopic resection for instance of the left lateral segment has quickly become the gold standard treatment [48-52]. The metabolic complexity of the hepatic system in combination with the pathology of the underlying diseases presents a particular challenge for the performing surgeon. Nevertheless, studies have shown a fast-learning curve and the fast expansion of resection size [53,54]. Minor resections are responsible for the successful start of minimal invasive liver surgery, with it shortly becoming a routine operation [55-57]. The location of the mass plays an essential role in the development of the surgical treatment plan. Masses in so called “non laparoscopic” segments posterior and superior in the liver prove to be challenging. Lesions located in these segments are proven to be associated with higher conversion rates, prolonged operation time, higher blood loss and narrow surgical margins [27,55,58-60]. An individual evaluation of strategy and risk management as well as the use of specialized techniques like assisted laparoscopy are a possible answer to the challenges [55]. The conversion rate in this study of 11,8% was within published range of 0% - 20% [55,61]. In our analysis, we chose to leave laparoscopically scheduled but converted patients in the laparoscopic group, following the intention to treat principle, to see how conversion would affect the surgical statistics. Large European and Asian studies analyzing explicitly converted cases have shown that unplanned conversions have a worse perioperative outcome but no significant difference in complications compared with planned open liver resections [62,63]. Our laparoscopic group does not support this trend with on average shorter operation times and fewer complications. Supporting the thesis of benefits of laparoscopic surgery even with the intention to treat principle and the inclusion of converted patients in the laparoscopic group.

At our centre an increase of laparoscopic hepatobiliary surgery occurred after the year 2010. The numbers in this study seem

to be in average fair comparison to other national and international study population. Large series have been published after the year 2010 as international reviews formed combined collectives [35,64]. With these studies the problem of indication and choice of the different surgical approaches cannot be addressed. The bias of preferring conventional surgery in difficult cases can in our opinion never be completely ruled out. Large groups and retrospective data can provide an estimate of the developments in addition to the possibility of reviewing the current standards. However, to date, there is no uniform guideline for surgical approaches. Most of the series published, derive from retrospective data. Reasons of complexity and time sensitivity seem to make large, randomised studies unpractical. This might be one of the reasons for the wider use of propensity score analysis [31,65]. The rather complex tool was developed during the 1990ties to minimize bias while observing causal effects in retrospective data [66,67]. In this study we were able to show a significant shorter operation time in the laparoscopic group, with no significant difference in resection size. These findings are in concert with numerous European, Asian, and American studies [55,56,68-71]. One explanation can possibly be found in the time spared for the laparotomy and abdominal wall closure. Furthermore, a laparoscopic approach was shown to be safe and even favourable in major resections concerning a reduced rate of blood loss, fewer complications and a shorter length of hospital stay [55,56,68-71].

Despite more anatomical resections in the conventional group our data showed a higher rate of bile leakage. Bile leakage is one of the most common specific complication in hepatobiliary surgery. The positive pressure of the pneumoperitoneum and the better exposure in laparoscopy could be an explanation for fewer bile leakages. Large series have shown fewer complications in laparoscopically operated patients [61,72]. Other retrospective studies reported no significant difference in bile leakage [52,64]. A recent study investigated the influence of different devices for transection. The authors found no significant difference between a cavitron ultrasonic surgical aspirator and a bipolar device (CUSA vs. Ligasure) [73]. A recent systematic review containing larger

series of open hepatectomies dating back until 2001 found the bipolar cautery to be the best device to prevent blood loss and the harmonic scalpel to have the least overall and major complications [74]. There is a myriad of different studies introducing new energy devices in rather small groups [75-77]. With the lack of large prospective randomised trials, the question of the right device remains controversial. On the other hand, the diversity of devices can be seen as an important asset. In lack of comprehensive clinical data our in-house standard used a CUSA for almost all conventional liver resections and either the Ligasure or Harmonic device in laparoscopic surgery. In cirrhotic liver parenchyma we preferred the Harmonic device.

Complications wise the two groups were in fair comparison. A clear trend of more minor complications Dindo I and IIIa and more overall complications in the conventional group can be shown. We found more cases of postoperative AKI, which may be caused by intraoperative volume management, hypotension, and the preexisting conditions. Other large studies did not show these findings mostly for not explicitly displaying the data. Overall complications in the laparoscopic groups were lower or equal to the conventional groups [31,52,61,64]. The conventional group showed significantly more surgical site infections. These findings are in concert with other authors [55,61].

Major complications did not differ significantly in our cases. The number of in hospital mortality, due to septic complications in relation to surgery showed a slightly higher number of conventional treated patients. A review of large series by Nguyen et al. published an overall morbidity rate of 10,5% (range from 0%-50%) for laparoscopic liver resections [78]. Jackson et al. found no significant differences in comparison between the groups [61]. There are no studies indicating clear inferiority of laparoscopic resections. The overall length of hospital stays, which is an important economic factor showed a significant longer stay for conventional operated patients. Other studies show similar or equal durations. Furthermore, different authors clearly described a superiority of laparoscopic operations in matters of wound pain in connection with the surgical management and length of hospital stay [64,79]. In addition to economic factors and a smaller wound area, biopsychosocial factors that can accelerate discharge should not be ignored. A large metanalysis concerning Enhanced Recovery (ERAS) after liver surgery showed a significant shorter length of hospital stay and lower complication rates in the laparoscopic and conventional ERAS groups compared to standard care. In the subgroup analysis laparoscopic patients even showed significantly lower complications rates compared to standard treatment. A trend that could not be shown in conventional ERAS patients [80].

Limitation

A clear limitation of this study is the retrospective design.

Concerns about different training- and skill-levels of surgeons and personal preferences can also not be fully addressed in this setting.

Conclusion

Laparoscopic surgery proved to be a safe and practical method of operation. Our study provides another comparison of LH vs. CH operation technique and depicted the advancement and development of indications in laparoscopic liver resections in over a decade in a relatively large population. Overall, we found, a better recovery. In our opinion, there is no doubt that technological progress and robotic engineering will ensure the further development of laparoscopic surgery in this field in the future. In concert with the current publications, we believe that major laparoscopic resections or laparoscopic resections in less exposed areas should be performed in high volume centers. The introduction of large nationwide registries for quality control could provide a better orientation.

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