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ORIGINAL ARTICLE

Safety of laparoscopic hepatectomy in patients with severe comorbidities - A propensity score matched analysis

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Abstract

Background: Laparoscopic hepatectomy (LH) is nowadays considered as the standard of care for various liver malignancies. However, studies focusing on perioperative outcome after LH in patients with severe comorbidities are still sparse.

Methods: 247 patients, who underwent LH between January 2016 and March 2020 at European surgical center Aachen Maastricht (ESCAM) were retrospectively analyzed regarding surgical outcome. All patients were categorized according to the ASA guidelines and a propensity score matched (PSM) analysis was performed to compare patients with severe comorbidities with patients with minor or no comorbidities.

Results: After PSM, no statistically significant differences regarding clinical characteristics were observed. We performed major resections in 26.4% of h-ASA (ASA > 2) patients and 19.4% of l-ASA (ASA≤2) patients, respectively ($P = .322$). Overall morbidity (Clavien-Dindo≥1) was observed more frequently in the h-ASA group (h-ASA: 25.0% vs. l-ASA: 8.3%; $P = .007$) while analysis of major morbidity (Clavien-Dindo≥3b) showed a non-significant tendency for more complications in h-ASA patients (h-ASA: 8.3% vs. l-ASA: 1.4%; $P = .053$). A subgroup analysis identified major resection (HR = 5.05; $P = .006$) as an independent risk factor for the occurrence of any postoperative complication and chronic kidney disease (HR = 22.59; $P = .030$) and liver fibrosis (HR = 30.16; $P = .031$) as risk factors for the occurrence of major complications in h-ASA patients.

Conclusion: LH in patients with severe systemic comorbidities shows a strong tendency towards an increased rate of major complications. Careful patient selection with respect to the planned extent of resection and the presence of chronic kidney disease and liver fibrosis should be performed to improve perioperative results.

KEYWORDS

ASA, comorbidity, complications, laparoscopic hepatectomy, postoperative outcome

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1 | INTRODUCTION

Various studies have identified laparoscopy as the standard technique for the treatment of various diseases in different surgical fields.[1,2] A decrease in postoperative pain, a decline in hospital stay and reduced morbidity while maintaining high-quality oncologic outcomes are the major advantages of laparoscopy.[3,4] Whether these benefits would be transferable to liver surgery was viewed skeptically at the beginning. However, due to the development of specially designed laparoscopic instruments and parenchymal transection techniques combined with the constantly growing expertise across many HPB centers, laparoscopic hepatectomy (LH) is nowadays considered a crucial part of the hepatobiliary surgeon's armamentarium.[5,6] Despite the widespread use of LH in recent years, the safety in patients with severe comorbidities has not been sufficiently investigated so far.

The American Society of Anesthesiologists (ASA) score is useful and widely established in evaluating the general physical health of patients. As patients categorized ASA 3 or higher have been shown to display increased postoperative mortality and morbidity, reducing surgical risk by implementation of minimally invasive techniques may have a beneficial impact on postoperative outcome after LH.[7] In this study, we therefore compared the short-term results of LH between patients with and without severe comorbidities defined by the ASA score. Additionally, we aimed to identify risk factors for postoperative complications in patients with severe comorbidities to further improve postoperative results in this high-risk cohort.

2 | PATIENTS AND METHODS

This retrospective study evaluating postoperative outcome after LH in patients with or without severe comorbidities is based on patients undergoing surgery at the European Surgery Center Aachen Maastricht (ESCAM). We compared short-term outcome and postoperative complications of patients with severe comorbidities defined as ASA 3 or higher (h-ASA)) with patients with minor or no comorbidities (ASA 2 or lower (l-ASA)). The study was approved by the local Institutional Review Board before analysis of the data (EK 423/19).

A total of 247 patients, who underwent LH between January 2016 and March 2020 at the Department of Surgery and Transplantation of the RWTH Aachen University Hospital (Germany) and the Department of surgery of the Maastricht University Medical Centre (The Netherlands)) were included in the analysis. All patients were categorized according to the current ASA guidelines by an experienced anesthesiologist.[8] In case of severe comorbiditiy, the decision for surgery has been made on an interdisciplinary basis.

2.1 | Preoperative workup

The indication for surgery was approved by a multidisciplinary tumor board including surgeons, hepatologists, oncologists, and radiologists. The extent of resection was defined according to the segmental anatomic description by Couinaud and the type of hepatectomy was classified according to Brisbane 2000 terminology.[9] Resections of three or more liver segments were categorized as a major liver resection. All assigned patients were preoperatively examined in detail. For staging, gadolinium-based magnetic resonance imaging (MRI) and/or contrast-material enhanced computed tomography (cmCT) were performed to assess the number, size, and location of liver lesions and to exclude potential distant metastases or other pathologies.

2.2 | Surgical technique

The general laparoscopic approach as well as the number and size of trocars were selected depending on tumor entity, size, and localization of the hepatic lesions. All resections were performed fully laparoscopic without the use of any hybrid techniques. By default, the first 12mm trocar was placed in direction or next to the resection plane to ensure optimal triangulation after placement of two additional 5 or 12mm trocars. Additional trocars were inserted if needed. Resection specimens were extracted through a suprapubic Pfannenstiel incision in a plastic recovery bag or via an extended 12mm trocar incision. The attending surgeon was positioned between the patient's legs (French position) and the patient was positioned in a left tilted supine position. The pneumoperitoneum was maintained at 12 mmHg intraperitoneal pressure. Intrahepatic lesions were routinely located by laparoscopic ultrasound. Parenchymal transection was commonly performed either by Thunderbeat ® (Olympus KK, Tokyo, Japan) or Harmonic Ace ® (Ethicon Inc Somerville, NJ, USA). If necessary, a laparoscopic ultrasonic surgical aspirator (CUSA, Integra life sciences, New Jersey, USA) was chosen for deeper parenchymal transection in close proximity to major vascular structures or bile ducts. Vascular staplers (Echelon, Ethicon, Somerville, New Jersey, USA) or Weck ® Hem-o-lok ® polymer clips (Teleflex Inc, Pennsylvania, USA) were used for the dissection of large vessels and bile ducts.

2.3 | Data collection

All study data including demographics, tumor characteristics, clinical chemistry, and operative and postoperative data of every patient was prospectively collected within an institutional database. The postoperative course was reviewed for

complications and rated according to the Clavien-Dindo classification over a follow-up period of 90 days.[10]

2.4 | Propensity score analysis

We performed a PS matched analysis to avoid confounding differences due to baseline varieties between the two groups. Patients' characteristics were compared before and after propensity score matching (PSM) between h-ASA and l-ASA cohorts. Due to different covariate distribution among the groups, one-to-one matching without substitution was conducted for bias reduction. The propensity score was created with the preoperative characteristics including sex, age, BMI, steatosis, fibrosis and cirrhosis grade of the liver, extent of resection, and tumor diagnosis. The 1:1 nearest neighbor matching without replacement was carried out using the SPSS propensity score matching extension command (SPSS Statistics 25, IBM Corp., Armonk, NY, USA).

2.5 | Statistical analysis

The primary endpoint of this study was the occurrence of postoperative complications in l-ASA patients compared with h-ASA patients undergoing LH. Additionally, a subgroup analysis of the h-ASA cohort was performed to identify risk factors for the occurrence of general (Clavien-Dindo ≥1) and major (Clavien-Dindo ≥3b) complications. Categorical data are presented as counts and percentages and compared using the chi-square test. Data derived from continuous variables are presented as mean and standard deviation and are analyzed by the Mann-Whitney U test. Associations between perioperative variables and complications in the subgroup analysis were assessed by means of binary logistic regression. Variables being statistically significant in univariate analysis were transferred into a multivariable model and analyzed with multivariable binary logistic regression. For this purpose, continuous and categorical data were recoded into scaled dummy variables. The level of significance was set to $P < .05$, and p values are given for two-sided testing. Analyses were performed using SPSS Statistics 25 (IBM Corp., Armonk, NY, USA).

3 | RESULTS

A total of 247 patients who underwent LH between 2016 and 2020 at ESCAM, of whom 73 have been categorized as h-ASA and 174 as l-ASA, were eligible for the analysis. Before propensity score matching (PSM), we observed statistically significant differences regarding sex ($P = .014$), age ($P = .006$), the presence of steatosis ($P = .003$), and tumor diagnosis ($P = .001$) between h-ASA and l-ASA groups. Baseline characteristics of both groups are summarized in Table 1. After PSM, no statistically significant differences were observed with 72 patients remaining in each group. Common diagnosis in both groups were colorectal liver metastasis (CRLM) (h-ASA: 49.3% vs. l-ASA: 59.2%) followed by hepatocellular carcinoma (HCC) (h-ASA: 24.7% vs. l-ASA: 12.7%), liver metastasis other than CRLM (LM (other)) (h-ASA: 15.1% vs. l-ASA: 8.5%), intrahepatic cholangiocellular carcinoma (iCC) (h-ASA: 4.1% vs. l-ASA: 1.4%) and benign lesions (h-ASA: 6.8% vs. l-ASA: 18.3%). We performed major resections in 26.4% of h-ASA patients and 19.4% of l-ASA patients, respectively ($P = .322$). The mean operation time was 201±100min for the h-ASA and 197±134min for the l-ASA group ($P = .839$).

3.1 | Perioperative outcomes after PSM

Overall morbidity, defined as the occurrence of any postoperative complication (Clavien Dindo ≥1), was observed more frequently in the h-ASA group (h-ASA: 25.0% vs. l-ASA: 8.3%; $P = .007$) as shown in Table 2. Regarding major postoperative complications (Clavien-Dindo ≥3b), our comparative analysis displayed a tendency for more complications in h-ASA patients than in l-ASA patients, but marginally failed to gain statistical significance (h-ASA: 8.3% vs. l-ASA: 1.4%; $P = .053$). Mortality was seldomly observed with 3 h-ASA patients (4.2%) and 1 l-ASA patient deceasing within 90 days after LH.

3.2 | Uni- and multivariable analysis of postoperative morbidity

For a more detailed assessment of the postoperative morbidity of h-ASA patients, a univariate binary logistic regression analysis including all available pre- and intraoperative variables was carried out (Table 3). Examination of the existing comorbidities revealed cardiovascular disease in 61.6%, chronic kidney disease in 16.4%, Diabetes in 28.8%, chronic respiratory disease in 35.6%, and cerebrovascular disease in 19.2% of the h-ASA patients. In our cohort, chronic kidney disease (HR = 3.69; $P = .047$), major resection (HR = 4.89; $P = .006$), and operation time >180 min (HR = 4.40; $P = .012$) were associated with the occurrence of any postoperative complication (Clavien Dindo ≥1). These variables were subsequently included in a multivariable binary logistic regression model which determined major resection (HR = 5.05; $P = .006$) as the single significant predictor of postoperative morbidity (Table 4). A complementary analysis on major postoperative morbidity (Clavien-Dindo ≥3b) was also carried out.

TABLE 1 Patients' characteristics in ASA > 2 and ASA ≤ 2 groups before and after PSM

	ASA > 2 (n = 73)	ASA ≤ 2 (n = 174)	*P*-value	Matched-ASA > 2 (n = 72)	Matched-ASA ≤ 2 (n = 72)	*P*-value
Demographics						
Sex, n (%)						
Male	41 (56.2)	68 (39.1)	**.014**	40 (55.6)	34 (47.2)	.317
Female	32 (43.8)	106 (60.9)		32 (44.4)	38 (52.8)	
Age (years)	64.0 ± 11.3	58.6 ± 14.5	**.006**	63.8 ± 11.2	62.0 ± 13.6	.384
BMI (kg/m^2)	26.5 ± 6.3	26.1 ± 4.9	.602	26.5 ± 6.3	26.3 ± 4.8	.834
ASA, n (%)						
I	0 (0)	33 (19.0)		0 (0)	30 (41.7)	
II	0 (0)	141 (81.0)		0 (0)	42 (58.3)	
III	65 (89.0)	0 (0)		65 (89.0)	0 (0)	
IV	8 (11.0)	0 (0)		8 (11.0)	0 (0)	
V	0 (0)	0 (0)		0 (0)	0 (0)	
Steatosis, n (%)	14 (19.2)	66 (39.1)	**.003**	14 (19.4)	17 (23.6)	.543
Fibrosis, n (%)	20 (27.4)	50 (29.8)	.710	20 (27.8)	15 (20.8)	.331
Cirrhosis, n (%)	10 (13.7)	14 (19.2)	.191	10 (13.9)	7 (9.7)	.438
Major resection, n (%)	20 (27.4)	29 (16.7)	.054	19 (26.4)	14 (19.4)	.322
Diagnosis, n (%)						
CRLM	36 (49.3)	77 (44.5)	**.001**	36 (49.3)	42 (59.2)	.051
LM (other)	11 (15.1)	16 (9.2)		11 (15.1)	6 (8.5)	
HCC	18 (24.7)	21 (12.1)		18 (24.7)	9 (12.7)	
iCC	3 (4.1)	9 (5.2)		3 (4.1)	1 (1.4)	
Benign	5 (6.8)	50 (28.9)		5 (6.8)	13 (18.3)	
Operative time (min)	203 ± 100	199 ± 97	.781	203 ± 100	197 ± 134	.766
Blood loss (mL)	284 ± 365	225 ± 283	.264	284 ± 364	306 ± 367	.764

Note: Data presented as median and standard deviation if not noted otherwise. Categorical data were compared using the chi-squared test, fisher's exact test or linear-by-linear association according to scale and number of cases. Data derived from continuous variables of different groups were compared by Mann-Whitney-*U*-Test. *P*-values < . 05 are marked bold.

Abbreviation: PSM, propensity score matched.

Univariable analysis showed a significant association of chronic kidney disease (HR = 14.75; $P < .004$), liver fibrosis (HR = 1.80; $P = .015$), liver cirrhosis (HR = 20.33; $P = .002$), conversion (HR = 10.67; $P = .024$), intraoperative blood transfusion (HR = 10.17; $P = .016$), and albumin ≤3.0mg/dl (HR = 33.00; $P = .008$) with major postoperative complications (Table 3). These variables were also included in the corresponding multivariable binary logistic regression model which identified the presence of chronic kidney disease (HR = 22.59; $P = .030$) and liver fibrosis (HR = 30.16; $P = .031$) as independent predictors of major postoperative morbidity (Table 5).

4 | DISCUSSION

In this study, we analyzed the perioperative outcomes after LH in l-ASA and h-ASA patients in a comparative analysis and provided evidence that h-ASA patients showed a significant higher rate of overall complications (Clavien Dindo ≥1) after LH and a tendency to also an elevated incidence of major complications (Clavien-Dindo ≥3b). Additionally, we identified major resection as an independent risk factor for the occurrence of any postoperative complication (Clavien Dindo ≥1) and chronic kidney disease and liver fibrosis as risk factors for the occurrence of major complications (Clavien-Dindo ≥3b) in h-ASA patients.

A variety of studies with large patient cohorts have already demonstrated the advantages of LH regarding the occurrence of complications compared to open procedures.[11,12] In addition, the feasibility and non-inferiority of LH has also been demonstrated for specific populations such as obese or elderly patients.[13,14] However, data focusing on LH in patients with severe comorbidities is very limited. In this study, the patients were categorized according to the ASA-classification. In 1941, the classification scheme of the

TABLE 2 Perioperative clinical data comparing ASA > 2 and ASA≤2 groups after PSM

	Matched-ASA > 2 (n = 72)	Matched-ASA≤2 (n = 72)	*P*-value
Operation time (min)	201 ± 100	197 ± 134	.839
Postoperative complications, n (%)			
No complications	54 (75.0)	66 (91.7)	.088
Clavien-Dindo I	4 (5.6)	0 (0)	
Clavien-Dindo II	4 (5.6)	1 (1.4)	
Clavien-Dindo IIIa	4 (5.6)	4 (5.6)	
Clavien-Dindo IIIb	2 (2.8)	0 (0)	
Clavien-Dindo IVa	1 (1.4)	0 (0)	
Clavien-Dindo IVb	0 (0)	0 (0)	
Clavien-Dindo V	3 (4.2)	1 (1.4)	
Clavien ≥IIIb n (%)	6 (8.3)	1 (1.4)	.053
Clavien ≥I n (%)	18 (25.0)	6 (8.3)	**.007**
Acute kidney injury (%)	2 (2.7)	0 (0.0)	.497
Urinary tract infection (%)	3 (4.1)	0 (0.0)	.245
Hypokalemia (%)	2 (2.7)	0 (0.0)	.497
Surgical site infection (%)	3 (4.1)	3 (4.1)	.999
Biliary leakage (%)	4 (5.5)	1 (1.4)	.366
Acute liver failure (%)	1 (1.4)	0 (0.0)	.999
Wound infection (%)	3 (4.1)	0 (0.0)	.245
Pneumonia (%)	4 (5.5)	2 (2.8)	.681

Note: Data presented as median and standard deviation if not noted otherwise. Categorical data were compared using the chi-squared test, fisher's exact test or linear-by-linear association according to scale and number of cases. Data derived from continuous variables of different groups were compared by Mann-Whitney-U-Test. *P*-values < .05 are marked bold.

American Society of Anesthesiologists in Physical Position (ASA-PS) was first proposed.[15] It has been revised over the years and now comprises 6 PS classification categories.[16,17] Categories 1-5 (6 denotes an organ donor) represent the levels of patient impairment, with ASA 1 representing a "usually stable patient" and ASA 5 representing a "moribund patient who is not expected to survive without surgery".[16,17] The evaluation of the individual patient status based on the ASA classification is nowadays established worldwide. Several studies have found it significantly linked to postoperative morbidity and mortality in general surgery.[7,18,19] However, studies who investigate LH in high-risk patients stratified according to ASA-classification are limited. A study by Tranchart et al found an ASA score of 3 or higher significantly related to elevated overall complications in an analysis of 140 patients who underwent LH. A stratification regarding ASA score has not been carried out in that publication. Only one case series by Sotiropoulos et al investigates LH in high-ASA patients.[20] However, this work is of considerably limited significance, as only 5 cases were examined in which minor resections were performed. The authors conclude that laparoscopic liver resection in this case series as feasible and safe. To the best of our knowledge, the present study is the first to examine LH in a cohort of significant size stratified according to ASA classification. The analysis was conducted after PSM, a statistical technique used in the sense of observational comparative research to eliminate bias in the patient distribution, thereby offering evidence, which is considerably superior to a case-control study.[21,22] Additionally, our findings are obtained from a population of h-ASA patients who underwent LH at two specialized HPB centers. Having a sizeable population in both comparative groups with a large proportion of major hepatectomies has allowed effective PSM.

Moreover, a subgroup analysis identified individual risk factors for postoperative complications, which may be targets of preoperative conditioning or optimization. Patients with chronic kidney disease and liver fibrosis should be carefully considered for LH, as both have been identified to be significant predictors for major complications in h-ASA patients. However, both risk factors are not easily addressed preoperatively. So far, the published literature does not provide any formal guidelines, which specifically address preoperative evaluation for individuals with advanced chronic kidney disease. This study by Bahrainwala et al generally recommends a preoperative assessment that includes glomerular filtration rate, cardiopulmonary fitness, hypertension and anemia

TABLE 3 Univariable analysis of perioperative morbidity in ASA > 2 patients

		Major morbidity (Clavien Dindo ≥3b)			Morbidity (Clavien Dindo ≥1)		
	n (%)	Hazard Ratio	95% CI	*P* value	Harzard Ratio	95% CI	*P* value
Gender							
Male	41 (56.2			.571			.718
Female	32 (43.8)						
Cardiovascular disease							
Present	45 (61.6)			.279			.215
Absent	28 (38.4)						
Chronic kidney disease							
Present	12 (16.4)	14.75	2.32-93.91	**.004**	3.69	1.02-13.37	**.047**
Absent	61 (83.6)	1			1		
Diabetes							
Present	21 (28.8)			.245			.140
Absent	52 (71.2)						
Chronic respiratory disease							
Present	26 (35.6)			.332			.493
Absent	47 (64.4)						
Cerebrovascular disease							
Present	14 (19.2)			.871			.809
Absent	59 (80.8)						
Steatosis							
Present	14 (19.2)			.369			.362
Absent	59 (80.8)						
Fibrosis							
Present	20 (27.4)	17.33	1.88-160.00	**.012**			.100
Absent	53 (72.6)	1					
Cirrhosis							
Present	10 (13.7)	20.33	3.06-135.03	**.002**			.074
Absent	63 (86.3)	1					
Previous abdominal surgery							
Yes	30 (41.7)			.667			.099
No	42 (58.3)						
Extent of resection							
Major	20 (27.4)			.211	4.89	1.58-15.17	**.006**
Minor	53 (72.6)				1		
Conversion							
Yes	5 (6.8)	10.67	1.37-83.24	**.024**			-
No	68 (93.2)	1					
Intraoperative blood transfusion							
Yes	9 (12.3)	10.17	1.67-61.92	**.016**			.242
No	64 (87.7)	1					
Intensive care							
Yes	53 (72.6)			.734			.071
No	32 (43.8)						

TABLE 3 (Continued)

		Major morbidity (Clavien Dindo ≥3b)			Morbidity (Clavien Dindo ≥1)		
	n (%)	Hazard Ratio	95% CI	*P* value	Harzard Ratio	95% CI	*P* value
Age							
≤65	35 (47.9)			.144			.102
>65	40 (54.8)						
BMI							
≤25	32 (43.8)			.075			0.718
>25	41 (56.2)						
Operation time (min)							
≤180	38 (52.1)			.105	4.40	1.38-14.01	0.**012**
>180	35 (47.9)				1		
Blood loss (ml)							
≤300	46 (62.2)			.610			0.177
>300	28 (37.8)						
Alkaline Phosphatase (U/L)							
≤80	31 (42.5)			.212			.268
>80	42 (57.5)						
GGT (U/L)							
≤46	30 (41.1)			.233			.945
>46	43 (58.9)						
Haemoglobin (g/dL)							
≤12	23 (31.5)			.320			.561
>12	50 (68.5)						
Platelet count (/nL)							
≤250	36 (49.3)			.422			.210
>250	37 (50.7)						
Total bilirubin (mg/dL)							
≤0.3	29 (39.7)			.255			.401
>0.3	44 (60.3)						
INR							
≤1	39 (53.4)			.831			.052
>1	33 (45.2)						
Albumin (g/dL)							
≤3.0	8 (11.0)	33.00	2.44-446.08	**.008**			.200
>3.0	65 (89)	1					

Note: Various parameters are associated with major and general postoperative morbidity. Hazard ratios are shown for statistically significant variables.

ASA, American society of anesthesiologist's classification; BMI, body mass index; GGT, gamma glutamyltransferase; INR, international normalized ratio; *P*-values < .05 are marked bold.

management, and bleeding risk. A preoperative optimization potential is given especially for an adequate blood pressure adjustment below 140/90 mmHg and a preoperative hemoglobin level target range of 10-11.5 g/dL.[23] A study by Inoue et al examined LH in patients with cardiac diseases and concluded that preoperative treatment of a cardiac condition should be prioritized, as the postoperative outcome in patients with controlled severe cardiac disease did not differ compared to patients without coexisting cardiac disease.[24] However, the evidence is limited due to the small number of patients in the high-risk group (n = 16). More reliable data is available on the safety of laparoscopic colorectal resection in patients with severe comorbidities and an ASA-score of 3 or higher. Two studies by Tashiro et al and Ichikawa et al with

TABLE 4 Multivariable binary logistic regression of perioperative morbidity in ASA > 2 patients

	Morbidity (Clavien Dindo ≥1)		
Variable	**Hazard Ratio**	**95% CI**	**P value**
Chronic kidney disease			
Present			.054
Absent			
Extent of resection			
Major	5.05	1.58-15.17	**.006**
Minor	1		
Operation time			
≤180			.185
>180			

Note: All variables showing statistical significance in univariate binary logistic regression were included in a multivariable logistic regression. Hazard ratios are shown for statistically significant variables. *P*-values < .05 are marked bold.

TABLE 5 Multivariable binary logistic regression of major perioperative morbidity in ASA > 2 patients

	Morbidity (Clavien dindo ≥3b)		
Variable	**Hazard ratio**	**95% CI**	***P* value**
Chronic kidney disease			
Present	23.59	1.35–411.23	**.030**
Absent			
Fibrose	30.16	1.37–666.05	**.031**
Present			
Absent			
Cirrhosis			
Present			.373
Absent			
Conversion			
Yes			.061
No			
Intraoperative blood transfusion			
Yes			.126
No			
Albumin (g/dL)			
≤3.0			.589
>3.0			

Note: All variables showing statistical significance in univariate binary logistic regression were included in a multivariable logistic regression. Hazard ratios are shown for statistically significant variables. *P*-values < .05 are marked bold.

34 and 15 patients in the intervention group demonstrated that laparoscopic colorectal resection for high-risk patients was performed safely without an increase in postoperative complications.[25,26] Additionally, performing major resection was an independent risk factor for increased postoperative overall morbidity. The extent of resection in multimorbid patients should be adjusted if necessary, and the combination of parenchymal-sparing surgical resection and local ablation should be considered, as already recommended for patients with CRLM.[27]

In developed countries, the percentage of elderly individuals continues growing relative to the rest of population. In Germany, 22% of the population is aged 60 or older, while Japan currently has the highest percentage of elderly population with one-third of its population aged 60 years or older.[28] Meanwhile, with the rising incidence of primary and secondary liver tumors, the number of elderly patients who need liver resection treatment is estimated to be further increasing. Smith and colleagues reported an anticipated 67% increase in cancer incidence among patients 65 years and older from 2010 to 2030 compared with an 11% increase for younger patients.[29] Owing to comorbidities, underlying liver diseases, and advanced age, liver resection for elderly patients remains challenging. Our data provides important evidence evaluating the impact of LH in such high-risk cohorts. Tissue trauma and the consecutive inflammatory response are reportedly decreased after LH compared with open resection[30] and thereby contribute to a reduction in early postoperative systemic complications. However, it is worthwhile to highlight that a number of studies show that advanced age and the presence of comorbid illness are intrinsic host factors that often limit the application of surgery treatment for liver tumors.[7,8] This is analogous to the results of our study, which shows a strong tendency toward an increased rate of major complications in multimorbid patients.

Our analysis has certainly limitations that need to be discussed, including its retrospective design and restricted sample size. The power in terms of a sufficient risk analysis for the individual comorbidity is restricted and a multicenter large-scale study would be desirable. In addition, it might be assumable that cases with significant comorbidities did preferably undergo laparoscopic liver resection due to the reduced surgical trauma, resulting in a selection bias which needs to be considered. Moreover, a known limiting factor of PSM is the inability to address unknown confounders, which could have a significant impact on the postoperative outcome and limit the validity.

In conclusion, our study gives evidence that LH in patients with severe systemic comorbidities (ASA 3 or higher) shows a strong tendency towards an increased rate of major complications compared to l-ASA patients. Careful patient selection with respect to the planned extent of resection and the presence of chronic kidney disease and liver fibrosis should be performed to improve perioperative results.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

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