Original Article

First 100 minimally invasive liver resections in a new tertiary referral centre for liver surgery

Giuliano La Barba[1*], Leonardo Solaini[1,2*], Giorgia Radi[1], Maria Teresa Mirarchi[1], Fabrizio D'Acapito[1], Andrea Gardini[1], Alessandro Cucchetti[1,2], Giorgio Ercolani[1,2]

[1]Department of General Surgery, Morgagni-Pierantoni Hospital, Forli, Italy, [2]Department of Medical and Surgical Sciences, DIMEC; Alma Mater Studiorum, University of Bologna, Italy

*Joint first authors

Abstract

Background: In the last decades, there has been an exponential diffusion of minimally invasive liver surgery (MILS) worldwide. The aim of this study was to evaluate our initial experience of 100 patients undergoing MILS resection comparing their outcomes with the standard open procedures.

Materials and Methods: One hundred consecutive MILS from 2016 to 2019 were included. Clinicopathological data were reviewed to evaluate outcomes. Standard open resections were used as the control group and compared exploiting propensity score matching.

Results: In total, 290 patients were included. The rate of MILS has been constantly increasing throughout years, representing the 48% in 2019. Of 100 (34.5%) MILS patients, 85 could be matched. After matching, the MILS conversion rate was 5.8% (n = 5). The post-operative complication rates were higher in the open group (45.9% vs. 31.8%, P = 0.004). Post-operative blood transfusions were less common in the MILS group (4.7% vs. 16.5%, P = 0.021). Biliary leak occurred in 2 (2.4) MILS versus 13 (15.3) open. The median comprehensive complication index was higher in the open group (8.7 [0–28.6] vs. 0 [0–10.4], P = 0.0009). The post-operative length of hospital stay was shorter after MILS (median 6 [5–8] vs 8 [7–13] days, P < 0.0001).

Conclusions: The rate of MILS has been significantly increasing throughout the years. The benefits of MILS over the traditional open approach were confirmed. The main advantages include lower rates of post-operative complications, blood transfusions, bile leaks and a significantly decreased hospital stay.

Keywords: Laparoscopic liver resection, minimally invasive surgery, tertiary centre

Address for correspondence: Dr. Leonardo Solaini, Department of General Surgery, Morgagni-Pierantoni Hospital, Forlì, Italy.
Department of Medical and Surgical Sciences, DIMEC, Alma Mater Studiorum, University of Bologna, Italy.
E-mail: leonardo.solaini2@unibo.it

Submitted: 28-Nov-2020, **Revised:** 27-Apr-2021, **Accepted:** 05-May-2021, **Published:** 01-Nov-2021

INTRODUCTION

Minimally invasive liver surgery (MILS) has grown exponentially worldwide in the last decades.[1,2] The laparoscopic approach in liver surgery has been one of the major advances in surgery in recent years.[3]

Recently, several systematic reviews on laparoscopic liver resection (LLR) demonstrated fewer complications rate, decreased blood loss and transfusion rate, and a shorter hospital stay in the LLR group when compared to open liver resections and with comparable oncological outcomes.[2,4-7]

Access this article online

Quick Response Code:

Website: www.journalofmas.com

DOI: 10.4103/jmas.JMAS_310_20

How to cite this article: La Barba G, Solaini L, Radi G, Mirarchi MT, D'Acapito F, Gardini A, *et al*. First 100 minimally invasive liver resections in a new tertiary referral centre for liver surgery. J Min Access Surg 2022;18:51-7.

However, the increase of laparoscopic approach for liver surgery is not homogeneous worldwide.

At the same time, the relationship between outcome and hospital volume in digestive cancer surgery has been investigated.[8,9] El Amrani *et al*. have recently determined the minimal number of procedures required to define a high-volume hospital. Based on these results, the authors noted that post-operative mortality in digestive cancer surgery was lower in high-volume hospitals. In addition, they showed that the benefits of high volumes were transferable across procedures. They proposed a new minimal cut-off for several surgical procedures, setting in 76 resections per year to perform liver surgery.[8] In liver surgery, the association between the hospital volume and the operative outcome has been largely explored.[10,11] These data prompted that these procedures should be centralised in high-volume hospitals to reduce post-operative mortality and improve survival outcomes.

Recent literature aimed to define a minimum number of annual resections to be carried out to identify those centres that should perform this type of surgery. These are defined as reference centres.[8]

In 2016, a regional re-organisation of our health system identified our centre as the HPB hub of our catchment area. In particular, four trusts representing 1.300.000 inhabitants/72 municipalities, were united in the 'Romagna health trust'.

After the first 4 years of activity, we performed an audit on our results to continue a path of improvement. The aim of this study was to evaluate the clinical outcomes of our first 100 MILS performed in a new referral centre for Hepato-Pancreatico-Biliary (HPB) surgery in Italy. In doing so, we exploited our database on liver resections, using the standard open resections as a control group to verify the outcomes.

MATERIALS AND METHODS

This study was performed according to the Strengthening the Reporting of Cohort Studies in Surgery.[12]

Data were extracted by an Institutional Review Board-approved retrospective database.

Design and patients

All consecutive patients who underwent hepatic resection (minimally invasive or open) between January 1, 2016, and January 1, 2020, were screened for inclusion. Patients were excluded if they had a biliary reconstruction and if no resections were performed. Patients were grouped as per the method of surgery: MILS or open. All patients were evaluated preoperatively for the laparoscopic approach. Performance status, tumour size and location were evaluated in the process of selecting those patients eligible for laparoscopy.

Variables and definitions

Collected outcomes were procedure type (open, MILS), conversion to open surgery, operative time (minutes), intra-operative blood transfusions, synchronous colo-rectal resection, overall complications, and major complications, length of hospital stay (days), in-hospital mortality. Complications, readmissions and mortality were all collected up to patient's discharge.

Post-operative complications were graded with the classification proposed by Dindo *et al*.[13] Liver failure was defined, according to the International Study Group of Liver Surgery classification, as any alteration of international normalised ratio and bilirubin values after post-operative day 5.[14]

The comprehensive complication index (CCI) was used to calculate the grade of severity and number of post-operative complications.[15,16]

Matching

To minimise the impact of treatment allocation bias, laparoscopic resections were matched to open resections exploiting propensity scores. Multivariable logistic regression was performed to estimate the propensity to undergo laparoscopic resection for all patients, regardless of the actual treatment received. Propensity scores were based on predictors of treatment or on those baseline variables which differed with a $P = 0.05$. In this analysis, the calculation of the propensity scores was based on the type of tumour (malignant versus benign) and the number of nodules (≥3 vs. <3). Nearest neighbour matching was performed in a 1:1 ratio without replacement and with a calipre width of 0.2 standard deviation.

Statistical analyses

Data were analysed using IBM SPSS Statistics for Windows version 24.0 (IBM Corp., Armonk, NY, USA) and R Statistical Software version i386 3.3.3 (Foundation for Statistical Computing, Vienna, Austria). Analyses were performed according to the intention-to-treat principle. Before matching continuous variables were presented as median and interquartile range and were compared using the Mann–Whitney U-test. Categorical data were presented as frequencies with percentages and were compared using the Chi-square or Fisher's exact test, as appropriate. In the post-match analyses, the Wilcoxon signed-rank test was used to compare continuous variables while McNemar's test was used for categorical data. In the matched cohort logistic regression was used to calculate the odds ratio (OR) for post-operative complications of perioperative variables (age, American Statistical Association (ASA) score, nodule size, number of nodules, malignant tumour, laparoscopic approach, synchronous resections and intra-operative transfusions). All variables showing $P < 0.05$ were included in a multivariate analysis performed in stepwise manner.

RESULTS

Total cohort

In total, 356 patients were screened, of whom 66 were excluded for reasons [Figure 1], leaving 290 patients for analysis.

The rate of MILS has been constantly increasing throughout the years, representing the 48% in 2019 [Figure 2]. The MILS procedures, which included 12 robotic liver resections, were grouped according to Kawaguchi's difficulty score[17] in Table 1. There was no differences with regards to the complexity of the procedure (Group 1 n = 19, 76% Group 2 3, 12% Group 3 3, 12% vs, 55, 73%; 14, 19%; 6, 8%; P = 0.656) and the complications rates (overall n = 4, 16% vs. 8, 11%; P = 0.444 – Clavien-Dindo >2 2, 8% vs. 6, 8%; P = 0.488) between the MILS procedure performed during the first (2016–2017) and the second interval (2018–2019) of the study period.

Patients' characteristics grouped according to the approach are shown in Table 2. Liver status at operation was available only for 220 patients: there were 19 (14.1%) cases of liver cirrhosis in the MILS group versus 15 (21.4%) in the open group (P = 0.356). The diagnosis of malignancy was less common in the laparoscopic group (72.0 vs. 86.8%, P < 0.002). Three or more nodules were more commonly seen in the open group (7.0 vs. 32.6%, P = 0.00001). Intra-operative outcomes are shown in Table 3. Conversion from MILS to open occurred in five patients (5.0%). Major resections were more common in the open group (13.8, vs. 8.0%; P < 0.00001). The post-operative outcomes are shown in Table 4. Overall mortality was 0.7% (two patients in the open group). The overall complication rate was significantly higher after open liver resection (47.8% vs. 12.0%, P = 0.026). Bile leak was less often seen after MILS (2.0 vs. 10.0%, P = 0.015). Median CCI was higher after open liver resections (median 8.7 [0–26.2] vs. 0 [0–8.7] days, P = 0.0002). Post-operative length of hospital stay was shorter after MILS (median 6 [4–8] vs. 8 [7–13] days, P < 0.0001).

Matched cohort

Of all MILS, 94.4% could be matched successfully to an open control. Differences (P < 0.05) in baseline characteristics were no longer present after matching. Intra-operative outcomes are presented in Table 2. Conversion from to open liver resection occurred in five patients (5.8%). Post-operative outcomes are shown in Table 3. The post-operative complication rates were higher in the open group (45.9% vs. 31.8%, P = 0.004). Post-operative blood transfusions were less common in

Table 1: Minimally invasive liver surgery procedures grouped according to the Kawaguchi's difficulty score

	n
Group 1 (wedge resection and left lateral sectionectomy)	74
Group 2 (anterolateral segmentectomy and left hepatectomy)	17
Group 3 (postero-superior segmentectomy, right posterior sectionectomy, right hepatectomy, central hepatectomy, and extended left/right hepatectomy)	9

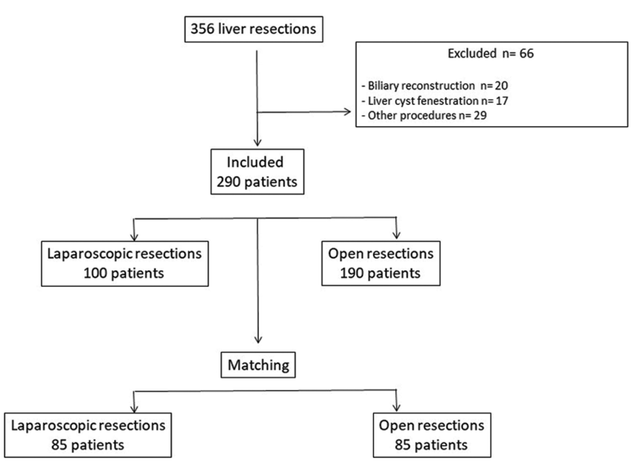

Figure 1: Flowchart summarizing the patients and the propensity score matching

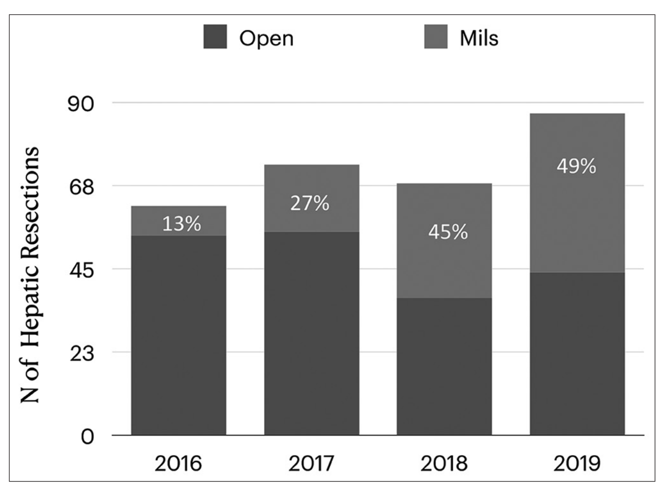

Figure 2: Trend of the Minimally Invasive Liver Surgery rate per year

Table 2: Patients' characteristics

Variables	Total cohort		P	Matched cohort		P
	MILS (*n*=100), *n* (%)	Open (*n*=190), *n* (%)		MILS (*n*=85), *n* (%)	Open (*n*=85), *n* (%)	
Age>70						
Yes	36 (36.0)	67 (35.2)	0.898	30 (35.3)	28 (36.9)	0.868
No	64 (64.0)	123 (64.8)		55 (64.7)	57 (67.1)	
Female						
Yes	50 (50.0)	82 (43.1)	0.321	43 (50.6)	42 (49.4)	0.753
No	50 (50.0)	108 (46.9)		42 (49.4)	43 (50.6)	
ASA>2						
Yes	45 (45.0)	80 (42.1)	0.708	38 (44.7)	34 (40.0)	0.617
No	55 (55.0)	110 (67.9)		47 (55.3)	51 (60.0)	
Malignancy						
Yes	72 (72.0)	165 (86.8)	0.002	63 (74.1)	63 (74.1)	1.000
No	28 (28.0)	25 (13.2)		22 (25.9)	22 (25.9)	
Nodules≥3						
Yes	7 (7.0)	62 (32.6)	<0.0001	6 (7.1)	8 (9.4)	1.000
No	83 (92.2)	128 (67.4)		79 (92.9)	77 (90.6)	
Tumor size (cm)						
<2	16 (16.0)	38 (20)	0.470	16 (18.8)	20 (23.5)	0.785
≥2-<5	49 (49.0)	76 (40)		41 (48.2)	36 (42.3)	
≥5	31 (31.0)	56 (29.4)		28 (32.9)	29 (34.1)	
NA	4 (4.0)	20 (10.6)				
Neoadjuvant chemotherapy°						
Yes	14 (29.8)	45 (37.8)	0.427	10 (11.8)	15 (17.6)	0.332
No	33 (70.2)	74 (62.2)		75 (88.2)	70 (82.3)	

°Calculated only on metastases (*n*=47 in MILS vs. 119 in open). MILS: Minimally invasive liver surgery, NA: Not applicable ASA: American Society of Anaesthesiologists

Table 3: Intra-operative variables

Variables	Total cohort		P	Matched cohort		P
	MILS (*n*=100), *n* (%)	Open (*n*=190), *n* (%)		MILS (*n*=85), *n* (%)	Open (*n*=85), *n* (%)	
Type of procedure						
Wedge resection	47 (47.0)	96 (50.5)	<0.00001	30 (35.3)	23 (27.1)	0.067
Segmentectomy	19 (19.0)	45 (23.6)		20 (23.5)	26 (30.6)	
Right hepatectomy	5 (5.0)	15 (7.8)		5 (5.9)	8 (9.4)	
Left hepatectomy	4 (3.0)	11 (5.7)		2 (2.3)	6 (7.1)	
Right posterior sectionectomy	4 (4.0)	16 (8.4)		4 (4.7)	6 (7.1)	
Left lobectomy	21 (21.0)	7 (3.6)		18 (20.0)	6 (7.1)	
Conversion to open						
Yes	5 (5)			5 (5.9)		
No	95 (95)			80 (94.1)		
Syncronous resection						
Right colectomy	5 (5.0)	4 (2.1)	0.097	4 (4.7)	1 (1.2)	0.581
Left colectomy	1 (1.0)	10 (5.2)		0	5 (5.9)	
Anterior rectal resection	2 (2.0)	8 (4.2)		1 (1.2)	3 (3.6)	
Other	1 (1.0)	5 (2.6)				
Operative time (min)						
Median (IQR)	292 (195-380)	306 (175-420)	0.329	266 (245-304)	290 (263-309)	0.942
Intraoperative blood trasfusion						
Yes	3 (3)	9 (4.7)	0.554	3 (3.6)	4 (4.7)	0.726
No	97 (97)	181 (95.3)		82 (96.7)	81 (95.3)	

MILS: Minimally invasive liver surgery, IQR: Interquartile range

the MILS group (4.7% vs. 16.5%, $P = 0.021$). Biliary leak occurred in 2 (2.4) MILS vs. 13 (15.3) open. The median CCI was significantly higher in the open group (8.7 [0–28.6] vs. 0 [0–10.4], $P = 0.0009$). The post-operative length of hospital stay was shorter after MILS [median 6 (5–8) vs 8 (7–13) days, $P < 0.0001$].

The multivariable analysis showed that synchronous resections (8.21, 1.73–38.0; $P = 0.008$) and MILS (0.49, 0.25–0.95; $P = 0.036$) were factors influencing the post-operative complications rate.

DISCUSSION

The advances in techniques and technology have allowed the spreading of the laparoscopic approach over the last three decades and its employ even in complex surgical procedures.

Table 4: Post-operative outcomes

Variables	Total cohort			Matched cohort		
	MILS (*n*=100), *n* (%)	Open (*n*=190), *n* (%)	*P*	MILS (*n*=85), *n* (%)	Open (*n*=85), *n* (%)	*P*
Post-operative complications						
Yes	12 (12.0)	91 (47.8)	0.026	27 (31.8)	39 (45.9)	0.004
No	88 (88.0)	99 (52.2)		58 (69.2)	46 (54.1)	
Clavien dindo Grade≥3						
Yes	8 (8.0)	25 (13.1)	0.319	9 (10.6)	17 (20)	0.124
No	92 (92.0)	165 (86.9)		76 (89.4)	68 (80)	
Mortality						
Yes	0	2 (1.1)	0.546	0	1 (1.2)	1.000
No	100 (100)	188 (98.9)		85 (100)	84 (98.8)	
Post-operative blood transfusion						
Yes	5 (5.0)	23 (12.1)	0.060	4 (4.7)	14 (16.5)	0.021
No	95 (95.0)	167 (87.9)		81 (95.3)	71 (83.5)	
Ascites						
Yes	2 (2.0)	11 (5.7)	0.231	2 (2.4)	7 (8.2)	0.180
No	98 (98.0)	179 (94.3)		83 (97.6)	78 (91.8)	
Liver failure						
Yes	0	2 (1.0)	0.545	0	1 (1.2)	0.500
No	100 (100)	187 (98.4)		85 (100)	84 (98.8)	
Subphrenic abscess						
Yes	5 (5.0)	15 (7.8)	0.621	5 (5.9)	9 (10.6)	0.065
No	85 (85.0)	174 (92.2)		80 (94.1)	76 (89.4)	
Biliary fistula						
Yes	2 (2.0)	19 (10)	0.015	2 (2.4)	13 (15.3)	0.007
No	98 (98.0)	170 (90)		83 (97.6)	72 (84.7)	
CCI						
Median (IQR)	0 (0-8.7)	8.7 (0-26.2)	0.0002	0 (0-10.4)	8.7 (0-28.6)	0.0009
Length of hospital stay						
Median (IQR)	6 (4-8)	8 (7-13)	<0.0001	6 (5-8)	8 (7-13)	<0.0001

MILS: Minimally invasive liver surgery, IQR: Interquartile range, CCI: Comprehensive complication index

Considering its complexity, the centralisation of patients who need liver surgery deemed necessary. There is a strong evidence that complex surgical procedures performed in high-volume tertiary centres for digestive cancer surgery as a part of multidisciplinary teams are associated with lower mortality risk.[8,11,18]

In this context, our early experience has shown that MILS in a 'young' HPB center could be associated with adequate safety parameters while maintaining the benefits of minimally invasive surgery. This was also associated with a rate of complex procedure which was in line with that of large multicentre series.[19]

To validate our results we performed a propensity score match comparison with the standard open resections performed in the same study period confirming that MILS was associated with improved post-operative outcomes. These included mortality and overall post-operative complications, the rate of biliary fistula and the need of blood transfusions after surgery. Similar findings were shown by a recent meta-analysis by Jin *et al.*;[5] those authors, analysing eight randomised controlled trials with a total of 554 patients, found that laparoscopy was associated with lower complication rates than open surgery.

This was also confirmed by logistic regression analysis in which the open approach and synchronous resections were found to be risk factors for complications. This is a recurrent finding in liver surgery literature. As such, a recent analysis by Wang *et al.*[20] found that the incidence of severe complications was doubled after synchronous resection (26.7%) when compared with the delayed liver resections (11.2%).

In our series, complication rates were higher than those set by Rössler 2016 *et al.* in their benchmark analysis.[21] This could be explained by the fact that our series represent a population of patients in which more than 40% were ASA >2 and this is in contrast with that reported by Rossler including only healthy living donors.

As reported above, the biliary leak occurred less commonly after LLRs (2.4 vs. 15.3%) and this is consistent with what has been reported in literature. A recent study by Smith *et al.*[22] showed a bile leak rate of 2.8% after 1388 consecutive liver resections: the authors found that the minimally invasive approach significantly reduced the odd of bile leak with an OR of 0.48 (95% confidence interva 0.23–0.99).

The conversions rate was 5.6% in the current series and this is in line with those reported in literature. In all

5 cases conversions were due to bulky tumours which is a well-established risk factor for conversion to open surgery.[23-25]

As expected, the length of hospital stay was significantly shorter after the laparoscopic approach. This may reflect the improved post-operative functional outcomes which have a major impact on the decision to discharge a patient. In addition, a shorter hospital stay significantly decrease total post-operative costs as suggested by Medbery *et al*.[26] who reported a $ 7000 savings in the laparoscopic group in their comparative analysis of right hepatectomies. Similar findings were found by Polignano *et al*.[27] who analysed the overall hospital costs after segmentectomies and found that it was significantly lower in the laparoscopic group by an average of 2,571 pounds sterling.

In light of our results and of those reported by the most recent meta-analyses, we can support the use of the laparoscopic approach whenever technically feasible and oncologically appropriate.

This study presents a few limitations. First, some of the included laparoscopic procedures may have been part of the learning curve of one of the surgeons performing these procedures as he was trained after our centre became an HPB hub. However, the impact of the learning curve may have been limited in the outcomes of the MILS group. This could be supported by the fact that the complication rate and the level of complexity of the laparoscopic procedures were similar between the first and the second period of the study interval.

Second, this was a retrospective study and it could be affected by biases linked to its nature. In particular, patients' pre-operative clinical status was represented mostly by ASA score in this study and this might have been underestimated some characteristics which could have influenced the morbidity rate in the open group.

The strengths of this study are linked to the short study interval which minimise the time-related differences in perioperative care and operative factors. In addition, the propensity score matching mitigated the impact of the treatment allocation bias which significantly affects the outcomes in retrospective studies.

CONCLUSIONS

Our analysis confirmed the benefits of laparoscopic liver surgery over the traditional open approach in expert centres. The main advantages include lower rates of post-operative complications, blood transfusions, bile leaks and a significantly decreased hospital stay. Synchronous resections remain the procedures with the greater risk of complications and should be performed with caution even in the laparoscopic approach.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Buell JF, Cherqui D, Geller DA, O'Rourke N, Iannitti D, Dagher I, *et al*. The international position on laparoscopic liver surgery: The Louisville statement, 2008. Ann Surg 2009;250:825-30.
2. Ciria R, Cherqui D, Geller DA, Briceno J, Wakabayashi G. Comparative short-term benefits of laparoscopic liver resection: 9000 cases and climbing. Ann Surg 2016;263:761-77.
3. Bryant R, Laurent A, Tayar C, Cherqui D. Laparoscopic liver resection-understanding its role in current practice: The Henri Mondor Hospital experience. Ann Surg 2009;250:103-11.
4. Aldrighetti L, Guzzetti E, Pulitanò C, Cipriani F, Catena M, Paganelli M, *et al*. Case-matched analysis of totally laparoscopic versus open liver resection for HCC: Short and middle term results. J Surg Oncol 2010;102:82-6.
5. Jin B, Chen MT, Fei YT, Du SD, Mao YL. Safety and efficacy for laparoscopic versus open hepatectomy: A meta-analysis. Surg Oncol 2018;27:A26-34.
6. Mirnezami R, Mirnezami AH, Chandrakumaran K, Abu Hilal M, Pearce NW, Primrose JN, *et al*. Short- and long-term outcomes after laparoscopic and open hepatic resection: Systematic review and meta-analysis. HPB (Oxford) 2011;13:295-308.
7. Solaini L, Bocchino A, Cucchetti A, Ercolani G. Anatomic laparoscopic liver resection in the scenario of the hepatocellular Carcinoma: A systematic review and meta-analysis. J Laparoendosc Adv Surg Tech A 2020;30:1076-81.
8. El Amrani M, Lenne X, Clement G, Delpero JR, Theis D, Pruvot FR, *et al*. Specificity of procedure volume and its association with postoperative mortality in digestive cancer surgery: A nationwide study of 225,752 patients. Ann Surg 2019;270:775-82.
9. Garcea G, Breukink SO, Marlow NE, Maddern GJ, Barraclough B, Collier NA, *et al*. A systematic review of the impact of volume of hepatic surgery on patient outcome. Surgery 2009;145:467-75.
10. Dimick JB, Cowan JA Jr., Knol JA, Upchurch GR Jr. Hepatic resection in the United States: indications, outcomes, and hospital procedural volumes from a nationally representative database. Arch Surg 2003;138:185-91.
11. Torzilli G, Viganò L, Giuliante F, Pinna AD. Liver surgery in Italy. Criteria to identify the hospital units and the tertiary referral centers entitled to perform it. Updates Surg 2016;68:135-42.
12. Agha RA, Borrelli MR, Vella-Baldacchino M, Thavayogan R, Orgill DP, STROCSS Group. The STROCSS statement: Strengthening the reporting of cohort studies in surgery. Int J Surg 2017;46:198-202.
13. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: A new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-13.
14. Rahbari NN, Reissfelder C, Koch M, Elbers H, Striebel F, Büchler MW, *et al*. The predictive value of postoperative clinical risk scores for outcome after hepatic resection: A validation analysis in 807 patients. Ann Surg Oncol 2011;18:3640-9.
15. Slankamenac K, Graf R, Barkun J, Puhan MA, Clavien PA. The

comprehensive complication index: A novel continuous scale to measure surgical morbidity. Ann Surg 2013;258:1-7.

16. Slankamenac K, Nederlof N, Pessaux P, de Jonge J, Wijnhoven BP, Breitenstein S, *et al*. The comprehensive complication index: A novel and more sensitive endpoint for assessing outcome and reducing sample size in randomized controlled trials. Ann Surg 2014;260:757-62.
17. Kawaguchi Y, Fuks D, Kokudo N, Gayet B. Difficulty of laparoscopic liver resection: Proposal for a new classification. Ann Surg 2018;267:13-7.
18. Learn PA, Bach PB. A decade of mortality reductions in major oncologic surgery: The impact of centralization and quality improvement. Med Care 2010;48:1041-9.
19. Russolillo N, Maina C, Fleres F, Langella S, Lo Tesoriere R, Ferrero A. Comparison and validation of three difficulty scoring systems in laparoscopic liver surgery: A retrospective analysis on 300 cases. Surg Endosc 2020;34:5484-94.
20. Wang LJ, Wang HW, Jin KM, Xing BC. Comparison of sequential, delayed and simultaneous resection strategies for syncronous colorectal liver metastases. BMC Surg 2020;20:16.
21. Rössler F, Sapisochin G, Song G, Lin YH, Simpson MA, Hasegawa K, *et al*. Defining benchmarks for major liver surgery: A multicenter analysis of 5202 living liver donors. Ann Surg 2016;264:492-500.
22. Smith AA, Monlezun DJ, Martinie J, Iannitti D, Konstantinidis I, Darden M, *et al*. Bile leak reduction with laparoscopic versus open liver resection: A multi-institutional propensity score-adjusted multivariable regression analysis. World J Surg 2020;44:1578-85.
23. Abu Hilal M, Aldrighetti L, Dagher I, Edwin B, Troisi RI, Alikhanov R, *et al*. The southampton consensus guidelines for laparoscopic liver surgery: From indication to implementation. Ann Surg 2018;268:11-8.
24. Ban D, Tanabe M, Ito H, Otsuka Y, Nitta H, Abe Y, *et al*. A novel difficulty scoring system for laparoscopic liver resection. J Hepatobiliary Pancreat Sci 2014;21:745-53.
25. Shelat VG, Cipriani F, Basseres T, Armstrong TH, Takhar AS, Pearce NW, *et al*. Pure laparoscopic liver resection for large malignant tumors: Does size matter? Ann Surg Oncol 2015;22:1288-93.
26. Medbery RL, Chadid TS, Sweeney JF, Knechtle SJ, Kooby DA, Maithel SK, *et al*. Laparoscopic vs open right hepatectomy: A value-based analysis. J Am Coll Surg 2014;218:929-39.
27. Polignano FM, Quyn AJ, de Figueiredo RS, Henderson NA, Kulli C, Tait IS. Laparoscopic versus open liver segmentectomy: Prospective, case-matched, intention-to-treat analysis of clinical outcomes and cost effectiveness. Surg Endosc 2008;22:2564-70.