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Defining global benchmarks for laparoscopic liver resections: an international multicenter study.

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Abstract

Objective: To establish global benchmark outcomes indicators after laparoscopic liver resections (L-LR).

Background: There is limited published data to date on the best achievable outcomes after L-LR.

Methods: This is a post hoc analyses of a multicenter database of 11983 patients undergoing L-LR in 45 international centers in 4 continents between 2015-2020. Three specific procedures: left lateral sectionectomy (LLS), left hepatectomy (LH) and right hepatectomy (RH) were selected to represent the 3 difficulty levels of L-LR. Fifteen outcome indicators were selected to establish benchmark cutoffs.

Results: There were 3519 L-LR (LLS, LH, RH) of which 1258 L-LR (40.6%) cases performed in 34 benchmark expert centers qualified as low-risk benchmark cases. These included 659 LLS (52.4%), 306 LH (24.3%) and 293 RH (23.3%). The benchmark outcomes established for operation time, open conversion rate, blood loss ≥ 500 mls, blood transfusion rate, postoperative morbidity, major morbidity and 90-day mortality after LLS, LH and RH were 209.5 min, 302 min and 426 min; 2.1%, 13.4% and 13.0%; 3.2%, 20% and 47.1%; 0, 7.1% and 10.5%; 11.1%, 20% and 50%; 0%, 7.1% and 20%; and 0%, 0% and 0%, respectively.

Conclusion: This study established the first global benchmark outcomes for LLR in a large-scale international patient cohort. It provides an up-to-date reference regarding the "best achievable" results for L-LR for which centers adopting L-LR can use as a comparison to enable an objective assessment of performance gaps and learning curves.

Key words: laparoscopic liver resection; benchmark; global; hepatectomy; minimally-invasive; quality assessment

Introduction

Benchmarking is a tool used for quality assessment and improvement in fields such as the manufacturing industry but its application in medicine and surgery remains more limited and ill-defined [1,2]. The objective of applying benchmarking in surgery is to assess the best possible outcome for a particular surgical procedure [2,3]. Formulation of standardized benchmarks [4] for key outcome indicators in surgery serve as important reference values for comparison when evaluating the implementation of novel surgical procedures and auditing outcomes. This has been recently defined for several major abdominal surgical procedures such as pancreas surgery [5], bariatric surgery [6], liver transplantation [7] and open major liver surgery [8].

The adoption of laparoscopic liver resections (L-LR) has been expanding rapidly world-wide over the past decade [9,10]. Hence, it has become critical to define benchmark values for the key outcome indicators of L-LR in order to promote the safe dissemination of the procedure. To date, there is limited data available in the literature on benchmarking outcomes in L-LR [11,12]. The absence of standardized benchmarks is a major shortcoming as there is lack of reference data for which surgeons embarking on L-LR can determine if they have overcome the learning curve and achieved competency [13,14].

In the present study, we aimed to establish various clinically-relevant intraoperative and postoperative benchmark values for L-LR from low-risk patients [3,5] who underwent surgery at high-volume expert centers from around the globe. It is difficult to benchmark liver resections including L-LR as these are composed of a wide-range of different procedures of varying complexities and outcomes [15-18]. Hence, to

reduce the heterogeneity of the procedures and outcomes, 3 specific types of procedures; laparoscopic left lateral sectionectomy (L-LLS), left hepatectomy (L-LH) and right hepatectomy (L-RH)] were selected to represent each of the 3 difficulty groups of L-LR as defined by Kawaguchi et al [15].

Methods

This is a post-hoc analysis of an international multicenter database of 11,893 patients who underwent pure L-LR between January 2015 to December 2020 at 45 centers. Of note, only pure L-LR were included and other approaches such as robotic assisted, hand-assisted and laparoscopic-assisted (hybrid) LR were excluded in this study. Three specific L-LR procedures were selected to represent each of the 3 levels of difficulty of L-LR according to the Institute Mutualiste Montsouris (IMM) classification [13]. L-LLS for low difficulty, L-LH for intermediate difficulty and L-RH for high difficulty resections (11,13). Hence, 3519 L-LR performed at 43 centers, from 16 countries in 4 continents. The flow chart demonstrating he selection of cases is summarized in **Supplementary Figure 1**, Supplemental Digital Content 1, http://links.lww.com/SLA/D884.

All institutions obtained their respective approvals according to their local requirements. Each individual center's collaborators and investigators collected and entered their deidentified data into a standard excel datasheet. This deidentified data were collated and analyzed centrally at the Singapore General Hospital. The data was stored in a password protected computer in a locked office. All data was audited and checked for accuracy by the first author with assistance from his study team. In the event of ambiguity, the contributing center was contacted to verify the accuracy of data. The

Singapore General Hospital Institution Review Board provided waiver for this study due to its retrospective nature and the use of only deidentified data.

Study Design

High volume experienced centers

A standardized methodology previously reported for procedures such as major liver resection [8], liver transplant [7], pancreatic surgery [5] and bariatric surgery [6] was used as a guide to develop the benchmark outcomes in this study. Centers which met the following criteria 1) Cumulative experience of over 80 L-LR prior to January 2015, 2) Average case load ≥ 20 L-LR per annum between 2015-2020 [11,12,19] and 3) academic interest in L-LR as evidenced by ≥ 1 Pubmed-indexed publication on L-LR were defined as a high-volume expert center in this study. 32 centers from 4 continents met the study criteria for high volume expert center. These included 17 from Europe, 13 from Asia, 1 from North America and 1 from South America. Additionally, 2 relatively new L-LR centers (1 Asia, 1 Europe) which did not meet criteria 1 were included as the L-LR programs in these 2 centers were initiated and the cases were performed by 2 world renown highly experienced pioneering L-LR surgeons who had relocated to these centers. Hence, finally, 34 centers were included and the other 9 centers which did not meet the criteria formed the control group. In agreement with all centers, the identity of the centers was anonymized.

Low risk procedures

In order to select patients with a low-preoperative risk profile for benchmarking [2], only patients aged between 18 to 70 years old [5] and with a low American Society of Anesthesiology (ASA) classification ≤2 were included [5]. Patients with very large

tumors ≥10 cm [20], Child's B liver cirrhosis or portal hypertension were excluded [17,21]. We also excluded patients who had L-LR for gallbladder cancer, donor hepatectomies, previous liver resections (repeat liver resections) [22], associating liver partition and portal vein ligation for staged hepatectomy [11], bilio-enteric anastomoses, hilar lymph node clearance and those who underwent LLR with concomitant major operations such as colectomies, bowel resections and stoma reversals [11,23,24]. Additionally, patients who underwent multiple minor liver resections with L-LLS were also excluded [11]. Notably, patients who underwent concomitant minor procedures such as cholecystectomy, hernia repair or ablations were included. The selection criteria is summarized in **Supplementary Table 1**, Supplemental Digital Content 2, http://links.lww.com/SLA/D885.

Definitions

LLS, LH and RH were classified according to the 2000 Brisbane classification.[25]. Notably, both LH and RH with caudate lobe resections were included as per the IMM classification [15]. Non-anatomical extended RH (partial segment 4) and extended LH (partial 5/8) and anatomical trisectionectomies were excluded. Post-operative complications were classified according to the Clavien-Dindo classification [26] and recorded for up to 90 days. Major complications were defined as complications > Clavien-Dindo grade 2. R1 resection was defined as a close resection margin of less than 1 mm. Difficulty of resections were also graded according to the Iwate score [16,18]. Failure-to-rescue rate was defined as the ratio of the number of 90-day mortalities in patients with major complications (numerator) to the total number of patients with major complications (denominator) [27].

Outcome indicators

Fifteen clinically relevant intra- and postoperative outcomes indicators were selected to establish benchmark cutoffs. The intra-operative outcomes selected were operation duration, estimated blood loss, blood loss ≥ 500mls, blood loss ≥ 1000mls, intraoperative blood transfusion and open conversion. The postoperative outcomes selected were postoperative 90-day morbidity, postoperative 90-day major morbidity (> Clavien-Dindo grade 2), reoperation, postoperative 30-day and 90-day mortality, postoperative length of stay, 30-day unplanned readmission rates, R1 resection (< 1mm margin for malignant tumors) and failure to rescue.

Benchmark values and statistical analysis

A benchmark value was established for each of the 15 outcome indicators from patients who underwent LLLS, LLH and LRH. This was set at 75^{th} percentile (indicators of poor outcome) of the overall median value of the outcome indicator as previously described [2,11]. Mann-Whitney U test for continuous variables, while Fisher's exact test and Pearson's $\chi 2$ test were used for categorical variables. All statistical analyses were performed using IBM SPSS V23.0 and Stata V17.0 (StataCorp, College Station, TX, USA.

Comparative cohorts

To test the benchmark values, we analyzed 2 separate cohort of patients. The first cohort was non-low-risk cases who underwent L-LR in the 34 experienced expert centers. The second cohort were low risk LLR meeting our study criteria for benchmark outcomes who underwent LLR at centers which did not meet our inclusion criteria as an expert center.

Results

3098 LLR were performed in the 34 centers which met the study criteria as an expert center. Of these, there were 1543 LLS, 755 LH and 800 RH. 1258 L-LR (40.6%) cases performed in benchmark expert centers met the criteria for low risk benchmark cases. These included 659 LLS (52.4%), 306 LH (24.3%) and 293 RH (23.3%).

The proportion of benchmark cases in the 34 expert centers ranged from 7.2% to 62.5% (**Figure 1**). The overall patient baseline clinicopathological features and outcomes are summarized in **Tables 1 and 2.**

Benchmark outcomes

The 15 benchmark cutoffs derived from the 75th percentile of the medians of each outcome indicator for each center are summarized in **Table 3**. The benchmark outcomes established for open conversion rate, blood loss ≥ 500 mls, blood transfusion rate, postoperative morbidity, major morbidity and 90-day mortality after LLS, LH and RH were 2.1%, 13.4% and 13.0%; 3.2%, 20% and 47.1%; 0, 7.1% and 10.5%; 11.1%, 20% and 50%; 0, 7.1% and 20%; and 0, 0 and 0, respectively. **Supplementary Table 2**, Supplemental Digital Content 3, http://links.lww.com/SLA/D886 summarizes the liver specific major morbidities.

Outcome comparisons

We subsequently tested the applicability of the benchmark outcomes in 2 separate cohort of patients; non-low-risk L-LR performed in benchmark expert centers and low-risk L-LR performed in non-benchmark centers (**Table 4**).

In the cohort of high-risk cases performed in benchmark centers, blood transfusion rate, blood loss ≥ 1000 mls, reoperation rate, failure to rescue and 90-day mortality were

outside the benchmark values for all 3 procedures: LLS, LH and RH. For LLS, blood loss ≥ 500 mls, open conversion rate. 30-day readmission, morbidity and major morbidity were also outside the cutoff. Furthermore, for LH, postoperative stay, morbidity, major morbidity, reoperation and R1 resections were also beyond the benchmark cutoff. Finally, with regards to RH, open conversion rate and reoperation also exceeded the benchmark cutoff.

In the 2nd comparison cohort of low-risk cases performed at non-benchmark centers; for LLS, postoperative morbidity and major morbidity exceeded the cutoff. With regards to LH, postoperative stay, 90-day mortality and failure to rescue rates exceeded the benchmark values. Finally, for RH, blood loss ≥ 1000 mls, postoperative stay, readmission rate, major morbidity rate, reoperation rate and 90-day mortality were beyond the benchmark cutoffs.

Impact of center volume on benchmark cases

Twenty-one centers had an annual case volume of ≥50 L-LR/ annum and 13 centers had an annual case volume of < 50 cases/ annum. Comparison between outcomes of L-LR stratified by annual volume is summarized in **Table 5**. Centers performing ≥50 L-LR per annum had a significantly shorter operation time for LLS, LH and RH; lower 90-day morbidity for LH; lower major morbidity for LLS and LH; lower reoperation for LLS; lower 30-day readmission and R1 resection for RH; but increased median blood loss for LLS. Comparison between the proportion of benchmark cases in centers performing ≥50 L-LR/ annum with centers performing <50 cases/ annum demonstrated no significant difference between both groups [1008/2493 (40.4%) vs 250/605 (41.3%), P=0.690). There was no significant correlation between the proportion of benchmark cases and key

outcomes such as operation time, open conversion rate and postoperative morbidity (results not shown).

Geographical differences in benchmark cases

The proportion of non-benchmark cases performed in centers in Asia, Europe and Americas were 765/1440 (53.1%), 1016/1543 (65.8%) and 59/115 (48.7%), respectively. Comparison between Asian and non-Asian centers demonstrated a significantly higher proportion of benchmark cases in Asian centers (P<0.001). Comparison between Asian and non-Asian centers also demonstrated a significantly higher proportion of cases performed in centers with an annual case volume ≥50 cases/annum in Asian centers compared to non-Asian cemters [571/675 (84.6%) vs 432/583 (74.1%), P<0.001]

Table 6 summarizes the 15 benchmark outcomes stratified by the geographical location of the benchmark centers. In general, comparison between Asian versus non-Asian benchmark centers demonstrated superior outcomes in Asian centers in terms of significantly shorter operation time (LLS and LH), lower median blood loss (LLS and LH), lower open conversion rate (LH), lower 90-day morbidity and major morbidity (LLS, LH and RH). However, Asian centers were associated with a longer postoperative stay (LLS, LH and RH) and increased blood loss for RH.

Discussion

To our knowledge, this is the first attempt to identify global benchmark cut-offs for L-LR. In this study, we established 15 benchmark values for the short-term perioperative outcomes after L-LR based on 3 specific procedures representing each difficulty level of L-LR. The benchmark values were tested in 2 different cohorts of

patients, 1 in higher risk patients who underwent L-LR at the benchmark centers and 1 in low-risk patients who were operated in non-bench centers. The results of this study demonstrate that L-LR can be performed safely today in expert centers with excellent outcomes. Low difficulty procedures such as L-LLS can be performed with low morbidity, major morbidity, mortality and open conversion rate. For procedures of intermediate and high difficulty such as LH and RH, although mortality rate was low, these were still associated with significant morbidity, major morbidity and open conversion rate. These findings suggest that L-LLS is currently an established and mature procedure in benchmark centers but procedures of intermediate and high difficulty such as LH and RH may not have completely matured. It is also important to emphasize that these reported benchmarks values are supposed to reflect the best possible outcomes of L-LR today and were obtained from low risk cases performed at high volume expert centers. These values would serve as useful guide for centers and surgeons embarking on L-LR and would help to determine their progress along the learning curve.

Presently, despite the advantages if L-LR [28,29] and its increasing adoption worldwide [9] there remains limited data on the benchmark outcomes of L-LR with only 2 recently published studies to date [11,12]. However, the 2 studies [11,12] reporting benchmark outcomes of L-LR based on the French and Italian nation-wide studies have several major limitations which are worth highlighting. Firstly, as both studies analyzed outcomes of centers limited to a single country, this limited the generalization of the results [12]. Secondly, the sample size of L-LR in each study was modest compared to the present analysis. Hence, these 2 studies could not implement the stringent inclusion and exclusion criteria as in the present study.

Another major limitation of the French study [11] was the long study period spanning from 2000 to 2017. Hence, a significant proportion of the benchmark cases were performed during the pioneering phase of LLR and during a center's learning curve which would unlikely be representative of the best possible outcome of L-LR today [30]. This was evident from the reportedly high benchmark values for open conversion rate of ≤ 7.2% for L-LLS and ≤ 29.8% for L-RH reported in the study. The reported benchmark values for blood loss ≥1000 ml for L-LS and L-RH were also relatively high at ≤8.3% and ≤17.7% respectively. Similarly, the benchmark blood transfusion rate was ≤3.8% and ≤14.6%. In the Italian nationwide study [12], the authors used the Achievable Benchmark of Care (ABC) method to identify the best achievable outcomes in L-LR [31]. However, benchmark outcomes were only reported for 2 outcome indicators ie. overall morbidity and major morbidity. These benchmark outcomes were reporting according to the difficulty of L-LR utilizing the IMM score. Hence, a notable limitation of this study was that within each difficulty group in the IMM scale, each group is heterogenous and made up of a wide range of different types of L-LR making comparison of benchmark values difficult. For example, within the IMM III group, procedures such as right hepatectomy, segmentectomy of posterosuperior segments, central hepatectomy and extended left hepatectomy are grouped together although each of these would likely be associated with very different postoperative outcomes [15,18,32]. Furthermore, the authors also included cases which underwent concomitant intestinal resection which they demonstrated had a significant impact on outcomes. Subsequently, the Italian group reported their benchmark outcomes for L-LLS (n=341) and L-RH (n=167) whereby the reported benchmark

outcomes for morbidity, major morbidity and open conversion rate for L-LLS and L-RH were 4.5%, 0% and 0% and 17.3%, 4.1% and 8.3%, respectively [33].

Interestingly, the benchmark outcomes reported in the present study compared favorably to that reported recently by Rossler et al [8] for open liver surgery. The authors reported benchmark 90-day morbidity and major morbidity values of 31.2% and 8.1%, respectively in a cohort of 5202 living donor hemihepatectomies (4206 RH, 996 LH). This was unexpected, as one would expect poorer outcomes for hepatectomies performed for liver pathology such as malignancy due to the higher risk population and underlying liver disease compared to living donors. This was evident in our study population whereby the median age was 57 years compared to 31 years in the living donor group. Furthermore, 22% of our patients had liver cirrhosis and 13% had prior chemotherapy. It is difficult to explain this observation definitively although it is plausible that the advantages of laparoscopy over open surgery accounted for these favorable results.

In this study not unexpectedly, comparison between low-risk benchmark cases performed in benchmark expert centers with the 2 control groups (high-risk non-benchmark cases performed in benchmark expert centers and low-risk benchmark cases performed in non-benchmark centers) demonstrated inferior outcomes in the 2 control groups. Notably, the outcomes of high-risk cases performed in benchmark expert centers tended to deviate more from the benchmark values compared to the low-risk benchmark cases performed in non-benchmark centers. This observation suggests that patient and procedure risk level are major factors which affects the performance and achievement of pre-defined quality standards even in the presence of adequate expertise.

Several recent studies have demonstrated a volume-outcome relationship with regards to liver resections and specifically L-LR [8,12,19]. Although this study was not designed specifically to examine the impact of center volume on outcomes, we observed a significant influence of center volume on the perioperative outcomes of L-LR. When we arbitrarily stratified centers according to a cutoff of 50 L-LR cases/annum, the higher volume centers were associated with significantly superior perioperative outcomes such as lower operation time, postoperative morbidity and readmission rate. In this study, unlike previous benchmark studies on pancreatectomy [5] and liver transplant [6] and we did not observe a correlation between the proportion of benchmark cases performed in a center and outcomes after L-LR.

Similar to the results of a previous studies on liver resections [34]] and surgery for perihilar cholangiocarcinoma [23], we observed that L-LR performed in Asian centers were associated in general with better perioperative outcomes compared to the rest of the world in terms of significantly lower operation time, median blood loss, open conversion rate, 90-day morbidity and major morbidity. It is difficult to determine the exact reasons accounting for the better outcomes observed with Asian centers although it must be acknowledged that there remains the potential for residual confounding factors despite the benchmark approach being utilized in this study. Notably, the higher proportion of L-LR in Asia being performed in centers with an annual case volume ≥50 cases/ annum in this study was likely to be a major contributing factor for the better perioperative outcomes observed. The longer postoperative stay observed in Asian centers was not surprising as it is well-known that this is due to the differences in culture and health care systems including reimbursement.

There are several limitations associated with the current study which should be highlighted. Firstly, this is a retrospective study which is associated with the usual limitations of information bias although most of the centers had a prospective database. However, this limitation can only be mitigated by performing a prospective clinical trial. Secondly, at present although L-LR has been rapidly increasing worldwide [35-37], it is possible that the procedure has not completely matured even in many of the high-volume expert centers in this study especially for difficult resections such as L-RH. Hence, with the rapid evolution of L-LR, the current benchmark outcomes will need to be regularly updated in future. Thirdly, as this study focused on short-term perioperative outcomes; we could not report on long-term oncologic outcomes which would be an important benchmark indicator for L-LR as these are usually performed for malignancies. Fourthly, unlike previous benchmark studies only age and ASA score was used in this study as information on specific comorbidities and use of anticoagulation was not collected. Finally, the comprehensive complications index which is an important indicator of cumulative morbidity was not used in this retrospective study. This index should ideally be used in future benchmark studies to emphasize the importance of reporting on multiple complications in a single patient. Nonetheless despite these limitations, this is the first global international multi-center study to provide benchmark outcomes for L-LR. Another strength of this study is the large sample size, which enabled us to focus the analysis on a relatively homogenous group of low-risk patients undergoing 3 specific L-LR procedures: LLS, LH and RH. Furthermore, we could also apply a stringent inclusion criteria by excluding L-LR with various confounding factors such as multiple resections,

concomitant major surgery, previous liver resections (redo hepatectomy), huge tumors, portal hypertension and Childs B cirrhosis.

In conclusion, this large international multicentric study is the first to provide global benchmark values for L-LR. It provides an up-to-date reference regarding the “best achievable” results for L-LR for which centers adopting L-LR can use as a comparison to enable an objective assessment of performance gaps and learning curves. It may also allow meaningful comparison of outcomes between centers, countries and different surgical techniques.

Declarations

There was no funding for this study

We confirm all the authors are accountable for all aspects of the work

i) Dr Goh BK has received travel grants and honorarium from Johnson and Johnson, Olympus and Transmedic the local distributor for the Da Vinci Robot.

ii) Dr Marino MV is a consultant for CAVA robotics LLC.

iii) Johann Pratschke reports a research grant from Intuitive Surgical Deutschland GmbH and personal fees or non-financial support from Johnson & Johnson, Medtronic, AFS Medical, Astellas, CHG Meridian, Chiesi, Falk Foundation, La Fource Group, Merck, Neovii, NOGGO, pharma-consult Peterson, and Promedicis.

iv) Moritz Schmelzle reports personal fees or other support outside of the submitted work from Merck, Bayer, ERBE, Amgen, Johnson & Johnson, Takeda, Olympus, Medtronic, Intuitive.

v) Asmund Fretland reports receiving speaker fees from Bayer.

vi) Fernando Rotellar reports speaker fees and support outside the submitted work from Integra, Medtronic, Olympus, Corza, Sirtex and Johnson & Johnson.

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Figure 1. Proportion of benchmark cases performed across the 34 included benchmark centers.

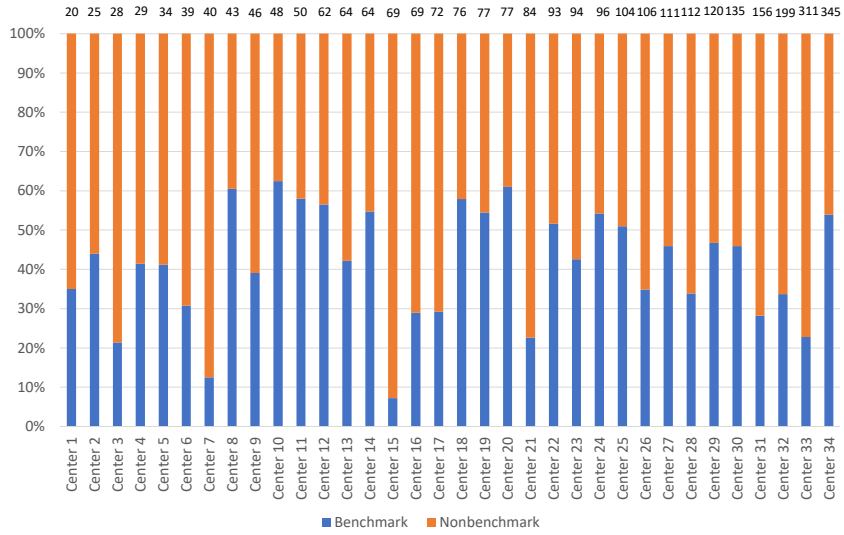

Table 1. Baseline clinicopathological features of the 1258 low risk patients operated in the 34 expert centers selected for benchmarking

	All L-LR N=1258	**LLS** N=659	**LH** N=306	**RH** N=293
Centers, n	34	34	34	34
Median body mass index, kg/cm^2 (IQR)[a]	24.1 (21.5-26.7)	24.0 (21.5-26.6)	24.0 (21.3-26.8)	24.4 (21.7-27.1)
Median age (IQR)	57 (49-65)	56 (47-64)	58 (48-64)	57 (47-63)
Male Sex, n (%)	696 (55.3)	362 (54.9)	175 (57.2)	159 (54.3)
ASA score, n (%) I II	 270 (21.5) 988 (78.5)	 133 (20.2) 526 (79.8)	 75 (24.5) 231 (75.5)	 62 (21.2) 231 (78.8)
Previous abdominal surgery, n (%)	372/1229 (29.6)	171 (26.9)	97 (31.7)	104 (35.5)
Concomitant minor surgery, n (%)	43 (3.4)	22 (3.3)	14 (4.6)	7 (2.4)
Malignancy, n (%)	885 (70.3)	426 (64.6)	213 (69.6)	246 (84.0)
HCC, n (%) CRLM, n (%) ICC, n (%) Other LM, n (%) Other malignancy, n (%)	471 (37.4) 263 (20.9) 69 (5.5) 62 (4.9) 20 (1.6)	251 (38.1) 110 (16.7) 24 (3.6) 32 (4.9) 9 (1.4)	115 (37.6) 54 (17.6) 28 (9.2) 10 (3.3) 6 (2.0)	105 (35.8) 99 (33.8) 17 (5.8) 20 (6.8) 5 (1.7)
Childs A cirrhosis, n (%)	271 (21.5)	152 (23.1)	58 (19.0)	61 (20.8)
Neoadjuvant chemotherapy for CRLM, n (%)	159 (12.6)	53 (8.0)	29 (9.5)	77 (26.3)
Multifocal tumors, n (%)	258/1257 (20.5)	89 (13.5)	64 (20.9)	105 (35.8)
Multiple resections, n (%)	37 (2.9)	0 (0.0)	20 (6.5)	17 (5.8)
Median tumor size (mm) (IQR)	36 (18-56)	35 (20-52)	35 (20-50)	41 (25-65)
Iwate score, n (%) Low Intermediate High Expert	 35 (2.8) 656 (52.1) 306 (24.3) 260 (20.7)	 35 (5.3) 622 (94.4) 2 (0.3) 0 (0)	 0 (0.0) 30 (9.8) 217 (70.9) 59 (19.3)	 0 (0.0) 4 (1.4) 87 (29.8) 201 (68.6)

[a] missing n = 42; [b] missing n =1

CRLM, colorectal liver metastases; HCC, hepatocellular carcinoma; ICC, intrahepatic cholangiocarcinoma; IQR, interquartile range; LM, liver metastases

Table 2. Clinical outcomes of the 1258 low risk patients operated in the 34 expert centers selected for benchmarking

	All L-LR N=1258	**LLS** N=659	**LH** N=306	**RH** N=293
Median operation time (IQR), min Missing data	200 (113-288) 1	145 (91-200) 0	245 (180-320) 1	330 (265-412) 0
Median estimated blood loss (IQR), cc Missing data	100 (0-225) 90	50 (50-150) 58	140 (50-300) 19	330 (200-500) 13
Blood loss ≥ 500 mls, %	144/1168 (12.3)	17/601 (2.8)	39/287 (13.6)	88/280 (31.4)
Blood loss ≥1000 mls, %	23/1168 (2.0)	1/601 (0.2)	6/287 (2.1)	18/280 (6.4)
Intraoperative blood transfusion, %	55 (4.4)	14 (2.1)	11 (3.6)	30 (10.2)
Open conversion, %	60 (4.8)	10 (1.5)	23 (7.5)	27 (9.2)
Postoperative 90-day morbidity, %	174 (13.8)	56 (8.5)	39 (12.8)	79 (27.0)
Postoperative 90-day major morbidity, %	51 (4.1)	8 (1.2)	13 (4.3)	30 (10.2)
Reoperation, %	18 (1.4)	4 (0.6)	6 (2.0)	8 (2.7)
30-day readmission, %	32 (2.5)	10 (1.5)	6 (2.0)	16 (5.5)
Median postoperative length of stay (IQR), d Missing data	5 (4-7) 4	5 (4-6) 0	6 (5-7) 1	6.5 (5-8) 3
R1 resection (<1mm) (malignancy only)	57/1197 (4.5)	18/424 (4.2)	11/212 (5.2)	28/245 (11.4)
Failure to rescue, n (%)	3 (5.4)	1 (12.5)	0(0.0)	2 (6.7)
30-day mortality, %	2 (0.2)	1 (0.2)	0(0-0)	1 (0.3)
90-day mortality, %	3 (0.2)	1 (0.2)	0(0-0)	2 (0.7)

Table 3. Fifteen benchmark outcome measures after LLR in 1258 low risk cases from 34 international high-volume centers

	LLS		**LH**		**RH**	
Variables	Median across 34 centers (range)	Benchmark cutoff (75^{th} percentile)	Median across 34 centers (range)	Benchmark cutoff (75^{th} percentile)	Median across 34 centers (range)	Benchmark cutoff (75^{th} percentile)
Operation time, min	167 (60-412)	209.5	270 (120-703)	302	358 (180-742)	426
Estimated blood loss, cc	50 (15-353)	100	150 (0-900)	300	350 (50-800)	400
Blood loss ≥ 500 mls, %	0 (0-18.2)	3.2	6.7 (0-58.3)	20	25 (0-100)	47.1
Blood loss ≥ 1000 mls, %	0 (0-3.2)	0	0 (0-25)	0	0 (0-30.8)	0
Intraoperative blood transfusion, %	0 (0-15.7)	0	0 (0-25)	7.1	0 (0-100)	10.5
Open conversion, %	0 (0-11.1)	2.1	0 (0-35.7)	13.4	0 (0-50)	13.0
Postoperative 90-day morbidity, %	6.3 (0-40)	11.1	9.1 (0-66.7)	20	23.1 (0-100)	50
Postoperative major morbidity, %	0 (0-16.7)	0	0 (0-33.3)	7.1	6.3 (0-50)	20
Reoperation, %	0 (0-16.7)	0	0 (0-33.3)	0	0 (0-50)	0
30-day readmission, %	0 (0-10)	0	0 (0-22.2)	0	0 (0-50)	8.3
Postoperative length of stay	4 (2-10)	5	5.5 (3-16.5)	7	6.5 (2-32)	7.5
R1 (<1 mm) resection (malignancy only)	0 (0-66.7)	7.1	0 (0-100)	10.5	0 (0-100)	18.2
Failure to rescue	0(0-0)	0	0(0-0)	0	0 (0-100)	0
30-day mortality, %	0 (0-3.3)	0	0(0-0)	0	0 (0-5.3)	0
90-day mortality, %	0 (0-3.3)	0	0(0-0)	0	0 (0-5.3)	0

Table 4. Comparison of the 15 benchmark outcome measures in 2 cohorts: non-bench mark cases in the benchmarking centers and benchmark low risk cases in the centers which did not meet our inclusion criteria as a high-volume expert center

	LLS			**LH**			**RH**		
Variables	High risk non-benchmark cases N=884	Benchmark patients in non-benchmark centers N = 58	Benchmark cutoff	High risk non-benchmark cases N = 449	Benchmark patients in non-benchmark centers N = 37	Benchmark cutoff	High risk non-benchmark cases N = 507	Benchmark patients in non-benchmark centers N = 34	Benchmark cutoff
% benchmark cases	NA	28	NA	NA	28.5	NA	NA	40.5	NA
Operation time, min (IQR)	169 (115)	180 (106)	209.5	275 (139)	225 (119)	302	315 (128)	345 (169)	427
Intraop blood transfusion, n (%)	**4.2**	0	0	**13.2**	0	7.1	**15.6**	2.9	10.5
Median blood loss, mls	100 (200)	40 (100)	100	200 (300)	130 (200)	300	300 (327)	225 (250)	400
Blood loss ≥ 500 mls, n (%)	**9.4**	1.7	3.2	18.2	10.8	20	30.5	20.6	47.1
Blood loss ≥ 1000 mls, n (%)	**3.0**	0	0	**6.3**	0	0	**9.9**	**5.9**	0
Open conversion, n (%)	**4.0**	1.7	2.1	11.1	5.4	13.4	**13.8**	8.8	13.0
Postoperative LOS, days (IQR)	5 (4)	5 (3)	5	**6 (6)**	**7 (4)**	5	7 (5)	**8 (7)**	7.5
30-day readmission, n (%)	**3.2**	**1.7**	0	5.6	5.4	7	8.1	**11.8**	8.3
90-day morbidity, n (%)	**16.9**	**15.5**	11.1	**23.4**	18.9	20	38.5	35.5	50
Postoperative major morbidity, n (%)	**3.8**	**6.9**	0	**7.4**	5.4	7.1	17.8	**26.5**	20

Reoperation, n (%)	**1.6**	**1.7**	0	**1.1**	0	0	**3.4**	**11.8**	0
30-day mortality, n (%)	**0.6**	0	0	**0.9**	0	0	**1.0**	0	0
90-day mortality, n (%)	**0.9**	0	0	**0.9**	**5.4**	0	**1.8**	**2.9**	0
Failure to rescue, n (%)	**17.6**	0	0	**9.1**	**33.3**	0	**10.0**	0	0
R1 (<1 mm) resection for malignancy (%)	6.7	4.3	7.1	**12**	5.6	10.5	13	8.3	18.2
Bold indicates values outside benchmark cutoffs									

Table 5. Comparison between the 15 benchmark outcome measures in low risk cases performed at the 34 benchmark centers stratified by center annual volume

	LLS			LH			RH		
Variables	Center volume ≤ 50/yr N=144	Center volume > 50/yr N=515	P-value	Center volume ≤ 50/yr N=58	Center volume > 50/yr N=248	P-value	Center volume ≤ 50/yr N=53	Center volume > 50/yr N=240	P-value
Operation time, min (IQR)	153 (97)	144 (108)	**0.023**	290 (143)	240 (142)	**<0.001**	365 (204)	330 (156)	**0.006**
Intraop blood transfusion, n (%)	1 (0.7)	13 (2.5)	0.323	0	11/247 (4.5)	0.133	4 (7.5)	26 (10.8)	0.620
Median blood loss, mls (IQR)	50 (80)	50 (120)	**0.010**	100 (194)	150 (250)	0.219	350 (453)	300 (300)	0.720
Blood loss ≥ 500 mls, n (%)	0	17/494 (3.4)	0.053	4 (8.5)	35 (14.6)	0.267	15/41 (36.6)	73/239 (30.5)	0.441
Blood loss ≥ 1000 mls, n (%)	0	1/494 (0.2)	1.000	0	4 (1.7)	1.000	1/41 (2.4)	17/239 (7.1)	0.487
Open conversion, n (%)	0	10 (1.9)	0.129	1 (1.7)	22 (8.9)	0.092	7 (13.2)	20 (8.3)	0.267
Postoperative LOS, days (IQR)	4 (2)	5 (2)	0.244	6 (2)	6 (2)	0.979	7 (3)	6 (3)	0.800
30-day readmission, n (%)	1 (0.7)	9 (1.7)	0.699	2 (3.4)	4 (1.6)	0.319	6 (11.3)	10 (4.2)	**0.049**
90-day morbidity, n (%)	17 (11.8)	39 (7.6)	0.107	14 (24.1)	25 (10.1)	**0.004**	18 (34.0)	61 (25.4)	0.205
Postoperative major morbidity, n (%)	5 (3.5)	3 (0.6)	**0.015**	6 (10.3)	7 (2.8)	**0.011**	8 (15.1)	22 (9.2)	0.212
Reoperation, n (%)	3 (2.1)	1 (0.2)	**0.034**	3 (5.2)	3 (1.2)	0.084	1 (1.9)	7 (2.9)	1.000
30-day mortality, n (%)	1 (0.7)	0	0.219	0	0	NC	0	1 (0.4)	1.000
90-day mortality, n (%)	1 (0.7)	0	0.219	0	0	NC	0	2 (0.8)	1.000
Failure to rescue, n (%)	1 (20.0)	0	0.408	0	0	NC	0	2 (9.1)	1.000
R1 (<1 mm) resection for malignancy (%)	5 (3.5)	13 (2.5)	0.564	3 (5.2)	8 (3.2)	0.443	10 (18.9)	18/239 (7.5)	**0.011**

Table 6. Summary of the 15 benchmark outcome measures in low risk cases performed at the 34 benchmark centers stratified by geographical location: Americas, Europe and Asia and statistical comparison between Asian and non-Asian centers

	LLS				**LH**				**RH**			
Variables	Americas N=29	Europe N=274	Asia N=356	P-value	Americas N=14	Europe N=106	Asia N=186	P-value	Americas N=13	Europe N=147	Asia N=133	P-value
Operation time, min (IQR)	160 (90)	180 (100)	115 (85)	**<0.001**	380 (131)	271 (131)	220 (136)	**<0.001**	480 (188)	330 (130)	325 (168)	0.432
Intraop blood transfusion, n (%)	0	4 (1.5)	10 (2.8)	0.279	0	6 (5.7)	5 (2.7)	0.349	2 (15.4)	13 (8.8)	15 (11.3)	0.593
Median blood loss, mls (IQR)	50 (48)	100 (170)	50 (50)	**0.035**	150 (225)	200 (300)	100 (150)	**<0.001**	350 (688)	300 (300)	400 (350)	**0.046**
Blood loss ≥ 500 mls, n (%)	0	6 (2.8)	11 (3.1)	0.632	2 (14.3)	19 (21.8)	18 (9.7)	**0.011**	5 (41.7)	33 (24.4)	50 (37.6)	**0.035**
Blood loss ≥ 1000 mls, n (%)	0	0	1 (0.3)	1.000	0	2 (2.3)	2 (1.1)	0.615	1 (8.3)	4 (3.0)	13 (9.8)	**0.048**
Open conversion, n (%)	0	6 (2.2)	4 (1.1)	0.525	2 (14.3)	13 (12.3)	8 (4.3)	**0.008**	0	14 (9.5)	13 (9.8)	0.763
Postoperative LOS, days (IQR)	3 (2)	4 (2)	5 (3)	**<0.001**	5 (2)	5 (3)	6.5 (3)	**<0.001**	6 (2)	6 (4)	7 (4)	**<0.001**
30-day readmission, n (%)	0	3 (1.1)	7 (2.0)	0.356	0	4 (3.8)	2 (1.1)	0.215	0	10 (6.8)	6 (4.5)	0.514
90-day morbidity, n (%)	1 (3.4)	32 (11.7)	23 (6.5)	**0.042**	1 (7.1)	22 (20.8)	16 (8.6)	**0.007**	4 (30.8)	50 (34.0)	25 (18.8)	**0.004**
Postoperative major morbidity, n (%)	0	7 (2.6)	1 (0.3)	**0.027**	1 (7.1)	8 (7.5)	4 (2.2)	**0.038**	2 (15.4)	20 (13.6)	8 (6.0)	**0.030**
Reoperation, n (%)	0	4 (1.5)	0	**0.044**	1 (7.1)	3 (2.8)	2 (1.1)	0.215	0	5 (3.4)	3 (2.3)	0.732
30-day mortality, n (%)	0	1 (0.4)	0	NC	0	0	0	NC	0	1 (0.7)	0	1.00
90-day	0	1	0	NC	0	0	0	NC	0	2	0	0.50

mortality, n (%)		(0.4)								(1.4)		3
Failure to rescue, n (%)	NC	1 (14.3)	0	1.000	NC	NC	NC	NC	0	2 (10.0)	0	1.000
R1 (<1 mm) resection for malignancy (%)	2 (6.9)	10 (3.7)	6 (1.7)	0.072	0	7 (6.7)	4 (2.2)	0.116	1 (7.7)	20 (13.7)	7 (5.3)	**0.022**
P-value: comparison between Asian vs non-Asian centers												