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Propensity-score matched and coarsened-exact matched analysis comparing robotic and laparoscopic major hepatectomies: an international multicenter study of 4822 cases

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Abstract

Objective: To compare the outcomes between robotic major hepatectomy (R-MH) and laparoscopic major hepatectomy(L-MH).

Background: Robotic techniques may overcome the limitations of laparoscopic liver resection. However, it is unknown whether robotic major hepatectomy (R-MH) is superior to laparoscopic major hepatectomy (L-MH).

Methods: This is a post hoc analysis of a multicenter database of patients undergoing R-MH or L-MH at 59 international centers from 2008 to 2021. Data on patient demographics, center experience/ volume, perioperative outcomes and tumor characteristics were collected and analyzed. 1:1 propensity score matched (PSM) and coarsened-exact matched (CEM) analysis was performed to minimize selection bias between both groups

Results: A total of 4822 cases met the study criteria, of which 892 underwent R-MH and 3930 underwent L-MH. Both 1:1 PSM, (841 R-MH vs 841 L-MH) and CEM (237 R-MH vs 356 L-MH) were performed. R-MH was associated with significantly less blood loss (PSM:200.0 [IQR:100.0, 450.0] ml vs. 300.0 [IQR:150.0, 500.0] ml; *P*=0.012; CEM:170.0 [IQR: 90.0, 400.0] ml vs. 200.0 [IQR:100.0, 400.0] ml; *P*=0.006), lower rates of Pringle maneuver application (PSM: 47.1% vs 63.0%; *P*<0.001; CEM: 54.0% vs 65.0%; *P*=0.007) and open conversion (PSM: 5.1% vs 11.9%; *P*<0.001; CEM: 5.5% vs 10.4%, *P*=0.04) compared to L-MH. On subset analysis of 1273 cirrhotic patients, R-MH was associated with a lower postoperative morbidity rate (PSM: 19.5% vs 29.9%; *P*=0.02; CEM 10.4% vs 25.5%; *P*=0.02) and shorter postoperative stay (PSM: 6.9 [IQR:

5.0, 9.0] days vs. 8.0 [IQR: 6.0 11.3] days; *P*<0.001; CEM 7.0 [IQR: 5.0, 9.0] days vs. 7.0 [IQR: 6.0, 10.0] days; *P*=0.047).

Conclusion: This international multicenter study demonstrated that R-MH was comparable to L-MH in safety and was associated with reduced blood loss, lower rates of Pringle maneuver application and conversion to open surgery.

Key words: Laparoscopic liver resection; Robotic liver resection; right hepatectomy; extended right hepatectomy; major hepatectomy

Introduction

With the application of laparoscopic techniques to liver resection(LR) in the early 1990s,[1] the extent of resection for laparoscopic liver resection(LLR) has become increasingly extensive, including most of the region from the left lateral segment to the posterosuperior segment.[2-4] Various international consensuses also recommended LLR as the standard approach for benign and malignant liver tumors, with the advantages of minimally invasive and rapid recovery.[5-9] However, the limited motion and flexibility of laparoscopic instruments, the high technical skills required, and its long learning curve have resulted in laparoscopic major hepatectomy(L-MH) remaining in the exploratory phase in many centers and it being associated with a significant open conversion rate. [10,11]

The robotic system was designed to overcome the limitations of traditional laparoscopic surgery.[12,13] Its increased dexterity from the stable endo-wrist instruments enables precise dissection and complex manipulation with high-definition three-dimensional (3D) visualization.[14] Specifically to MH, this theoretically enables accurate dissection of the vessels at the hilar and hepatocaval region, as well as easier fine suturing especially of torn venous tributaries during intraoperative bleeding.[15] In recent years, there have been an increasing number of studies comparing LLR and robotic liver resection (RLR) which on the whole have demonstrated mixed results in terms of advantages of the perioperative outcomes between the two approaches.[16-21] It has been suggested that RLR may increase the proportion of major hepatectomy (MH) performed in a purely minimally invasive manner and have some advantages in patients with higher difficulty level compared to LLR.[22,23] However, these studies were mostly from small single single-center experience. Preliminary early data from our international collaboration involving 21 centers had suggested there were some advantages with the robotic platform with regards to right hepatectomy (RH), right posterior sectionectomy (RPS) and right anterior sectionectomy (RAS).[15,24-26] However, a limitation of these studies was that a center's learning curve experience and annual volume were not taken into consideration.

Hence with these limitations in mind, we performed this large international multicenter study with the primary objective of comparing the outcomes of robotic major hepatectomy (R-MH) with L-MH. We also sought to compare the outcomes of both modalities in the subset of patients with cirrhosis.

Methods

This is an international multicenter retrospective case-control analysis of patients undergoing pure L-MH or R-MH at 59 centers between 2008-2021. All institutions obtained their respective approvals according to their local center's requirements. This study was approved by the Singapore General Hospital Institution Review Board and the need for patient consent was waived. The deidentified data were collected in the individual centers. These were collated and analyzed centrally at the Singapore General Hospital.

In this study, only patients who underwent pure L-MH or R-MH were included. Laparoscopic-assisted (hybrid) and hand-assisted laparoscopic resections were excluded. Similarly, patients undergoing donor hepatectomy for transplant, associating liver partition and portal vin ligation for staged hepatectomy (ALPPS) were excluded. Patients who had concomitant major operations such as bilio-enteric anastomosis, portal vein ligation, colectomies, stoma reversals, bile duct explorations, gastrectomies and splenectomies were also excluded. Notably, hilar lymph node dissection and concomitant minor surgeries such as hernia and ablations were included. Patients with multiple simultaneous LRs were included only if they had 1 concomitant minor LR.

Definitions

MHs included conventional MHs and technical MHs in this study. Conventional MHs was defined according to the 2000 Brisbane classification as resection of 3 or more segments and included left/extended left hepatectomy, right/extended right hepatectomy (RH/ERH) and central hepatectomy.[27] Technical MHs included RAS and RPS as defined previously.[28] The recently proposed "New World" terminology for liver resections was not used as this definition was not used in most center's prospective databases.[29] Diameter of the largest lesion was used in cases of multiple tumors. Post-operative complications were recorded for up to 30 days or during the same hospitalization and included 30-day readmissions. These were classified according to the Clavien-Dindo classification.[30] The difficulty of resections was graded according to the Iwate score and Institute Mutualiste Montsouris (IMM) scoring system.[31,32] In order to mitigate confounding factors from historical bias and center experience, resections were classified into 3 periods: 2008-2012, 2013-2017 and 2018-2021. The average annual volume of minimally invasive LRs (MILR) performed at each center during the 3 periods of time was also recorded and each center was allocated to 1 of the following groups: < 20 cases/year, 20-75 cases/year and > 75 cases/year. Furthermore, the first 50 MILRs performed at each institution were recorded and were considered as cases performed during a center's learning curve.[33]

Statistical analysis

Propensity-score matching (PSM) was performed using a 1:1 nearest neighbour matching algorithm without replacement with distances determined by logistic regression. PSM was performed based on the following variables: gender, year of resection, center's annual case volume, cases performed during the learning curve (first 50 cases), age at operation, American Society of Anesthesiologists (ASA) status, size of tumour, single or multiple tumours, malignant or benign tumours, cirrhosis with Child Pugh score, presence of portal hypertension, previous liver surgery, previous open liver surgery, previous abdominal operation, multiple LRs, concomitant minor non-cholecystectomy operation, hilar lymph node dissection, histological diagnosis, posterosuperior segments, Iwate difficulty grade and IMM procedure code. Continuous variables such as age and tumour size were dichotomized into categorical variables in the logistic regression model.

Calibration, goodness-of-fit and discrimination were assessed with Lemeshow and Hosmer and area-under receiver operating curves with bootstrap validation (2,000 stratified bootstrap replicates were utilized). Sensitivity analyses were undertaken using coarsened exact matching (CEM), which identifies approximately-exact matches between patients and hence minimize co-variate imbalance and confounding bias.

Covariate distributions between patients undergoing robotic or laparoscopic right hepatectomy were found to be balanced after conditioning on the propensity score, where a difference of < 0.1 in absolute standard mean difference after matching was considered to indicate a good balance. In the unmatched cohort, comparisons of patient characteristics, and peri- and post-operative details between patients undergoing robotic or laparoscopic right hepatectomy were performed using Mann-Whitney U test for continuous variables, while Fisher's exact test and Pearson's χ2 test were used for categorical variables. Comparisons in the matched cohorts took into account the paired nature of the data; hence, paired analyses such as Wilcoxon signed-rank test, McNemar test and McNemar-Bowker test were respectively used for continuous, 2-by-2 categorical and 3-by-3 categorical variables. All analyses were done in R-4.1.0 with package 'MatchIt' and a two-sided $P < 0.05$ were regarded to indicate statistical significance.

Results

Comparison Between R-MH and L-MH in the Unmatched Cohorts

A total of 4822 cases met the study criteria, of which 892 underwent R-MH and 3930 underwent L-MH during the study period. Patient demographics and clinicopathological data are shown in **Supplementary Table 1**, Supplemental Digital Content 1, http://links.lww.com/SLA/E566. R-MH group was associated with a younger median patient age (61.0 [IQR: 51.0, 69.0] vs. 62.9 [IQR: 53.0, 71.0]; $P = 0.002$), a higher proportion of lower center experience (≤ 50 cases) (8.3% vs. 3.3%; $P < 0.001$), and a higher proportion of patients with ASA score III/IV (36.1% vs. 24.7%; $P < 0.001$). Between R-MH and L-MH, there was also a significant difference in the time period when the resection was undertaken ($P < 0.001$), and in the average center annual volume ($P < 0.001$). Of note, a higher proportion of R-MH were performed in 2018-2021 compared to L-MH (59.9% vs 45.6%). Likewise, a higher proportion of R-MH were performed in centers with <20 cases/year compared to L-MH (12.7% vs 5.7%).

Additionally, there were significantly higher proportions of patients in the R-MH group with benign tumor (19.5% vs. 16.4%; $P = 0.03$), concomitant minor operative procedures (10.7% vs. 6.5%; $P < 0.001$), higher rates of hilar lymph node dissection

(5.5% vs. 3.6%; *P* = 0.009) and high Iwate difficulty grade surgeries (34.1% vs 30.1%; *P* = 0.02). The L-MH group had significantly higher proportion of patients with previous liver surgery (7.1% vs. 5.0%; *P* = 0.03), multifocal tumors (30.3% vs. 20.9%; *P* < 0.001), and multiple concomitant LRs (7.3% vs. 3.5%; *P* < 0.001) **(Supplementary Table 1**, Supplemental Digital Content 1, http://links.lww.com/SLA/E566**).**

The perioperative outcomes in the unmatched cohort are presented in **Table 1**. The R-MH group was associated with less blood loss (median [IQR], 200.0 [100.0, 450.0] vs. 300.0 [150.0, 500.0]); *P* < 0.001), lower rates of blood loss ≥ 500ml (23.7% vs. 29.6%; *P* = 0.001), lower frequency of the application of Pringle maneuver (47.6% vs. 60.4%; *P* < 0.001), lower rates of open conversion (5.3% vs. 10.5%; *P* < 0.001) and shorter postoperative stay (median [IQR], 6.1 [4.8, 9.0] vs. 7.0 [5.0, 10.0]; *P* < 0.001). The two groups did not differ with regards to operative time, rate of blood transfusion, morbidity, major morbidity, reoperation, 30-day readmission, 30-day mortality, in-hospital mortality and 90-day mortality **(Table 1).**

Comparison Between R-MH and L-MH in the Matched Cohorts

After a 1:1 PSM, 841 patients who underwent R-MH was matched to 841 patients who underwent L-MH. After CEM, 237 patients who underwent R-MH was matched to 356 patients who underwent L-MH. Both groups were well balanced in demographics and tumor characteristics in the matched cohorts by PSM and CEM **(Supplementary Table 1**, Supplemental Digital Content 1, http://links.lww.com/SLA/E566**; eFigures S1-3 in Supplement**, Supplemental Digital Content 2, http://links.lww.com/SLA/E567**).**

There were no significant differences in terms of operative time, morbidity, major morbidity, reoperation, readmission and mortality (*P* > 0.05) **(Table 1).** R-MH was associated with significantly less blood loss compared to L-MH (PSM 200.0 [IQR: 100.0, 450.0] ml vs. 300.0 [IQR: 150.0, 500.0] ml; *P* = 0.01; CEM 170.0 [IQR: 90.0, 400.0] ml vs. 200.0 [IQR: 100.0, 400.0] ml; *P* = 0.006). However, due to the relatively low blood loss in both groups, there was no significant difference in the rates of patients with blood loss ≥ 500 ml and intraoperative blood transfusion between both groups. Postoperative stay was shorter in the R-MH group than in the L-MH group on PSM (6.1 [IQR: 4.3, 9.0] days vs. 7.0 [IQR: 5.0, 9.0] days, *P* = 0.002) however the magnitude of difference was small and shown to be insignificant on CEM (6.8 [IQR: 4.6, 9.0] days vs. 7.0 [IQR: 5.0, 8.0] days; *P* = 0.61). R-MH was associated with lower rates of Pringle maneuver application and open conversion compared to L-MH, and these differences were significant on both PSM (47.1% vs. 63.0%; *P* < 0.001; 5.1% vs. 11.9%; *P* < 0.001) and CEM (54.0% vs. 65.0%; *P* = 0.007; 5.5% vs 10.4%, *P* = 0.04) **(Table 1).**

Comparison Between R-MH and L-MH in the Subset of Patients with Cirrhosis

We performed subset analyses of 1273 patients with cirrhosis. There were significant differences in BMI, year of resection, average center annual volume, rates of cumulative center experience ≤ 50 cases, ASA score III/IV, multifocal tumor and IMM classification between the two groups in the unmatched cohort **(Supplementary Table 2**, Supplemental Digital Content 1, http://links.lww.com/SLA/E566**).** After PSM and CEM, the baseline clinicopathological characteristics of cirrhotic patients in the R-MH and L-MH groups were comparable **(Supplementary Table 2**, Supplemental Digital Content 1, http://links.lww.com/SLA/E566**; eFigures S4-6 in Supplement**, Supplemental Digital Content 2, http://links.lww.com/SLA/E567**).**

There was no longer a significant difference in blood loss (median [IQR], 200.0 [100.0, 600.0] ml vs. 300.0 [150.0, 585.0] ml; *P* = 0.004) after matching. On PSM, the R-MH group had a lower rate of major morbidity (4.1% vs. 9.5%; *P* = 0.03) compared to the L-MH group. However, this was insignificant on CEM (3.0% vs. 3.7%; *P* = 1.00). R-MH was associated with a significantly lower postoperative morbidity rate (PSM 19.5% vs. 29.9%; *P* = 0.02; CEM 10.4% vs. 25.5%; *P* = 0.02) and shorter length of postoperative stay (PSM 6.9 [IQR: 5.0, 9.0] days vs. 8.0 [IQR: 6.0, 11.3] days; *P* < 0.001; CEM 7.0 [IQR: 5.0, 9.0] days vs. 7.0 [IQR: 6.0, 10.0] days; *P* = 0.047) on both PSM and CEM. There was no significant difference in other perioperative outcomes between the two groups **(Supplementary Table 3**, Supplemental Digital Content 1, http://links.lww.com/SLA/E566**).** Missing values are summarized in **Supplementary Table 4**, Supplemental Digital Content 1, http://links.lww.com/SLA/E566**.**

Discussion

This international multicenter PSM and CEM study analyzed a relatively large number of patients undergoing R-MH and L-MH. It demonstrated that R-MH was associated with lower blood loss, lower frequency of the use of Pringle maneuver and lower open conversion rate compared to L-MH. R-MH and L-MH had comparable safety as evidence by the similar postoperative morbidity and mortality rates. In the subset of patients with cirrhosis, R-MH had similar short-term outcomes as L-MH, but with a significantly lower postoperative morbidity rate.

With the development of minimally invasive technique, laparoscopy has been increasingly used for liver resections. Previous studies have shown that LLR is associated with a shorter hospital stay and lower postoperative morbidity compared with open surgery. [34,35] Hence, some proponents have recommended LLR as the standard treatment for benign and malignant liver tumors .[5-8] However, LLR especially with regards to MH is a complex and technically demanding procedure with a steep learning curve that requires extensive training and experience, and is therefore only performed in high-volume centers and by experienced surgeons.[28,36]

Presently, there is some evidence suggesting that robotic surgery when applied to LR may overcome the limitations of laparoscopic surgery and is associated with a shorter learning curve.[33] Several previous studies demonstrated no significant difference in perioperative and oncological outcomes between RLR and LLR, with similar survival outcomes for malignancies.[16-21] However, a recent meta-analysis comparing 950 RLR and 1680 LLR patients demonstrated that the robotic technique was associated with less blood loss and lower readmission rate.[37] It is worth noting that the proportion of MH in the above studies was only 10-20% due to the high technical requirements of MH. Chong et al. compared 107 RLR vs. 94 LLR patients and found that the use of the robotic system enabled a higher proportion of minimally invasive hepatectomies of a higher difficulty level to be performed.[22] Cipriani et al. compared 288 RLR vs. 864 LLR patients after 1:3 PSM and concluded that RLR had lower blood loss, lower conversion rates and blood transfusion rates in the high difficulty group.[23] Tsung et al. also showed that the robotic approach increased the percentage of minimally invasive MHs from 7.1% to 81% compared to laparoscopy.[21] Although several studies have previously compared the outcomes of R-MH and L-MH, these studies had relatively small sample sizes and were mostly single-center experience.[38-40]

Data on blood loss from previous studies comparing R-MH and L-MH have provided mixed results. Chiow et al. compared 96 R-RPS and 244L-RPS and demonstrated that R-RPS was associated with lower blood loss than L-RPS.[26] Similarly, a meta-analysis comparing RLR and LLR found that robotic surgery was associated with less blood loss than LLR in a subgroup analysis of MHs.[41] However, a recent systematic review comparing 225 R-MH and 300 L-MH showed no significant differences in blood loss [38], which was consistent with the results of another multicenter study comparing R-RH/ERH and L-RH/ERH.[41] The theoretical advantages of the robotic system such as the magnified 3-d view, stable and dexterous endo-wrist instruments may facilitate identification, dissection and control of extrahepatic hilar, short hepatic veins and intrahepatic vessels which are critical steps during the performance of most MH. Additionally, it also facilitates intracorporeal fine suturing to be easily performed which allows for timely hemostasis in the event of intraoperative bleeding.[42,43] These advantages may contribute to the reduced blood loss and lower open conversion rate.

The Pringle maneuver is the simplest and standard technique of inflow occlusion and is effective in reducing intraoperative bleeding during hepatectomy.[44] Since R-MH was able to reduce blood loss in this study, the rate of Pringle maneuver application was accordingly lower than L-MH, which is consistent with a multicenter study comparing R-MH and L-MH.[39] Intraoperative bleeding is the main reason for open conversion in minimally invasive surgery.[45] In the present study, the conversion rate was significantly lower for R-MH than that of L-MH, even after PSM and CEM. This may possibly be attributed to the advantages of the robotic approach in reducing and controlling intraoperative bleeding. These findings were consistent with 2 recent international multicenter studies analyzing R-RH/ERH vs. L-RH/ERH and R-RPS vs. L-RPS, respectively, which also demonstrated that the robotic approach was associated with a lower open conversion rate compared to laparoscopy.[26,43]

In the setting of liver cirrhosis, hepatectomy has been considered a major challenge, even for experienced liver surgeons.[46] Patients with cirrhosis often have stiff, fibrotic parenchyma, which makes liver resection especially MH more challenging. Factors such as portal hypertension, thrombocytopenia and impaired coagulation function may lead to significant intraoperative and postoperative bleeding. Due to the impaired regenerative capacity of the cirrhotic liver after surgery, patients with cirrhosis also have a higher risk of serious complications such as refractory ascites, infection, and liver failure. Nonetheless, several studies including a recent meta-analysis have demonstrated the advantages of LLR over OLR even in patients with cirrhosis.[46-50] The recent meta-analysis comprising 690 LLR and 928 OLR demonstrated that laparoscopy was associated with less operative time, lower rates of overall and major complications, and shorter length of hospital stay.[48] This may be attributed to the fact that small abdominal incisions cause less disruption of the collateral circulation and lymphatic flow in the abdominal wall, and laparoscopic surgery does not require extensive mobilization, allowing more perihepatic collateral vessels to be preserved.[46] These advantages of LLR over OLR were also demonstrated in an international multicenter study of patients with Childs B cirrhosis.[50]

Of note, there has been no study to date comparing R-MH versus L-MH in patients with cirrhosis. In this study, we found that in the subset of patients with cirrhosis, R-MH was associated with a significantly lower postoperative morbidity rate and postoperative stay, while there was no significant difference between the two groups in terms of blood loss, operative time, length of stay, and rates of open conversion, major morbidity, and mortality.

To our knowledge, this is the largest study to date comparing between R-MH and L-MH. The large sample size, enabled matching for multiple baseline characteristics. Another strength of this study, was we also attempted to control for confounding factors related to the learning curve by including year of resection, center's cumulative experience with the first 50 cases and center annual volume.[13,24]

There are several limitations of this study which should be highlighted. First, the nonrandomized retrospective study design was subject to inevitable information and selection bias. Although PSM and CEM analyses were performed to minimize baseline differences between the two groups, there were still unmeasured confounders that may affect the results in the absence of randomization. Second, as this was an international multicenter study, there was substantial heterogeneity in terms of patient selection, surgeon/center experience, surgical technique and perioperative treatment among the centers. Nonetheless, these results are reflective of real-world data and contribute to the generalized applicability of this study. A third major limitation was that although we could control for center experience, individual surgeon experience within each center which is a potential major confounding factor was not known. It is conceivable that a higher proportion of R-MH cases were performed by more experienced liver surgeons with a special interest in MILR accounting for the observed advantages of R-MH such as lower open conversion rate and reduced blood loss observed in this study. Many surgeons who performed R-MH may have prior experience with laparoscopic surgery. The easier accessibility and lower costs of laparoscopy over robotic surgery may have also enabled more surgeons including less experienced surgeons to attempt laparoscopic rather than robotic surgery. The lower rate at which the Pringle maneuver was used for R-MH may be the result of variations in practice – routine versus selective Pringle maneuver between surgeons or may be due to residual selection bias which could not be mitigated completely by the matching process. Lastly, the combination of variables selected for the PSM analysis only discriminated patients between the treatment arms to a moderate extent (AUROC=0.673 for the overall cohort, 0.693 for patients with cirrhosis). This may have inadvertently compromised the integrity of the propensity-score computed for each participant, and subsequent downstream matching of participants. Nonetheless, the comparison of outcomes from the CEM analysis demonstrate largely concordant findings to the PSM analysis.

Conclusion

In conclusion, this large, international multicenter, match-controlled study demonstrated that R-MH was comparable to L-MH in safety and was associated with significantly lower blood loss, lower rate of application of the Pringle maneuver and lower open conversion rate. In patients with cirrhosis, R-MH was associated with significantly lower overall morbidity and postoperative length of stay compared to L-MH.

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Data access

Data will be available from the corresponding author on reasonable request. It is not available publicly due to ethical and privacy concerns.

Declarations

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.

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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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Table 1. Comparison of perioperative outcomes between R-MH and L-MH

Remarks: After matching, good balance was found amongst baseline covariates between arms (all absolute standard mean difference <0.1).

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Abbreviations: ASA, American Society of Anesthesiologists; Abdo, abdominal; CRLM, colorectal liver metastasis; LM, liver metastasis; op, operation; IMM, Institut Mutualiste Montsouris; Surg, surgery; RAS, right anterior sectionectomy; ELH, extended left hepatectomy; ERH, extended right hepatectomy; LH, left hepatectomy; RH, right hepatectomy.

Table 1. Comparison of perioperative outcomes between R-MH and L-MH before and after PSM and CEM adjustment

	Unmatched cohort (N = 4822)			**1:1 Propensity score matching (nearest neighbor matching; N = 1682)**			**Coarsened exact matching N = 593)**		
	R-MH N = 892	**L-MH N = 3930**	**P-value**	**R-MH N = 841**	**L-MH N = 841**	**P-value**	**R-MH N = 237**	**L-MH N = 356**	**P-value**
Median operating time [IQR], min	293.0 [224.8, 397.8]	300.0 [235.0, 381.0]	0.85	292.0 [225.0, 400.0]	300.0 [234.5, 390.0]	0.60	270.0 [209.0, 350.0]	282.5 [210.0, 360.0]	0.60
Median blood loss [IQR], ml	200.0 [100.0, 450.0]	300.0 [150.0, 500.0]	**<0.001**	200.0 [100.0, 450.0]	300.0 [150.0, 500.0]	**0.01**	170.0 [90.0, 400.0]	200.0 [100.0, 400.0]	**0.006**
Blood loss (categories), ml			**0.001**			0.32			0.99
< 500 ml	635 (76.3)	2648 (70.4)		593 (75.6)	572 (72.0)		183 (79.2)	266 (79.2)	
≥ 500 ml	197 (23.7)	1116 (29.6)		191 (24.4)	222 (28.0)		48 (20.8)	70 (20.8)	
Intraoperative blood transfusion, n (%)	114 (12.8)	551 (14.0)	0.33	114 (13.6)	119 (14.1)	0.77	18 (7.6)	31 (8.7)	0.63
Pringle maneuver applied, n (%)	425 (47.6)	2268 (60.4)	**<0.001**	396 (47.1)	520 (63.0)	**<0.001**	128 (54.0)	227 (65.0)	**0.007**
Open conversion, n (%)	47 (5.3)	411 (10.5)	**<0.001**	43 (5.1)	100 (11.9)	**<0.001**	13 (5.5)	37 (10.4)	**0.04**
Median postoperative stay, days [IQR]	6.1 [4.8, 9.0]	7.0 [5.0, 10.0]	**<0.001**	6.1 [4.3, 9.0]	7.0 [5.0, 9.0]	**0.002**	6.8 [4.6, 9.0]	7.0 [5.0, 8.0]	0.61
30-day readmission, n (%)	48 (5.4)	166 (4.3)	0.14	41 (4.9)	32 (3.8)	0.38	4 (1.7)	10 (2.8)	0.42
Postoperative morbidity, n (%)	219 (24.6)	1063 (27.1)	0.13	199 (23.7)	212 (25.2)	0.48	39 (16.5)	67 (18.8)	0.46
Major morbidity (Clavien-Dindo grade> 2), n (%)	69 (7.7)	416 (10.6)	**0.01**	62 (7.4)	79 (9.4)	0.16	9 (3.8)	14 (3.9)	0.93
Reoperation, n (%)	13 (1.5)	92 (2.3)	0.10	12 (1.4)	20 (2.4)	0.22	2 (0.8)	7 (2.0)	0.33
30-day mortality, n	9 (1.0)	34 (0.9)	0.68	9 (1.1)	13 (1.5)	0.52	1 (0.4)	1 (0.3)	1.00

(%)									
In-hospital mortality, n (%)	7 (0.8)	44 (1.1)	0.38	7 (0.8)	15 (1.8)	0.14	1 (0.4)	2 (0.6)	1.00
90-day mortality, n (%)	15 (1.7)	59 (1.5)	0.69	15 (1.8)	19 (2.3)	0.61	3 (1.3)	3 (0.8)	0.69

For categorical variables, denominators may differ from total numbers due to missing data. Bold value: *P* < 0.05 (Statistically significant). Abbreviations: R-MH, robotic major hepatectomy; L-MH, laparoscopic major hepatectomy.