Original Article

Validation of the Institute Mutualiste Montsouris system for the stratification of laparoscopic liver resections: an international multicenter study

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Background: The Institut Mutualiste Montsouris (IMM) 3-level complexity classification has been validated for laparoscopic liver resection (LLR) in several studies with small sample size. However, it has not been well-validated in large studies down to the individual procedure type. Hence, in order to address current limitations in the studies validating the IMM complexity classification, we performed an international multicenter study to validate the IMM complexity classification across its three complexity levels and the categorization of the 11 distinct procedure types.

Methods: A retrospective cohort study of 22,252 patients undergoing LLR across 64 centers worldwide between 2005 and 2021 was performed. Baseline characteristics and perioperative outcomes were analyzed across the three difficulty levels and 11 procedure types of the IMM complexity classification.

Results: A total of 14,765 patients were included in our final analysis. The main indications for LLR in our study was hepatocellular carcinoma or intrahepatic cholangiocarcinoma (n=7,781, 52.7%) followed by liver metastasectomy (n=3,911, 26.5%). In terms of underlying liver pathology, 5,127 (34.7%) cases had cirrhosis, and 1,214 (8.3%) had portal hypertension. Perioperative outcomes including operative time, open conversion rate, intraoperative blood loss, need for intraoperative blood transfusion, need for Pringle's application, length of stay, postoperative morbidity, major postoperative morbidity and 90-day mortality all demonstrated a significant increasing trend with increasing IMM complexity grades (P<0.001). These trends remained significant following adjustment for baseline characteristics (P<0.001). Notably, when examining the 11 LLR procedure types, all procedures within each IMM complexity grade were individually higher than all procedures in the preceding complexity grade for operative time, blood loss, length of stay, postoperative morbidity and major postoperative morbidity.

Conclusions: The three IMM complexity grades were well associated with LLR complexity as determined by key surrogate perioperative measures. Our findings also supported the categorization of the 11 distinct LLR procedures into the three complexity levels.

Keywords: Laparoscopic liver resection (LLR); Iwate criteria; validation; international multicenter study; perioperative outcomes

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Introduction

Laparoscopic liver resection (LLR) has become increasingly adopted across the world over the past two decades (1-4). The traction gained by LLR is largely attributable to the compelling amount of evidence to date that LLR is associated with improved perioperative outcomes compared with traditional open liver resections (OLRs) (3,5,6). The improved outcomes associated with LLR are however contingent upon the safe and proficient performance of LLR, which requires mounting a significant learning curve (7). To this end, several difficulty scoring systems (DSS) for LLR have been developed over the years which serve two key purposes (8-14). The first is to allow for risk stratification of liver resection cases to guide decision making on the choice of operative approach (open versus laparoscopic) for an individual surgeon depending on how far along he/she is along the LLR learning curve (7,8). The second is to provide an objective metric by which LLR cases can be assessed for inherent difficulty so as to facilitate evaluation of perioperative outcomes which is essential for auditing LLR programs and benchmarking against international standards (8).

The Institut Mutualiste Montsouris (IMM) 3-level complexity classification (*Table 1*) was developed in 2018 based on a single institutional retrospective review of 452 consecutive LLR performed over a 20-year period

Highlight box

Key findings

- This study sucessfully validated the three Institut Mutualiste Montsouris (IMM) complexity grades including the 11 invidual procedures within each grade.

What is known and what is new?

- Previous studies had only validated the three IMM complexity grades but not the individual procedures within each grade.
- This study is the first to validate the categorization of each of the 11 distinct procedure types.

What is the implication, and what should change now?

- This study supports the use of the IMM complexity classification system.
- Further studies are needed to determine if the IMM system can be further improved and optimized.

Table 1 IMM 3-level complexity classification

Grade of complexity	Procedures
Low	
I	Wedge AL Sg
II	Wedge PS Sg
III	Lt lateral Sect
Intermediate	
IV	Sgm AL Sg
V	Lt Hep
High	
VI	Sgm PS Sg
VII	Rt Hep
VIII	Ext Rt Hep
IX	Rt Post Sect
X	Central Hep/Rt Ant Sect
XI	Ext Lt Hep

AL, anterolateral (II, III, IVb, V, VI); Ant, anterior; Ext, extended; Hep, hepatectomy; IMM, Institut Mutualiste Montsouris; Lt, left; Post, posterior; PS, posterosuperior (I, IVa, VII, VIII); Rt, right; Sect, sectionectomy; Sg, segment; Sgm, segmentectomy.

(1995 to 2015) (14). Using the pre-existing Brisbane 2000 nomenclature and definitions of anterolateral (segments 2, 3, 4b, 5 and 6) and posterosuperior (segments 1, 4a, 7 and 8) segments put forth in preceding position statements, this DSS divided LLR into 11 distinct procedures (1,2,14,15). These 11 procedures were in turn grouped into three levels of complexity (grades I, II and III) based on a composite score derived from determining if each procedure was at or above the median value of the entire cohort for three perioperative variables (operative time, intraoperative blood loss and conversion rate), which served as a surrogate measure of technical complexity (14).

Since its conception, the IMM has been extensively validated by several studies and shown to be a significant discriminator for operative time, blood loss, need for transfusion, need for Pringle's maneuver and Pringle's time, conversion rate, postoperative complication rate, length of stay, liver failure rate and mortality for LLR (9,16-22). These studies however, including the initial study by Kawaguchi *et al.* which developed the complexity classification, had limited sample sizes which only permitted evaluation of the IMM DSS across its three difficulty levels and not down to the granularity of the 11 distinct procedures. Additionally, they are predominantly single institutional cohorts which limit the generalizability of the validation as key clinicopathologic variables such as the prevalence of cirrhosis and proportions of different indications for liver resection may differ internationally (9,13,23).

As such, this study was conducted as the first international multicenter study to validate the IMM complexity classification across its three complexity levels and to evaluate if the categorization of the 11 distinct procedure types into the 3 complexity levels was appropriate. We present this study in accordance with the STROBE reporting checklist (available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-24-304/rc).

Methods

Study design

This is an international multicenter post hoc study of 22,252 patients who underwent pure LLR at 64 centers between 2005 and 2021. All institutions obtained their respective approvals according to their local center's requirements. The study was performed in accordance with the Declaration of Helsinki and its subsequent amendments. This study was approved by the Singapore General Hospital Institution Review Board (2020/2802) 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.

Patients who underwent donor hepatectomy for transplant or associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) (n=70), had multiple simultaneous liver resections (n=2,308), previous liver resections (n=2,042) or concomitant major operations (n=1,958), were excluded. Notably, patients with concomitant minor operations such as hernia repair or ablations were included. Following the aforementioned exclusions, 14,765 cases of LLR with complete data were included in this study for analysis.

Definitions and outcomes

The types of LLR were defined in accordance with the original IMM complexity classification which utilised the pre-existing Brisbane 2000 nomenclature and definitions of anterolateral (segments 2, 3, 4b, 5 and 6) and posterosuperior (segments 1, 4a, 7 and 8) segments put forth in preceding position statements (1,2,14,15). The LLR procedures were ordered from 1 to 11 as originally presented in the IMM complexity classification as follows: (I) anterolateral wedge resection; (II) posterosuperior wedge resection; (III) left lateral sectionectomy; (IV) anterolateral segmentectomy; (V) left hepatectomy; (VI) posterosuperior segmentectomy; (VII) right hepatectomy; (VIII) extended right hepatectomy; (IX) right posterior sectionectomy; (X) central hepatectomy/right anterior sectionectomy; (XI) extended left hepatectomy (14). These 11 procedures were in turn grouped into three complexity levels as per the IMM system, with grade I (low difficulty) encompassing procedures 1 to 3, grade II (intermediate difficulty) encompassing procedures 4 and 5, and grade III (high difficulty) encompassing procedures 6 to 11 (14).

The baseline clinicopathological characteristics of patients were recorded and analyzed, including age, sex, year of resection, ASA score, previous abdominal surgery history, concomitant minor surgery, proportion of malignant pathology, pathology type, liver cirrhosis, Child-Pugh grade, portal hypertension, median tumor diameter, tumor number, and the difficulty index of the Iwate DSS. The diameter of the largest lesion was used in cases of multiple tumors. Cirrhosis was defined based on pathological examination (METAVIR F4) and portal hypertension was defined based on, as the presence of ascites, varices or splenomegaly with a platelet count of less than 100×10^9/L.

Postoperative complications were classified according to the Clavien-Dindo classification and recorded for up to 30 days or during the same hospitalization and included 30-day readmissions (24). Thirty-day and 90-day mortalities were recorded. To mitigate confounding factors from historical bias and center experience, the resections were classified into three periods: 2005–2010, 2011–2016 and 2017–2021.

Perioperative variables (both intraoperative characteristics and postoperative outcomes after LLR) were analyzed and evaluated according to both the three difficulty levels (low, intermediate, high) and across the 11 distinct LLR procedures delineated in the IMM complexity classification (14).

Statistical analysis

Continuous variables were summarized as medians and their interquartile ranges, while factor variables were summarised as percentages. The Cochran-Armitage and Jonckheere-Terpstra trend tests to assess presence of a monotonic association between the Iwate DSS and perioperative outcomes. To control for differences in baseline characteristics and enable comparability across strata, adjusted outcomes for each strata were obtained by conditioning the predictive margins on the baseline characteristics of the overall population. Bootstrapped quantile and Firth penalized-likelihood logistic regressions were employed for continuous and binary dependent variables respectively, and covariates included all baseline characteristics shown in *Table 2*. Statistical analyses were conducted in R version 4.2.1.

Results

A total of 14,765 LLR were performed across 64 international centers, comprising 3,890 anterolateral wedge resections, 2,020 posterosuperior wedge resections, 2,394 left lateral sectionectomies, 1,989 anterolateral segmentectomies, 1,029 left hepatectomies, 1,094 posterosuperior segmentectomies, 1,174 right hepatectomies, 75 extended right hepatectomies, 640 right posterior sectionectomies, 358 central hepatectomies/right anterior sectionectomies and 102 extended left hepatectomies. There was an increase in the number of LLR performed across the three pre-defined time periods, with 1,297 (8.8%), 5,486 (37.2%) and 7,982 (54.1%) LLR performed in 2005–2010, 2011–2016 and 2017–2021 respectively. The main indications for LLR in our study was hepatocellular carcinoma or intrahepatic cholangiocarcinoma (n=7,781, 52.7%) followed by liver metastasectomy (n=3,911, 26.5%). In terms of underlying liver pathology, 5,127 (34.7%) cases had cirrhosis, and 1,214 (8.3%) had portal hypertension. The overall and comparative baseline clinicopathologic characteristics across the three IMM DSS difficulty levels and 11 LLR procedure types are summarized in *Table 2*.

The overall and raw unadjusted comparative perioperative outcomes across the three IMM complexity levels and 11 LLR procedure types are summarized in *Table 3* and *Figures 1-3*, while the adjusted comparative outcomes are summarized in *Table 4* and *Figures 1-3*. Key perioperative outcomes including operative time, open conversion rate, intraoperative blood loss, need for intraoperative blood transfusion, need for Pringle's application, length of stay, postoperative morbidity, major postoperative morbidity and 90-day mortality all demonstrated a significant increasing trend with increasing

Table 2 Comparison between baseline clinicopathological characteristics stratified by IMM procedure type

Variable	Overall (N=14,765)	IMM I (low)			IMM II (intermediate)		IMM III (high)					
		1: Wedge AL Sg (N=3,890)	2: Wedge PS Sg (N=2,020)	3: Lt lateral Sect (N=2,394)	4: Segment AL (N=1,989)	5: Lt Hep (N=1,029)	6: Segment PS Sg (N=1,094)	7: Rt Hep (N=1,174)	8: Ext Rt Hep (N=75)	9: Rt Post Sect (N=640)	10: Central Hep/Rt Ant Sect (N=358)	11: Ext Lt Hep (N=102)
Median age, years [IQR]	62 [52–71]	63 [53–71]	63 [53–71]	61 [50–70]	62 [52–71]	63 [52–70]	64 [54–73]	62 [52–71]	64 [55–71]	62 [52–71]	62 [53–71]	63 [55–71]
Male sex	9,052 (61.3)	2,294 (58.9)	1,261 (62.4)	1,371 (57.2)	1,291 (64.9)	586 (56.9)	745 (68.1)	692 (58.9)	51 (68.0)	422 (65.9)	268 (74.8)	71 (69.6)
Year of resection												
2005–2010	1,297 (8.8)	462 (11.8)	127 (6.2)	309 (12.9)	136 (6.8)	76 (7.3)	31 (2.8)	100 (8.5)	5 (6.6%)	38 (5.9%)	5 (1.4%)	8 (7.8)
2011–2016	5,486 (37.2)	1,430 (36.7)	701 (34.7)	949 (39.6)	853 (42.8)	355 (34.5)	323 (29.5)	488 (41.5)	32 (42.6%)	221 (34.5%)	96 (26.8%)	38 (37.2)
2017–2021	7,982 (54.1)	1,998 (51.3)	1,192 (59.0)	1,136 (47.4)	1,000 (50.2)	598 (58.1)	740 (67.6)	586 (49.9)	38 (50.6%)	381 (59.5%)	257 (71.7%)	56 (54.9)
ASA score												
I/II	10,999 (74.5)	2,847 (73.2)	1,472 (72.9)	1,857 (77.6)	1,448 (72.9)	794 (77.2)	802 (73.3)	897 (76.4)	51 (68.0)	492 (76.9)	272 (76.0)	67 (65.7)
III/IV	3,758 (25.5)	1,040 (26.8)	546 (27.1)	536 (22.4%)	539 (27.1)	235 (22.8)	292 (26.7)	277 (23.6)	24 (32.0)	148 (23.1)	86 (24.0)	35 (34.3)
Previous abdominal surgery	4,691/14,409 (32.5)	1,305/3,756 (34.7)	745/1,967 (37.8)	661/2,315 (28.5)	578/1,933 (29.9)	326/1,022 (31.9)	357/1,082 (32.9)	405/1,164 (34.7)	18/75 (24.0)	184/635 (28.9)	80/358 (22.3)	32/102 (31.4)
Concomitant minor surgery	643/11,656 (5.5)	197/2,984 (6.6)	63/1,575 (4.0)	77/1,840 (4.1)	82/1,642 (4.9)	48/790 (6.0)	35/916 (3.8)	67/886 (7.5)	3/57 (5.2)	39/552 (7.0)	23/334 (6.8)	9/80 (11.3)
Malignant pathology	11,844/14,748 (80.3)	3,028/3,886 (77.9)	1,683/2,019 (83.4)	1,703/2,388 (71.3)	1,705/1,985 (85.9)	699/1,028 (68.0)	980/1,093 (89.7)	994/1,174 (84.7)	72/75 (96.0)	562/640 (87.8)	332/358 (92.7)	86/102 (84.3)
Pathology type												
Benign pathology	2,904 (19.7)	858 (22.1)	336 (16.6)	658 (28.7)	280 (14.1)	329 (32.0)	113 (10.4)	180 (15.3)	3 (4.0)	78 (12.2)	26 (7.26)	16 (15.7)
HCC/ICC	7,781 (52.7)	1,854 (47.7)	987 (48.8)	1,159 (48.4)	1,287 (64.8)	484 (47.0)	684 (62.6)	575 (48.98)	47 (62.7)	382 (59.7)	266 (74.3)	56 (54.9)
CRLM/LM	3,911 (26.5)	1,122 (28.9)	685 (33.9)	530 (22.2)	390 (19.6)	202 (19.6)	292 (26.7)	401 (34.2)	24 (32.0)	176 (27.5)	60 (16.7)	29 (28.4)
Other malignancies	152 (1.0)	52 (1.3)	11 (0.5)	14 (0.6)	28 (1.4)	13 (1.3)	4 (0.4)	18 (1.5)	1 (1.3)	4 (0.6)	6 (1.7)	1 (1.0)
Cirrhosis	5,127/14,760 (34.7)	1,375/3,889 (35.3)	754/2,020 (37.3)	739/2,393 (30.8)	835/1,987 (42.0)	256/1,029 (24.8)	462/1,094 (42.2)	290/1,173 (24.7)	24/75 (32.0)	206/640 (32.1)	165/358 (46.0)	21/102 (20.5)
Childs-Pugh score												
No cirrhosis	9,633/14,753 (65.3)	2,514/3,885 (64.7)	1,266/2,019 (62.7)	1,654/2,393 (69.1)	1,152/1,987 (57.9)	773/1,029 (75.1)	632/1,094 (57.7)	883/1,172 (75.3)	51/74 (68.9)	434/640 (67.8)	193/358 (53.9)	81/102 (79.4)
A	4,639/14,753 (31.4)	1,268/3,885 (32.6)	681/2,019 (33.7)	680/2,393 (28.4)	734/1,987 (36.9)	224/1,029 (21.7)	411/1,094 (37.5)	256/1,172 (21.8)	18/74 (34.3)	189/640 (29.5)	157/358 (43.8)	21/102 (20.6)
B	481/14,753 (3.3)	103/3,885 (2.7)	72/2,019 (3.6)	59/2,393 (2.5)	101/1,987 (5.1)	32/1,029 (3.1)	51/1,094 (4.7)	33/1,172 (2.8)	5/74 (6.8)	17/640 (2.7)	8/358 (2.23)	0/102 (0.0)
Portal hypertension	1,214/14,687 (8.3)	401/3,862 (10.4)	192/2,015 (9.5)	163/2,384 (6.8)	215/1,974 (10.8)	41/1,026 (4.0)	107/1,086 (9.8)	40/1,169 (3.42)	4/75 (5.3)	24/638 (3.7)	24/358 (6.7)	3/100 (3.0)
Median tumor size, mm [IQR]	30 [20–50]	25 [16–35]	25 [16–35]	37 [24–60]	31 [22–47]	45 [30–70]	30 [21–45]	50 [30–80]	58 [31–93]	40 [29–69]	35 [27–55]	48 [35–78]
Multiple tumors	1,989/14,759 (13.5)	324/3,890 (8.3)	175/2,019 (8.6)	353/2,392 (14.7)	199/1,989 (10.0)	170/1,027 (16.5)	123/1,094 (11.2)	391/1,173 (33.3)	37/75 (49.3)	126/640 (19.6)	62/358 (17.3)	26/102 (25.5)

Data are presented as n (%) unless otherwise specified. AL, anterolateral (II, III, IVb, V, VI); Ant, anterior; ASA, American Society of Anesthesiologists; CRLM, colorectal liver metastasis; Ext, extended; Hep, hepatectomy; HCC, hepatocellular carcinoma; Hep, hepatectomy; ICC, intrahepatic cholangiocarcinoma; IMM, Institut Mutualiste Montsouris; IQR, interquartile range; LM, liver metastasis; Lt, left; Post, posterior; PS, posterosuperior (I, IVa, VII, VIII); Rt, right; Sect, sectionectomy; Sg, segment.

Table 3 Raw unadjusted perioperative outcomes of LLR stratified by IMM procedure type

Variable	Overall (N=14,765)	IMM I (low)			IMM II (intermediate)		IMM III (high)					
		1: Wedge AL Sg (N=3,890)	2: Wedge PS Sg (N=2,020)	3: Lt lateral Sect (N=2,394)	4: Segment AL Sg (N=1,989)	5: Lt Hep (N=1,029)	6: Segment PS Sg (N=1,094)	7: Rt Hep (N=1,174)	8: Ext Rt Hep (N=75)	9: Rt Post Sect (N=640)	10: Central Hep/Rt Ant Sect (N=358)	11: Ext Lt Hep (N=102)
Median operating time, min [IQR]	204 [140–285]	150 [100–210]	186 [130–250]	165 [120–220]	219 [162–283]	252 [190–322]	270 [200–360]	320 [265–407]	360 [300–410]	310 [240–390]	304 [240–400]	348 [280–435]
Median blood loss, mL [IQR]	150 [50–300]	100 [30–200]	100 [50–300]	100 [50–200]	200 [100–350]	200 [80–350]	200 [100–500]	300 [200–550]	500 [225–1,000]	400 [200–700]	300 [200–600]	400 [200–800]
Blood loss (categories)												
<500 mL	11,609 (83.6)	3,298 (91.4)	1,675 (87.3)	2,045 (93.0)	1,553 (82.3)	829 (84.8)	766 (73.6)	765 (68.0)	34 (47.2)	359 (59.1)	228 (64.6)	57 (56.4)
≥500 mL	2,281 (16.4)	311 (8.6)	244 (12.7)	153 (6.9)	334 (17.7)	148 (15.2)	275 (26.4)	360 (32.0)	38 (52.8)	249 (40.9)	125 (35.4)	44 (43.6)
Intraoperative blood transfusion	1,163/14,774 (7.9)	130/3,880 (3.3)	153/2,017 (7.6)	78/2,391 (3.3)	172/1,986 (8.6)	72/1,028 (7.0)	145/1,094 (13.2)	187/1,173 (15.9)	24/75 (32.0)	127/640 (19.8)	53/358 (14.8)	22/102 (21.6)
Pringle maneuver applied	6,269/14,264 (43.9)	1,248/3,783 (32.9)	911/1,958 (46.5)	455/2,314 (19.6)	1,047/1,941 (53.9)	507/963 (52.6)	684/1,060 (64.5)	642/1,133 (56.6)	34/67 (50.7)	430/608 (70.7)	253/344 (73.5)	58/93 (62.3)
Open conversion	906/14,765 (6.1)	153/3,890 (3.9)	113/2,020 (5.6)	88/2,394 (3.6)	131/1,989 (6.5)	75/1,029 (7.2)	68/1,094 (6.2)	168/1,174 (14.3)	9/75 (12.0)	62/640 (9.6)	24/358 (6.7)	15/102 (14.7)
Median postoperative stay, days [IQR]	8 [5–11]	4 [3–6]	5 [3–7]	5 [3–7]	5 [4–8]	6 [5–8]	6 [4–9]	7 [5–10]	8 [6–16]	7 [5–9]	8 [6–11]	8 [5–11]
30-day readmission	390/14,700 (2.6)	71/3,878 (1.8)	48/2,019 (2.3)	44/2,383 (1.8)	47/1,980 (2.3)	38/1,024 (3.7)	38/1,093 (3.4)	58/1,150 (5.0)	2/75 (2.6)	16/640 (2.5)	23/356 (6.4)	5/102 (4.9)
Postoperative morbidity	2,586/14,746 (17.5)	471/3,881 (12.1)	291/2,020 (14.4)	302/2,392 (12.6)	374/1,987 (18.8)	181/1,028 (17.6)	260/1,092 (23.8)	411/1,173 (35.0)	28/75 (37.3)	139/640 (21.7)	102/356 (28.6)	27/102 (26.4)
Major morbidity (Clavien-Dindo grade >2)	805/14,747 (5.5)	118/3,881 (3.0)	74/2,019 (3.7)	68/2,392 (2.8)	112/1,987 (5.6)	61/1,028 (5.9)	86/1,092 (7.9)	164/1,174 (14.0)	18/75 (24.0)	51/640 (8.0)	37/357 (10.4)	16/102 (15.7)
Reoperation	175/14,764 (1.2)	25/3,890 (0.6)	10/2,020 (0.5)	25/2,394 (1.0)	14/1,989 (0.7)	18/1,028 (1.7)	16/1,094 (1.5)	44/1,174 (3.7)	6/75 (8.0)	10/640 (1.5)	3/358 (0.8)	4/102 (3.9)
30-day mortality	45/14,764 (0.3)	2/3,889 (0.05)	4/2,020 (0.2)	6/2,394 (0.2)	6/1,989 (0.3)	8/1,029 (0.8)	3/1,094 (0.3)	10/1,174 (0.8)	1/75 (1.3)	2/640 (0.3)	3/358 (0.8)	0/102 (0.0)
In-hospital mortality	70/14,765 (0.5)	5/3,890 (0.1)	8/2,020 (0.4)	7/2,394 (0.3)	10/1,989 (0.5)	5/1,029 (0.5)	5/1,094 (0.5)	17/1,174 (1.4)	4/75 (5.3)	6/640 (0.9)	3/358 (0.8)	0/102 (0.0)
90-day mortality	91/14,764 (0.5)	6/3,890 (0.1)	7/2,020 (0.3)	13/2,394 (0.5)	12/1,989 (0.6)	9/1,029 (0.8)	5/1,094 (0.4)	23/1,173 (1.9)	3/75 (4.0)	8/640 (1.2)	4/358 (1.1)	1/102 (0.9)
Close/involved margins (≤1 mm)	1,998/14,648 (13.6)	492/3,842 (12.8)	323/2,001 (16.1)	162/2,381 (6.8)	317/1,981 (16.0)	101/1,018 (9.9)	220/1,089 (20.2)	150/1,168 (12.8)	15/74 (20.3)	118/638 (18.5)	69/355 (19.4)	31/101 (30.7)

Data are presented as n (%) unless otherwise specified. AL, anterolateral (II, III, IVb, V, VI); Ant, anterior; Ext, extended; Hep, hepatectomy; IMM, Institut Mutualiste Montsouris; IQR, interquartile range; LLR, laparoscopic liver resection; Lt, left; Post, posterior; PS, posterosuperior (I, IVa, VII, VIII); Rt, right; Sect, sectionectomy; Sg, segment.

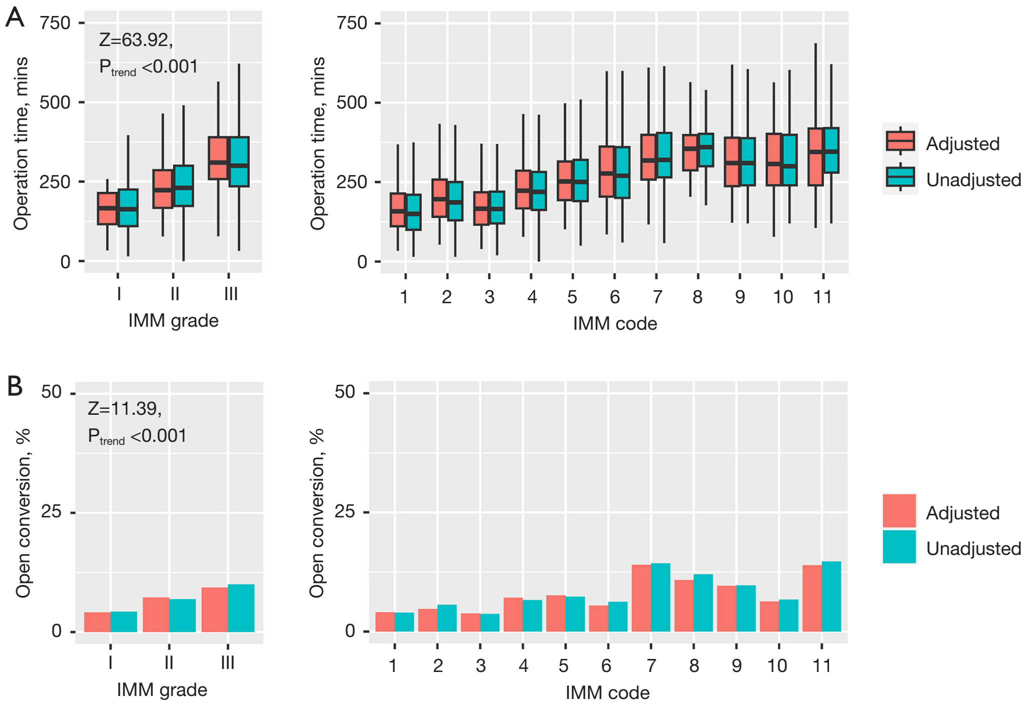

Figure 1 Unadjusted and adjusted comparative perioperative outcomes across the three IMM complexity levels and 11 LLR procedure types. (A) Operation time; (B) open conversion rate. IMM, Institut Mutualiste Montsouris; LLR, laparoscopic liver resection.

IMM DSS complexity grade (P<0.001). These trends remained significant following adjustment for baseline characteristics (P<0.001). Notably, when examining the 11 LLR procedure types, all procedures within each IMM complexity level were individually higher that all procedures in the preceding difficulty level for operative time, blood loss, length of stay, postoperative morbidity and major postoperative morbidity. Comparison between adjusted perioperative outcomes of procedures stratified by IMM difficulty level are summarized in *Table 5* which showed statistical significance for most outcome comparisons.

Missing data was generally inconsiderable and these are summarized in Table S1. The variables with the most missing data were blood loss (n=875) and tumor size (n=664). The pattern of missingness evaluated with Little's tests indicated the data was missing completely-at-random, P>0.99.

Discussion

Our current study demonstrates the increasingly widespread adoption of LLR for progressively more complex resections over the past two decades, with more than half the LLR cases performed in most recent five years from 2016 to 2021. This trend has been borne out of a growing body of evidence of the multitude of perioperative benefits afforded by a minimally-invasive approach not unprecedented in various other surgical subspecialties (1-3). Great caution is however advised when adopting LLR due to its steep inherent learning curve, an approach echoed consistently throughout the various international consensus statements (1-3,25). A well validated complexity classification system for LLR is essential for risk stratification of liver resection cases to influence the choice of operative approach (open versus laparoscopic) based on the expected difficulty in relation to a surgeon's LLR learning curve, as well as to facilitate audits of individual surgeons' and centers' LLR outcomes benchmarked against international standards (7,8). While the IMM 3-level complexity classification has been validated by several studies to date, they have been primarily limited to single center experiences, and validated only across its three difficulty levels. These studies however did not evaluate the categorization of the 11 distinct LLR procedural types (9,16-22). This limits the ability to generalize the IMM classification as a well validated system for predicting LLR difficulty across an international

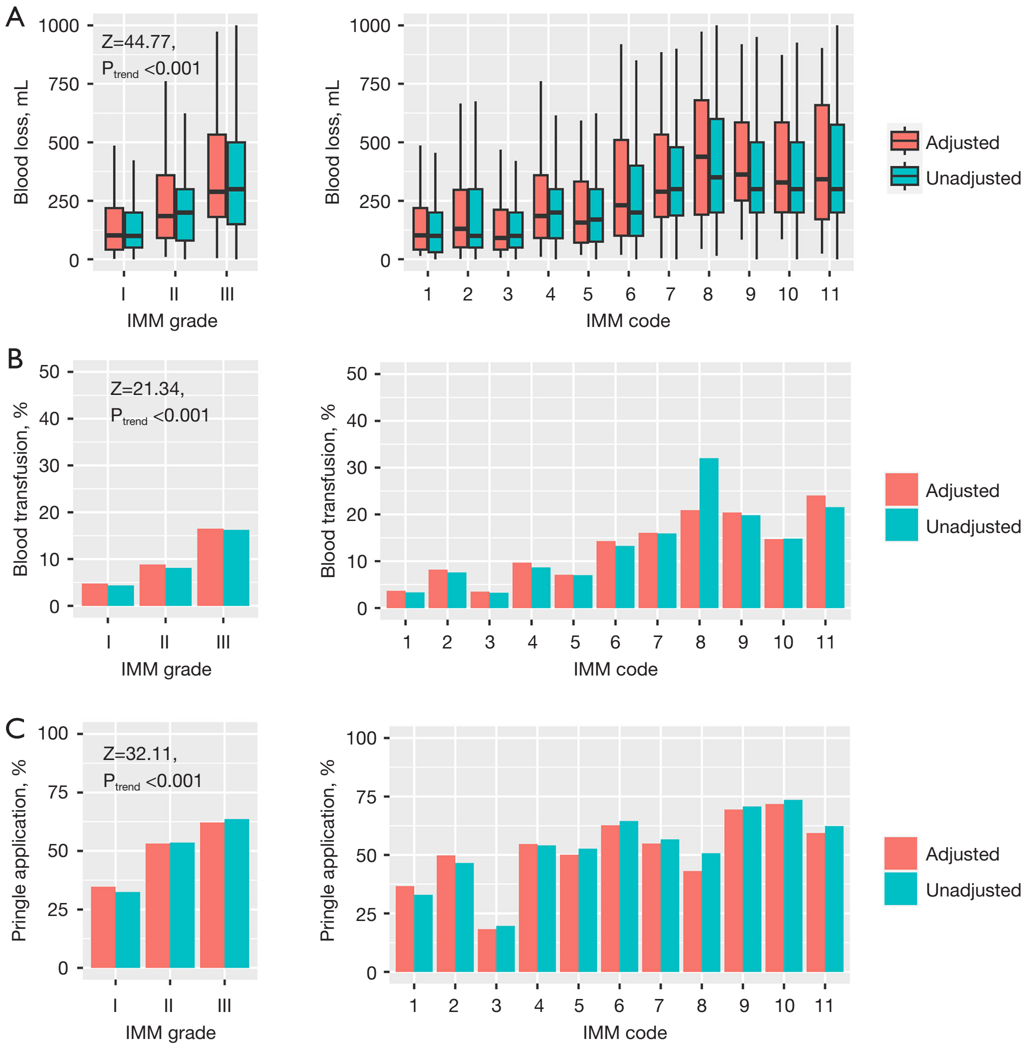

Figure 2 Unadjusted and adjusted comparative perioperative outcomes across the three IMM complexity levels and 11 LLR procedure types. (A) Estimated blood loss; (B) blood transfusion rate; (C) application of Pringles maneuver. IMM, Institut Mutualiste Montsouris; LLR, laparoscopic liver resection.

platform.

This present study addresses this gap through featuring the largest multicenter cohort of LLR to date, which provided a sample size large enough to evaluate the IMM system down to the granularity of its 11 LLR procedure types. Across the three complexity levels of the classification, a significant corresponding trend in key intraoperative (operative time, conversion rate, blood loss, need for transfusion and need for Pringle's application) and postoperative (length of stay, postoperative morbidity, major postoperative morbidity and 90-day mortality) outcomes was observed, with a higher difficulty level associated with worse outcomes. When examining the 11 LLR procedure types, we noted that every procedure within each difficulty level was individually higher than the preceding difficulty level for operative time, blood loss, length of stay, postoperative morbidity and major postoperative morbidity. These findings confirmed that the categorization of the 11 distinct procedures into the three difficulty levels was appropriate.

Within each difficulty level however, there were differing trends between the procedure types. Amongst the low complexity level (grade I) procedures, procedure 2 (posterolateral wedge resections) had worse intraoperative

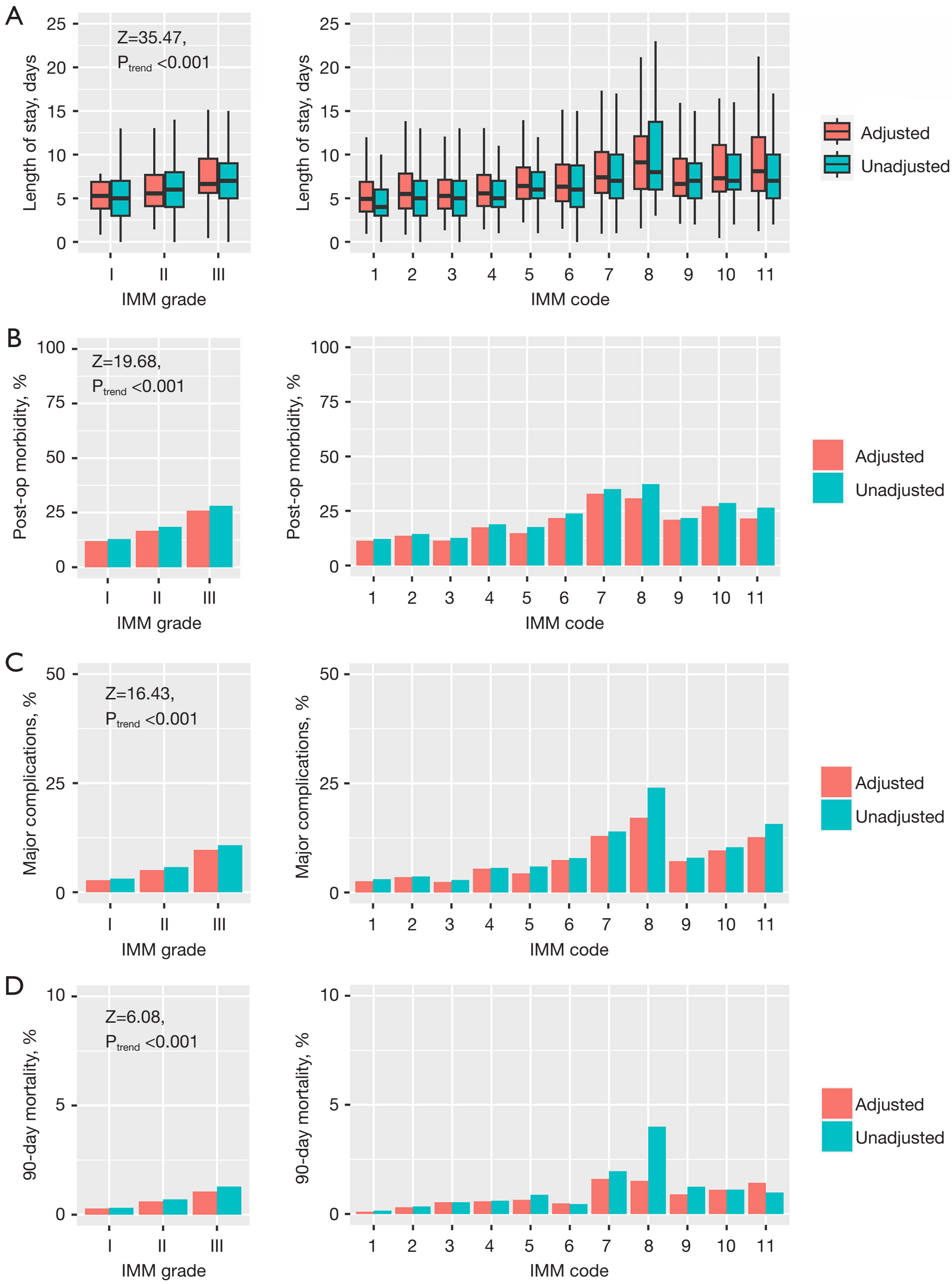

Figure 3 Unadjusted and adjusted comparative perioperative outcomes across the three IMM complexity levels and 11 LLR procedure types. (A) Postoperative length of stay; (B) postoperative morbidity; (C) Major complications; (D) 90-day mortality. IMM, Institut Mutualiste Montsouris; LLR, laparoscopic liver resection.

Table 4 Adjusted predictive margins† of perioperative outcomes of LLR stratified by IMM procedure type

Variable	IMM I (low)			IMM II (intermediate)		IMM III (high)					
	1: Wedge AL Sg (N=3,890)	2: Wedge PS Sg (N=2,020)	3: Lt lateral Sect (N=2,394)	4: Segment AL Sg (N=1,989)	5: Lt Hep (N=1,029)	6: Segment PS Sg (N=1,094)	7: Rt Hep (N=1,174)	8: Ext Rt Hep (N=75)	9: Rt Post Sect (N=640)	10: Central Hep/Rt Ant Sect (N=358)	11: Ext Lt Hep (N=102)
Median operating time [IQR], min	158 [111–214]	197 [142–259]	166 [117–219]	223 [168–286]	253 [193–315]	277 [204–362]	318 [259–400]	356 [287–398]	310 [238–390]	307 [240–402]	345 [238–420]
Median blood loss [IQR], mL	102 [41–219]	130 [51–298]	91 [41–213]	186 [91–359]	158 [71–332]	231 [101–511]	289 [181–533]	439 [191–680]	362 [251–585]	328 [201–585]	342 [171–659]
Blood loss (categories)											
<500 mL	7.5 (6.5–8.5)	11.7 (10.1–13.4)	6.8 (5.6–8.0)	15.7 (13.9–17.5)	12.8 (10.4–15.3)	25.3 (22.3–28.3)	28.7 (25.5–31.9)	45.3 (31.6–59.0)	39.6 (35.3–43.9)	34.2 (28.9–39.5)	37.7 (26.8–48.6)
≥500 mL	92.5 (91.5–93.5)	88.3 (86.6–89.9)	93.2 (92.0–94.4)	84.3 (82.5–86.1)	87.2 (84.7–89.6)	74.7 (71.7–77.7)	71.3 (68.1–74.5)	54.7 (41.0–68.4)	60.4 (56.1–64.7)	65.8 (60.5–71.1)	62.3 (51.4–73.2)
Intraoperative blood transfusion	3.2 (25.9–38.4)	7.6 (6.3–8.9)	31.4 (23.5–3.9)	8.3 (6.9–9.6)	71.8 (5.3–9.0)	13.4 (11.1–15.6)	15.6 (13.1–18.1)	20.9 (10.1–31.7)	20.2 (16.8–23.7)	14.3 (10.4–18.1)	24.4 (14.7–34.1)
Pringle maneuver applied	36.0 (34.2–37.9)	47.3 (44.7–49.8)	17.0 (15.2–18.8)	53.5 (50.9–56.1)	47.1 (43.4–50.7)	58.8 (55.4–62.2)	53.1 (49.6–56.7)	43.1 (28.6–57.5)	67.5 (63.3–71.7)	67.3 (61.8–72.9)	57.4 (45.6–69.4)
Open conversion	3.6 (3.0–4.37)	4.5 (3.52–5.63)	3.6 (2.76–4.51)	6.6 (5.39–7.84)	7.8 (5.90–0.09)	5.3 (0.03–9.78)	13.9 (11.5–16.3)	10.8 (2.52–19.0)	9.7 (7.1–12.2)	6.4 (3.7–9.1)	13.2 (5.8–20.6)
Median postoperative stay, days [IQR]	4.9 [4.8–5.1]	5.49 [5.3–5.6]	5.2 [5.1–5.4]	5.56 [5.4–5.7]	6.4 [6.1–6.6]	6.3 [6.1–6.5]	7.4 [7.1–7.6]	9.1 [8.2–10]	6.6 [6.3–6.9]	7.3 [6.9–7.6]	8.1 [7.3–8.8]
30-day readmission	1.6 (1.17–2.11)	20.9 (1.3–28.2)	2.0 (1.3–2.7)	2.0 (1.3–2.7)	1.8 (0.9–2.8)	2.6 (1.5–3.6)	4.1 (0.2–5.5)	0.8 (1.4–3.0)	2.3 (1.0–3.5)	6.6 (3.9–9.1)	4 (0.01–0.08)
Postoperative morbidity	10.5 (9.4–11.6)	12.8 (11.1–14.5)	11.1 (9.7–12.7)	16.2 (14.4–18.0)	15.1 (12.5–17.7)	20.6 (18.0–23.3)	32.2 (29.0–35.5)	30.8 (18.6–43.0)	21.2 (17.7–24.8)	27.0 (22.1–32.0)	20.7 (11.7–29.7)
Major morbidity (Clavien-Dindo grade >2)	2.4 (1.8–2.9)	3.3 (2.4–4.3)	2.3 (1.6–3.0)	5.1 (4.0–6.1)	4.3 (2.9–5.8)	7.1 (5.4–8.8)	12.1 (9.9–14.4)	17.1 (7.4–26.7)	7.2 (5.0–9.4)	9.7 (6.4–12)	11.8 (4.8–18.9)
Reoperation	0.4 (0.2–0.7)	0.3 (0.01–0.6)	0.9 (0.4–1.3)	0.6 (0.2–1.0)	1.1 (0.3–1.8)	1.3 (0.5–2.1)	3.1 (1.8–4.3)	9.4 (1.5–17.3)	1.2 (0.2–2.1)	0.8 (0.2–1.9)	2.9 (0.6–6.5)
30-day mortality	0.05 (0.03–0.13)	0.2 (0.01–0.4)	0.3 (0.06–0.6)	0.3 (0.06–0.6)	0.6 (0.09–1.2)	0.3 (0.02–0.06)	0.5 (0.09–1.0)	1.5 (1.0–4.2)	0.4 (0.1–0.9)	0.8 (0.08–1.7)	0.4 (0.8–1.7)
In-hospital mortality	0.1 (0.07–0.2)	0.3 (0.06–0.59)	0.3 (0.9–0.6)	0.4 (0.1–0.7)	0.2 (0.06–0.5)	0.4 (0.04–0.7)	0.9 (0.3–1.6)	1.2 (0.8–3.2)	0.6 (0.0–1.3)	0.7 (0.06–1.5)	0.4 (0.7–1.5)
90-day mortality	0.1 (0.006–0.2)	0.3 (0.04–0.5)	0.5 (0.2–0.8)	0.5 (0.2–0.9)	0.6 (0.09–1.1)	0.4 (0.06–0.9)	1.6 (0.7–2.4)	1.5 (0.9–4.01)	0.8 (0.13–1.6)	1.1 (0.05–2.1)	1.4 (0.8–3.7)
Close/involved margins (≤1 mm)	6.8 (5.2–8.0)	7.6 (5.9–9.4)	3.8 (2.8–4.8)	8.4 (6.6–10.3)	9.4 (7.2–11.6)	4.6 (33–6.0)	4.6 (3.3–6.0)	7.0 (2.2–11.8)	8.3 (6.0–10.6)	9.3 (6.4–12.2)	15.3 (8.0–22.6)

Data are presented as % (95% CI) unless otherwise specified. †, to control for differences in baseline characteristics and enable comparability across strata, adjusted outcomes for each strata were obtained by conditioning the predictive margins on the baseline characteristics of the overall population. I.e., the adjusted median operating time of 141 and 148 minutes for patients with IMM procedure 1 and IMM procedure 2 respectively represent the predicted OT time in a *hypothetical scenario* where 34.7% of patients in both strata had cirrhosis (as opposed to the actual cirrhosis rates of 35.4% and 37.3%) and 13.5% of patients in both strata had multifocal tumors (as opposed to the actual rate of 8.3% and 8.6% respectively), and so on. AL, anterolateral (II, III, IVb, V, VI); Ant, anterior; CI, confidence interval; Ext, extended; Hep, hepatectomy; IMM, Institut Mutualiste Montsouris; IQR, interquartile range; LLR, laparoscopic liver resection; Lt, left; Post, posterior; PS, posterosuperior (I, IVa, VII, VIII); OT time, operating time; Rt, right; Sect, sectionectomy; Sg, segment.

Table 5 Statistical comparisons between adjusted IMM difficulty groups

Variable	P value			
	IMM II *vs.* IMM I†	IMM III *vs.* IMM II†	IMM III *vs.* IMM I†	Monotonic trend‡
Median operating time	<0.001	<0.001	<0.001	<0.001
Median blood loss (continuous variable)	<0.001	<0.001	<0.001	<0.001
Blood loss (categorical variable: <500 *vs.* ≥500 mL)	<0.001	<0.001	<0.001	<0.001
Intraoperative blood transfusion	<0.001	<0.001	<0.001	<0.001
Pringle maneuver applied	<0.001	<0.001	<0.001	<0.001
Open conversion	<0.001	<0.001	<0.001	<0.001
Median postoperative stay	<0.001	<0.001	<0.001	<0.001
30-day readmission	<0.001	<0.001	<0.001	<0.001
Postoperative morbidity	<0.001	<0.001	<0.001	<0.001
Major morbidity (Clavien-Dindo grade >2)	<0.001	<0.001	<0.001	<0.001
Reoperation	0.10	<0.001	<0.001	<0.001
30-day mortality	0.003	0.73	<0.001	0.001
In-hospital mortality	0.04	0.02	<0.001	<0.001
90-day mortality	0.008	0.02	<0.001	<0.001
Close/involved margins (≤1 mm)	0.004	<0.001	<0.001	<0.001

†, pairwise comparisons were performed using Fisher's exact test and Mann-Whitney *U* test respectively for factor and continuous outcomes; ‡, two-sided Cochran-Armitage or Jonckheere-Terpstra trend tests were used to evaluate the presence of a monotonic increasing or decreasing gradation over the three IMM difficulty categories, which was treated as an ordinal variable. IMM, Institut Mutualiste Montsouris.

outcomes (operative time, conversion rate, blood loss, need for transfusion and need for Pringle's application) than procedure 3 (left lateral sectionectomy), which was in turn much more comparable to procedure 1 (anterolateral wedge resections). This is unsurprising in view of the significant technical challenges associated with accessing the posterosuperior segments as compared to a left lateral sectionectomy which has long been used as a landmark operation for surgeons at the earlier part of their LLR learning curve (1,10,26,27).

Amongst the intermediate complexity level (grade II) procedures, procedure 4 (anterolateral segmentectomy) and procedure 5 (left hepatectomy) were largely comparable for all key intraoperative and postoperative outcomes. This is likely attributable to similarities in the operative techniques required for both LLR procedure types, including ease of access to the transection lines and minimal requirement for right lobe mobilization and securing of short hepatic veins.

Amongst the high complexity level (grade III) procedures, a considerable amount of discordance in perioperative outcome trends was observed. As the biggest group in the IMM classification with six procedures included, the original IMM development cohort study also delved into a subgroup analysis comparing between the procedure types of this group, and found that when taken together, procedures 9 to 11 (right posterior sectionectomy, central hepatectomy, extended left hepatectomy) had worse perioperative outcomes in terms of operative time, blood loss, conversion rate, bile leak rate and fluid collection rate than procedures 6 to 8 (posterosuperior segmentectomy, right hepatectomy, extended right hepatectomy) (14). In our current study, with sufficient numbers of LLR performed to allow for a more granular evaluation of these six procedures, we found that procedure 8 (extended right hepatectomy) was associated with the worst perioperative outcomes in terms of operation time, blood loss, need for blood transfusion, length of stay, postoperative morbidity, major postoperative morbidity and 90-day mortality. This is likely due to a an interplay of technical factors (need for extensive liver mobilization including complete mobilization off the inferior vena cava), disease factors (large central tumors or cholangiocarcinomas requiring extended resections for oncologic margins) and higher rates of postoperative liver failure with the amount of parenchymal loss associated with this procedure. Conversely, procedure 6 (posterosuperior segmentectomy) was associated with the best perioperative outcomes in terms of operation time, conversion rate, blood loss, need for blood transfusion, length of stay and 90-day mortality. This is reflective of the more limited liver mobilization required, lack of need for hilar dissection and lower parenchymal loss associated with this procedure within grade III procedures. Interestingly, procedure 7 (right hepatectomy) is associated with the highest conversion rate, and has operation time similar to procedures 9 and 10 (right posterior sectionectomy and central hepatectomy/right anterior sectionectomy) in spite of a technically more challenging parenchymal transection plane in the latter two (28,29). This could be attributable to the fact that a conventional resection such as procedure 7 (right hepatectomy) is likely to be undertaken laparoscopically by a larger pool of surgeons with considerable inter-individual variation in technical expertise and procedural experience, while resections involving the right intersectional plane such as procedures 9 and 10 (right posterior sectionectomy and central hepatectomy/right anterior sectionectomy) are more likely to be undertaken laparoscopically by a smaller pool of experienced surgeons.

A common criticism of the IMM complexity classification compared to several other established DSS lies in its unidimensional nature as it only takes into account the type of resection, and not various other variables such as tumor size, proximity to major vessels, parenchymal quality such as presence of cirrhosis, body mass index and previous liver resections which have been found to correlate with perioperative outcomes (10-13). This however is advantageous in rendering the IMM classification as arguably the simplest system for daily usage when assessing individual cases of liver resections (9,17). Furthermore, the use of additional variables to predict LLR difficulty may not always be clinically relevant as the decision on the type of resection to undertake often already takes into account many of these factors. For instance, a segment 7 lesion that is close to the right hepatic vein would be relevant when considering a limited segmentectomy, but largely irrelevant when considering a right hepatectomy. Notably, in this analysis, the IMM classification was useful in stratifying LLR according to its complexity in both the raw and adjusted analyses suggesting that other factors played a more minor role in the complexity of LLR compared to the type and extent of liver resection. Hence, further studies are needed to determine if these other factors such as tumor size, liver cirrhosis and body mass index should be added on to the IMM system to improve its ability to stratify LLR according to its complexity level.

The IMM complexity classification is unique because it was originally devised for stratifying the surgical complexity of LLR procedures (14) and subsequently validated for OLR (30). As such, IMM complexity classification may be useful for adjusting intergroup differences of the surgical complexity (31) and developing risk-stratified posthepatectomy pathways in patients undergoing LLR and OLR (32-35). Furthermore, with the increasing adoption of robotic liver resections today, the utility of this system should also be validated for robotic procedures.

We recognize several limitations of our current study. Firstly, its retrospective nature lends itself to potential selection bias and missing data. Nonetheless, evaluation of *Tables 1,2* showed that the raw rate of missing data was relatively consistent between the variables and not proportional to the size of category nor the nature variable. Furthermore, Little's test indicated the data was missing in a random pattern. The heterogeneity in individual center and surgeon technical expertise, caseload, surgical technique and perioperative care may also confound our findings. However, our study remains the largest validation cohort by far of the IMM complexity system, with highly generalizable findings having been derived from an international multicenter collaboration, and offers the first evaluation of the 11 LLR procedure types dimension of the IMM system.

Conclusions

The three difficulty levels of IMM complexity classification correlate well with LLR complexity as determined by key surrogate perioperative measures. Our findings also supported the categorization of the 11 distinct LLR procedures into the 3 complexity levels. Hence, the IMM classification would serve as a robust tool in stratifying LLR for auditing and benchmarking purposes.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-24-304/rc

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was performed in accordance with the Declaration of Helsinki and its subsequent amendments. This retrospective study on anonymized patient data was approved by the Singapore General Hospital Institution Review Board (2020/2802) and the need for any further board review and patient consent was waived.

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