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Minimal Invasive Versus Open Surgery for Colorectal Liver Metastases

A Multicenter German StuDoQ|Liver Registry-Based Cohort Analysis in Germany

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Objective: To compare the outcome of minimally invasive liver surgery (MILS) to open liver surgery (OLS) for resection of colorectal liver metastases (CRLM) on a nationwide level.
Background: Colorectal cancer is the third most common malignancy worldwide. Up to 50% of all patients with colorectal cancer develop CRLM. MILS represents an attractive alternative to OLS for treatment of CRLM.
Methods: Retrospective cohort study using the prospectively recorded German Quality management registry for liver surgery. Propensity-score matching was performed to account for variance in the extent of resection and patient demographics.
Results: In total, 1037 patients underwent liver resection for CRLM from 2019 to 2021. MILS was performed in 31%. Operative time was significantly longer in MILS (234 *vs* 222 minutes, $P = 0.02$) compared with OLS. After MILS, median length of hospital stay (LOS) was significantly shorter (7 *vs* 10 days; $P < 0.001$). Despite 76% of major resections being OLS, postoperative complications and 90-day morbidity and mortality did not differ. The Pringle maneuver was more frequently used in MILS (48% *vs* 40%, $P = 0.048$). After propensity-score matching for age, body mass index, Eastern Cooperative Oncology Group, and extent of resection, LOS remained shorter in the MILS cohort (6 *vs* 10 days, $P < 0.001$) and operative time did not differ significantly ($P = 0.2$).
Conclusion: MILS is not the standard for resection of CRLM in Germany. Drawbacks, such as a longer operative time remain. However, if technically possible, MILS is a reasonable alternative to OLS for resection of CRLM, with comparable postoperative complications, reduced LOS, and equal oncological radicality.

Keywords: colorectal liver metastasis, liver resection, minimal invasive liver surgery

Colorectal cancer is the third most common malignancy worldwide.[1–3] One-fifth of patients present with distant metastases at the time of the diagnosis, most common hepatic. Despite recent advances in chemotherapy and immunotherapy, surgical resection of colorectal liver metastases (CRLM) remains the backbone of local treatment strategies for CRLM.

Minimal invasive liver surgery (MILS) represents an attractive alternative to conventional open liver surgery (OLS) for treatment of CRLM.[4] MILS reduces the surgical trauma and the extent of postoperative adhesions compared with OLS, which improves the postoperative outcome. In combination with parenchyma-sparing resections, MILS has been associated with less intraoperative blood loss, lower postoperative morbidity, and shorter length of hospital stay (LOS).[4–7] The Southampton Consensus Guidelines have defined MILS as a valid treatment option for CRLM in any location of the liver.[8] However, surgically complex and technically challenging cases—for example, due to the intrahepatic localization of the lesions or massive adhesions from prior surgery—might require open surgery. Two randomized controlled trials comparing laparoscopic MILS and OLS for resection of CRLM (OSLO-COMET and LapOpHuva) found no differences regarding the oncological outcomes.[7,9] Although improved 3-year overall survival rates were described for MILS in meta-analyses of retrospective data,[10] 3-year disease-free survival rates after surgical treatment of CRLM range between 55% and 58% and have not been shown to differ between OLS or MILS.[10,11]

New surgical strategies have been established in the last decade to treat CLRM patients that were previously thought of being unresectable. This included staged procedures for patients with bilobar CRLM such as associating liver partition with portal vein ligation for staged hepatectomy (ALPSS) or two-staged

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hepatectomy (TSH), which consists of surgical clear up of the left lobe followed by portal vein embolization and final second stage resection of the right lobe four to 6 weeks after the initial intervention. From a conceptional point of view, MILS should be the preferable approach for staged procedures, as postoperative adhesions are less likely to occur, rendering the second surgery easier. Moreover, robotic-assisted liver surgery has been developed to combine the advantage of open and laparoscopic surgery and has further advanced the implementation of the minimally invasive approach for the liver.[12–14] Robotic surgery allows for three-dimensional visualization and greater dexterity and flexibility during surgery and has already been well reported for treatment of CRLM.[15–17] The benefit of the articulated instruments and the superior visualization enable robotic liver resection in cases deemed too difficult for laparoscopic resection thus far. Several authors have described their learning curve and highlighted the benefits of the minimal invasive approach for CRLM.[18–20] Nevertheless, despite robotic surgery being available since the early 2000s, the implementation in liver surgery has taken a long time. This is equally true for laparoscopic liver surgery, which—despite its popularity and described benefits—still is not the standard of care.

The aim of the presented study was therefore to identify the actual implementation of MILS for CRLM in Germany using the newly established StuDoQ|Liver registry of the German Society of General and Visceral Surgery. Furthermore, we compared short-term postoperative morbidity and mortality on a nationwide level.

MATERIALS AND METHODS

Study Design

This is a retrospective cohort analysis of the prospectively recorded German Quality management registry for liver surgery (StuDoQ|Liver registry of the German Society of General and Visceral Surgery). From its implementation in April 2019, 3456 patients undergoing liver surgery were included in this database. Clinical data with a special focus on type of surgery and postoperative outcome are added by the local surgical centers. All patients receiving liver surgery for CRLM documented in the StuDoQ registry (30%) were included in this analysis. Due to the retrospective nature and analysis of anonymized registry data, this study was deemed exempt from the institutional review board. Data are anonymized and individual patients could not be identified.

Patients

Patient data entered in the registry included baseline demographics, such as age, body mass index (BMI), gender, American Society for Anesthesiologist (ASA) score, and Eastern Cooperative Oncology Group (ECOG) status. Furthermore, TNM staging of the primary tumor, the type of primary cancer, and the type of resection were documented. Liver resections with more than three segments were regarded as major resections. Procedures for stepwise clearing of the liver from CRLM were also documented, that is, ALPSS, single-staged partial hepatectomy (SSH) or TSH. Furthermore, the dissection technique used, and operative time were documented. Laparoscopic and robotic surgeries were regarded as MILS due to the relative low number of robotic cases and combined in downstream analysis.

Follow-up

Postoperative 90-day morbidity and mortality were recorded by the registry center if the patients presented for routine follow-up exams. Complications were documented according to the Clavien-Dindo classification system.[21]

Statistical Analysis

Statistical analyses were performed with R version 4.2.0 and RStudio (Version 2022.07.2 + 576 “Spotted Wakerobin”) for macOS (R Foundation for Statistical Computing, Vienna, Austria). Additional packages for graph plotting and tabular analysis of statistics were tidyverse and gtsummary. The Wilcoxon rank sum test was used to compare groups. Propensity-score matching was performed to account for variance in the extent of resection and patient demographics. We used nearest-neighbor matching with a caliper of 0.2. Included variables in creation of the propensity score were patient sex, age, BMI, ECOG status, the extent of resection and the complexity as calculated by the IWATE location score.[22] Results were adjusted for multiple testing by the method of Benjamini and Hochberg and are reported as q values. A P value ≤0.05 was considered significant. A positive false discovery rate (q value) cutoff of ≤0.05 was chosen.

RESULTS

Patient Demographics

In total, 1037 patients underwent liver resection for CRLM in the study period. Median age was 62 years, and most patients were male (64%). BMI was slightly higher (26.2 kg/m^2 *vs* 25.2 kg/m^2, P = 0.074) in patients undergoing MILS. ECOG and ASA scores were similar (Table 1). Diabetes mellitus was prevalent in 12.3% of all patients, liver cirrhosis (Child Pugh A or B) was present in 1% of cases. Median length of hospital stay (LOS) was shorter after MILS compared to OLS (7 d *vs* 10 d; P < 0.001) (Figure 1). However, complications such as bile leakage, liver failure or postoperative hemorrhage did not differ between both groups. The most frequently recorded complications were Clavien-Dindo grade 3b (3.7%) and grade 3a (2.9%). Ninety-day postoperative mortality was 2.7% (n=28), and three of those cases (10.7%) were from the MILS group.

Surgical Resection

MILS was performed in 31% of cases. Of these, 88% were performed laparoscopic, and 12% (n=49) were robotic-assisted liver resections. Liver resection was an elective procedure in 99% of cases (Table 2). Operative time was longer for MILS (234 *vs* 222 minutes, P = 0.02) and the Pringle maneuver was more frequently used (48% *vs* 40%, P < 0.001) during MILS. The most used method for parenchymal transection was ultrasonic dissection (53%) followed by bipolar coagulation (50%) or stapler hepatectomy (25%). Waterjet and sealing devices were used more frequently in MILS (both p < 0.001). Major resections were performed more frequently by OLS (35% OLS *vs* 25% MILS, P = 0.003). The complexity of the tumor location, as measured by the IWATE location score, did not differ between MILS and OLS. The minimally invasive approach was more frequently used for TSH (13% *vs* 1.5%, P < 0.001). In 50 cases (16%), conversion from MIS to OLS was necessary.

Tumor Characteristics

CRLM originated from a primary colon or rectal cancer in 65% and 35% of cases, respectively. MILS was more commonly used in patients with T3 colorectal cancer, while OLS was the preferred approach for patients with T4 cancer (Table 3). In case of multiple metastases, OLS was more frequently used (73% *vs* 45%, P < 0.001). In histological analysis of resected liver parenchyma, one in five patients had pathological parenchymal alterations, i.e., steatosis, fibrosis, or cirrhosis. R0 resection was achieved in 84% of patients receiving MILS compared to 78% receiving OLS (P = 0.03).

TABLE 1.
Patient demographics

Variable	Baseline Data					Propensity-Score Matching			
	Overall, n = 1,037*	MILS, n = 318*	OLS, n = 719*	P†	q value‡	MILS, n = 282*	OLS, n = 282*	P†	q value‡
Age (years)	62 (54, 70)	62 (54, 71)	62 (54, 69)	0.3	0.5	62 (54, 71)	60 (53, 69)	0.2	0.4
Sex (% female)	369 (36%)	115 (36%)	254 (35%)	0.8	0.8	100 (35%)	93 (33%)	0.6	0.7
BMI (kg/m^2)	25.5 (22.4, 28.6)	26.2 (22.8, 29.0)	25.2 (22.3, 28.4)	0.074	0.2	26.2 (23.0, 29.1)	25.6 (22.3, 28.4)	0.3	0.4
ECOG				0.12	0.2			0.5	0.6
1	318 (31%)	98 (31%)	220 (31%)			85 (30%)	84 (30%)		
2	64 (6.2%)	26 (8.2%)	38 (5.3%)			24 (8.5%)	25 (8.9%)		
3	11 (1.1%)	5 (1.6%)	6 (0.8%)			5 (1.8%)	1 (0.4%)		
4	1 (<0.1%)	1 (0.3%)	0 (0%)			1 (0.4%)	0 (0%)		
ASA				0.072	0.2			0.2	0.4
1	44 (4.2%)	17 (5.3%)	27 (3.8%)			16 (5.7%)	10 (3.5%)		
2	362 (35%)	121 (38%)	241 (34%)			103 (37%)	93 (33%)		
3	624 (60%)	180 (57%)	444 (62%)			163 (58%)	176 (62%)		
4	7 (0.7%)	0 (0%)	7 (1.0%)			0 (0%)	3 (1.1%)		
Diabetes mellitus				0.7	0.8			>0.9	>0.9
IDDM	48 (4.6%)	16 (5.0%)	32 (4.5%)			14 (5.0%)	14 (5.0%)		
NIDDM	80 (7.7%)	27 (8.5%)	53 (7.4%)			21 (7.4%)	20 (7.1%)		
Length of hospital stay (days)	9 (6, 14)	7 (5, 9)	10 (7, 16)	<0.001	<0.001	6 (5, 9)	10 (7, 16)	<0.001	<0.001
Bile leakage				0.7	0.8			0.9	>0.9
Grade A	17 (1.6%)	5 (1.6%)	12 (1.7%)			3 (1.1%)	5 (1.8%)		
Grade B	42 (4.1%)	12 (3.8%)	30 (4.2%)			12 (4.3%)	14 (5.0%)		
Grade C	33 (3.2%)	7 (2.2%)	26 (3.6%)			6 (2.1%)	5 (1.8%)		
Postoperative liver failure				0.5	0.6			0.7	0.7
Grade A	13 (1.3%)	2 (0.6%)	11 (1.5%)			2 (0.7%)	4 (1.4%)		
Grade B	4 (0.4%)	1 (0.3%)	3 (0.4%)			1 (0.4%)	0 (0%)		
Grade C	12 (1.2%)	2 (0.6%)	10 (1.4%)			1 (0.4%)	2 (0.7%)		
Postoperative hemorrhage				0.2	0.3			0.2	0.4
Grade A	13 (1.3%)	2 (0.6%)	11 (1.5%)			2 (0.7%)	4 (1.4%)		
Grade B	6 (0.6%)	0 (0%)	6 (0.8%)			0 (0%)	2 (0.7%)		
Grade C	10 (1.0%)	2 (0.6%)	8 (1.1%)			1 (0.4%)	4 (1.4%)		
Complications during the first 90 days				0.5	0.6			0.4	0.5
Grade 1	10 (1.0%)	3 (1.0%)	7 (1.1%)			3 (1.1%)	2 (0.7%)		
Grade 2	22 (2.3%)	8 (2.7%)	14 (2.1%)			7 (2.5%)	7 (2.5%)		
Grade 3a	28 (2.9%)	12 (4.0%)	16 (2.4%)			11 (3.9%)	6 (2.1%)		
Grade 3b	35 (3.7%)	8 (2.7%)	27 (4.1%)			8 (2.8%)	11 (3.9%)		
Grade 4a	4 (0.4%)	2 (0.7%)	2 (0.3%)			2 (0.7%)	0 (0%)		
Grade 4b	6 (0.6%)	1 (0.3%)	5 (0.8%)			1 (0.4%)	3 (1.1%)		
Grade 5	19 (2.0%)	3 (1.0%)	16 (2.4%)			3 (1.1%)	8 (2.8%)		
Cause of death during the first 90 days				0.12	0.2			0.2	0.4
Death due to non-surgical complications	3 (0.3%)	1 (0.3%)	2 (0.3%)			1 (0.4%)	2 (0.7%)		
Death due to other cause	4 (0.4%)	1 (0.3%)	3 (0.5%)			1 (0.4%)	1 (0.4%)		
Death due to primary disease	12 (1.3%)	0 (0%)	12 (1.8%)			0 (0%)	4 (1.4%)		
Death due to surgical complications	7 (0.7%)	1 (0.3%)	6 (0.9%)			1 (0.4%)	3 (1.1%)		
Unknown	2 (0.2%)	0 (0%)	2 (0.3%)			0 (0%)	1 (0.4%)		

*Median (IQR); n (%).
†Wilcoxon rank sum test; Fisher's Exact Test for count data; Fisher's Exact Test for count data with simulated *P* value (based on 2000 replicates).
‡False discovery rate correction for multiple testing.
ASA, American Society of Anesthesiologists; ECOG, Eastern Cooperative Oncology Group; f, female; MILS, minimal invasive liver surgery; OLS, open liver surgery.

Propensity-Score Matching

After propensity-score matching for age, BMI, ECOG, and extent of resection, 282 patient pairs remained. Median LOS remained shorter in MILS (6 d *vs* 10 d, *P* < 0.001), while the operative time did not differ (*P* = 0.2, Figure 2). Complications remained similar in the matched subgroup (12% MILS, 13% OLS, *P* = 0.4). Postoperative 90-day overall survival was 98% for all patients (99% MILS, 96% OLS, *P* = 0.2). Major resections were similarly distributed between MILS and OLS (25% *vs* 29%, *P* = 0.4).

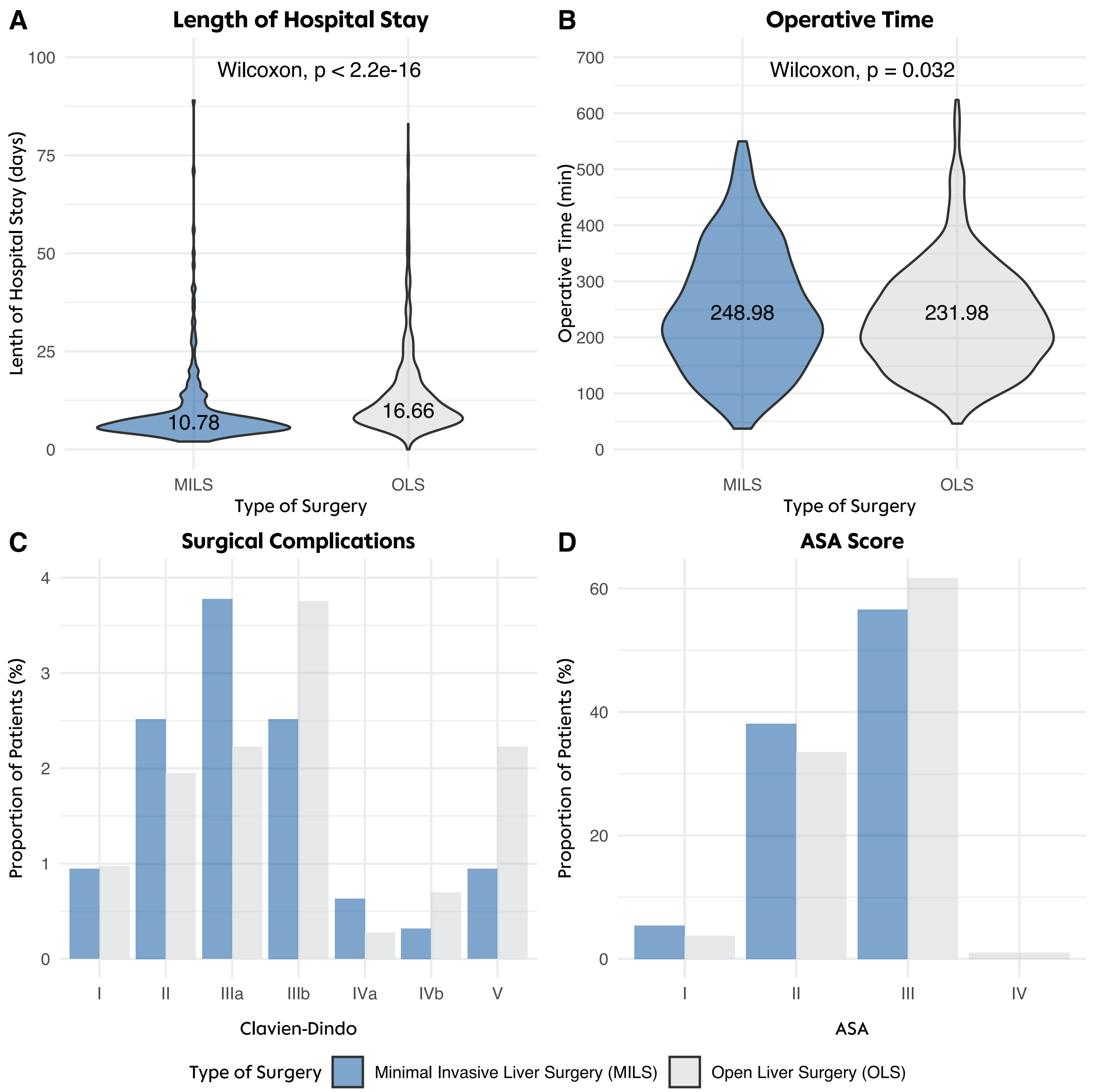

FIGURE 1. Comparison between MILS and OLS for colorectal liver metastases in the German Quality management registry for liver surgery (N = 1037). Mean length of hospital stay was significantly longer in OLS (A) and surgery duration shorter (B). There were no significant differences in surgical complications classified after Clavien-Dindo (C) or patient health prior to surgery as estimated by the ASA score (D). ASA, American Society of Anesthesiologists; MILS, minimal invasive liver; OLS, open liver surgery.

DISCUSSION

CRLM are one of the most common indications for liver surgery. Recent developments in laparoscopic and robotic-assisted surgery as well as the growing expertise of hepatobiliary surgeons have expanded the use-cases for MILS. In this study, we analyze German StuDoQ|Liver registry data to assess the utilization of MILS for CRLM in Germany. Moreover, we compare the perioperative morbidity and mortality of MILS versus OLS for CRLM.

Laparoscopic liver surgery was the primary type of MILS used, while the robotic approach was limited to a small number of cases. Moreover, our data indicate that even after matching for confounding factors such as extent of resection, complexity, and baseline characteristics of the patients, LOS is significantly shorter after MILS. However, operative times did not differ after matching, and we could not show a reduction in complication rate and mortality after MILS compared to OLS.

Thus, although drawbacks such as a longer operative time remain, MILS is superior to OLS for CRLM regarding LOS, if feasibly from a technical perspective. This has previously demonstrated for other entities.[7,23] LOS was similar to previously published data with a median of 9 days.[10,24] Despite adjusting for patient health and complexity of the surgery, LOS remained significantly higher in OLS. Importantly, postoperative morbidity was equivalent between the groups and therefore may not adequately account for the differences in LOS. We know that the reduced surgical trauma, fewer surgical site infections, and rapid postoperative mobilization can lead to earlier discharge after MILS. Furthermore, MILS causes less postoperative adhesions, which makes repeated liver resection less difficult. We therefore see MILS especially promising for patients with CRLM, which are known to benefit from repeated liver resections. We show that MILS is still not the standard of care in Germany, despite its apparent benefits.[25,26] Schneider et al.

TABLE 2.

Surgery

Variable	Baseline Data					Propensity-Score Matching			
	Overall, n = 1037*	MILS n = 318*	OLS n = 719*	*P*†	*q* value‡	MILS, n = 282*	OLS, n = 282*	*P*†	*q* value‡
Type of surgery				0.5	0.6			0.3	0.4
Elective surgery	1,026 (99%)	316 (99%)	710 (99%)			280 (99%)	276 (98%)		
Emergency surgery	11 (1.1%)	2 (0.6%)	9 (1.3%)			2 (0.7%)	6 (2.1%)		
Vascular exclusion				<0.001	0.004			0.051	0.2
No vascular exclusion	627 (60%)	167 (53%)	460 (64%)			146 (52%)	170 (60%)		
Pringle	407 (39%)	150 (47%)	257 (36%)			135 (48%)	112 (40%)		
Total vascular exclusion	3 (0.3%)	1 (0.3%)	2 (0.3%)			1 (0.4%)	0 (0%)		
Clamp-crush	91 (8.8%)	38 (12%)	53 (7.4%)	0.023	0.073	36 (13%)	22 (7.8%)	0.071	0.2
Ultrasonic dissector	554 (53%)	172 (54%)	382 (53%)	0.8	0.8	153 (54%)	165 (59%)	0.4	0.5
Waterjet	81 (7.8%)	48 (15%)	33 (4.6%)	<0.001	<0.001	43 (15%)	21 (7.4%)	0.005	0.023
Sealing	272 (26%)	110 (35%)	162 (23%)	<0.001	<0.001	98 (35%)	64 (23%)	0.002	0.011
Bipolar	519 (50%)	147 (46%)	372 (52%)	0.11	0.2	128 (45%)	157 (56%)	0.018	0.067
Stapler	261 (25%)	55 (17%)	206 (29%)	<0.001	<0.001	50 (18%)	77 (27%)	0.009	0.036
Resection type				0.067	0.2			0.7	0.8
Extended right hepatectomy	12 (1.2%)	1 (0.3%)	11 (1.5%)			0 (0%)	2 (0.7%)		
Left hepatectomy	55 (5.3%)	12 (3.8%)	43 (6.0%)			11 (3.9%)	13 (4.6%)		
Left lateral sectionectomy	51 (4.9%)	21 (6.6%)	30 (4.2%)			19 (6.7%)	15 (5.3%)		
Other	742 (72%)	236 (74%)	506 (70%)			211 (75%)	210 (74%)		
Right hepatectomy	177 (17%)	48 (15%)	129 (18%)			41 (15%)	42 (15%)		
Extent of resection				0.003	0.011			0.4	0.5
Major Resection	331 (32%)	81 (25%)	250 (35%)			71 (25%)	81 (29%)		
Minor Resection	706 (68%)	237 (75%)	469 (65%)			211 (75%)	201 (71%)		
Location Score (IWATE)				0.2	0.3			0.6	0.7
1	355 (34%)	111 (35%)	244 (34%)			99 (35%)	104 (37%)		
2	399 (38%)	127 (40%)	272 (38%)			113 (40%)	105 (37%)		
3	128 (12%)	38 (12%)	90 (13%)			33 (12%)	28 (9.9%)		
4	49 (4.7%)	10 (3.1%)	39 (5.4%)			10 (3.5%)	19 (6.7%)		
5	83 (8.0%)	29 (9.1%)	54 (7.5%)			24 (8.5%)	23 (8.2%)		
Other	23 (2.2%)	3 (0.9%)	20 (2.8%)			3 (1.1%)	3 (1.1%)		
Surgery technique				<0.001	0.002			<0.001	0.003
ALLPS	37 (3.6%)	4 (1.3%)	33 (4.6%)			4 (1.4%)	14 (5.0%)		
Other TSH	20 (1.9%)	9 (2.8%)	11 (1.5%)			7 (2.5%)	6 (2.1%)		
SSH	928 (89%)	264 (83%)	664 (92%)			236 (84%)	258 (91%)		
TSH	52 (5.0%)	41 (13%)	11 (1.5%)			35 (12%)	4 (1.4%)		
Conversion	50 (4.9%)	50 (16%)	0 (0%)	<0.001	<0.001				
Operative time (min)	225 (166, 298)	234 (169, 322)	222 (163, 290)	0.024	0.073	230 (166, 311)	222 (160, 289)	0.2	0.4

*Median (IQR); n (%)

†Wilcoxon rank sum test; Fisher's Exact Test for count data; Fisher's Exact Test for count data with simulated *P* value (based on 2000 replicates).

‡False discovery rate correction for multiple testing.

ALLPS, associated liver partition and portal vein ligation for staged hepatectomy; MILS, minimal invasive liver surgery; OLS, open liver surgery; TSH, two-staged hepatectomy.

analyzed data in Switzerland and found unequal access to minimal invasive surgery associated with patient age, comorbidities, type of insurance and geographic location. Unfortunately, this data is not available in this registry, but could further explain the differences in selection for MILS or OLS.

Overall, 90-day postoperative mortality was 2.7% in the study cohort and higher than the reported 0.5% in the multi-institutional Japanese study by Beppu et al.[24] However, only 3% of patients were regarded as ASA 3 in their data set, in comparison to 60% in our study cohort. This might be associated with overall population health, reflected in current life expectancy, which is 4 years lower in Germany than in Japan.[27] In addition, less than 10% of cases were major resections, compared to 32% in the presented dataset, which is most likely the main reason for this difference in postoperative mortality.

Fretland et al. reported a postoperative complication rate of 31% in the OLS group and 19% in the MILS group in the OSLO-COMET randomized controlled trial.[7] This was significantly higher than the reported 13% and 12% in our registry analysis. However, complications were recorded as dichotomous variable if a complication greater to Clavien-Dindo grade 2 occurred. The data are therefore not necessarily comparable.[28] The utilization of the Clavien-Dindo score for evaluating postoperative complications in the StuDoq registry is therefore one additional caveat of our data. While this is well established, the recently proposed Comprehensive Complication Index would have enabled a more detailed analysis of postoperative complications.[29]

Operating time differed in the baseline comparisons between MILS and OLS, which has previously been reported as a major drawback of MILS.[6,9] This was most likely due to the confounding effect of more major resections being performed in the open approach. After propensity-score matching, MILS resections and OLS did not differ in operating time. The decision for MILS or OLS was decided in each individual center and was

TABLE 3.

Tumor Characteristics of Primary

	Baseline Data					Propensity-Score Matching			
Variable	**Overall n = 1,037***	MILS n = 318*	OLS, n = 719*	***P*†**	***q* value‡**	MILS, n = 282*	OLS, n = 282*	***P*†**	***q* value‡**
Origin of primary				0.091	0.2			0.079	0.2
Colon cancer	670 (65%)	193 (61%)	477 (66%)			167 (60%)	188 (67%)		
Rectal cancer	367 (35%)	125 (39%)	242 (34%)			113 (40%)	92 (33%)		
T				<0.001	0.002			0.003	0.012
T0	50 (9.2%)	22 (16%)	28 (6.8%)			19 (17%)	10 (6.4%)		
T1	9 (1.7%)	3 (2.2%)	6 (1.5%)			3 (2.7%)	5 (3.2%)		
T2	45 (8.3%)	6 (4.4%)	39 (9.5%)			5 (4.4%)	20 (13%)		
T3	294 (54%)	79 (59%)	215 (52%)			65 (58%)	75 (48%)		
T4	76 (14%)	15 (11%)	61 (15%)			12 (11%)	22 (14%)		
Tx	71 (13%)	10 (7.4%)	61 (15%)			9 (8.0%)	25 (16%)		
N				0.2	0.3			0.4	0.5
N0	189 (40%)	54 (45%)	135 (38%)			47 (46%)	53 (39%)		
N1	283 (60%)	67 (55%)	216 (62%)			55 (54%)	82 (61%)		
M				0.001	0.006			0.010	0.034
M0	330 (36%)	97 (39%)	233 (35%)			85 (39%)	93 (36%)		
M1	486 (53%)	139 (56%)	347 (52%)			121 (56%)	131 (51%)		
Mx	101 (11%)	13 (5.2%)	88 (13%)			10 (4.6%)	32 (12%)		
Pulmonary metastases	70 (14%)	22 (16%)	48 (14%)	0.6	0.7	18 (15%)	21 (16%)	0.9	>0.9
Peritoneal metastases	45 (9.3%)	15 (11%)	30 (8.6%)	0.5	0.6	11 (9.1%)	12 (9.2%)	>0.9	>0.9
Other metastases				<0.001	0.002			<0.001	0.003
Multiple metastases	24 (4.9%)	3 (2.2%)	21 (6.1%)			2 (1.7%)	5 (3.8%)		
One other metastasis	317 (65%)	63 (45%)	254 (73%)			65 (54%)	29 (22%)		
G				0.2	0.3			0.2	0.4
G1	24 (3.9%)	4 (2.6%)	20 (4.3%)			2 (1.5%)	8 (4.3%)		
G2	312 (50%)	71 (46%)	241 (51%)			60 (46%)	93 (50%)		
G3	68 (11%)	19 (12%)	49 (10%)			18 (14%)	26 (14%)		
G4	7 (1.1%)	0 (0%)	7 (1.5%)			0 (0%)	3 (1.6%)		
Gx	212 (34%)	61 (39%)	151 (32%)			51 (39%)	56 (30%)		
L				0.7	0.7			0.8	>0.9
L0	271 (57%)	66 (55%)	205 (58%)			54 (53%)	79 (56%)		
L1	203 (43%)	53 (45%)	150 (42%)			47 (47%)	63 (44%)		
V				0.2	0.3			0.12	0.3
V0	374 (77%)	91 (73%)	283 (79%)			76 (72%)	113 (81%)		
V1	111 (23%)	34 (27%)	77 (21%)			29 (28%)	26 (19%)		
R				0.034	0.10			0.044	0.12
R0	740 (80%)	218 (84%)	522 (78%)			191 (85%)	200 (78%)		
R1	59 (6.4%)	15 (5.7%)	44 (6.6%)			13 (5.8%)	14 (5.4%)		
R2	19 (2.0%)	8 (3.1%)	11 (1.6%)			6 (2.7%)	5 (1.9%)		
Rx	111 (12%)	20 (7.7%)	91 (14%)			16 (7.1%)	39 (15%)		
Parenchyma pathological quality	127 (20%)	52 (24%)	75 (18%)	0.095	0.2	50 (25%)	31 (19%)	0.2	0.3

*Median (IQR); n (%)

†Wilcoxon rank sum test; Fisher's Exact Test for count data; Fisher's Exact Test for count data with simulated *P* value (based on 2000 replicates)

‡False discovery rate correction for multiple testing

MILS, minimal invasive liver surgery; OLS, open liver surgery.

not standardized across centers. Hence, a selection bias for less complex cases in MILS is likely and we assume that the higher rate of R0 in MILS is connected to this limitation in our study.

Another limitation of this study is the lack of external data validation. Data are entered by each participating study center to the registry and anonymized thereafter. We were therefore not able to control for data errors. However, as being one of the participating centers, we can confirm rigorous data entry and having additional checks in place before submission to the registry. We expect this to be the case in all other participating centers as well. On the other hand, we present results from a large and recent multicenter patient cohort, which is certainly one of the strengths of this study. A previous meta-analysis of Zhang et al. included 2,259 patients from 10 different studies[10] – compared to 1,037 patients in our registry analysis. Another limitation is that long-term data on survival and complications are unfortunately missing due to the nature of the registry. However, previously published data from Aghayan et al. showed comparable overall 5-year survival of 54% in the MILS group and 55% in the open group, even though the study was not powered for long-term survival.[30] Other retrospective studies have shown 5-year survival rates above 60%.[31–34]

In conclusion, our Germany-based registry analysis indicates that MILS is a reasonable alternative to OLS for resection of CRLM if technically feasible. MILS was associated with reduced LOS, comparable postoperative complication rates, and equal oncological radicality. These data further support the use of MILS for resection of CRLM, if technically feasible.

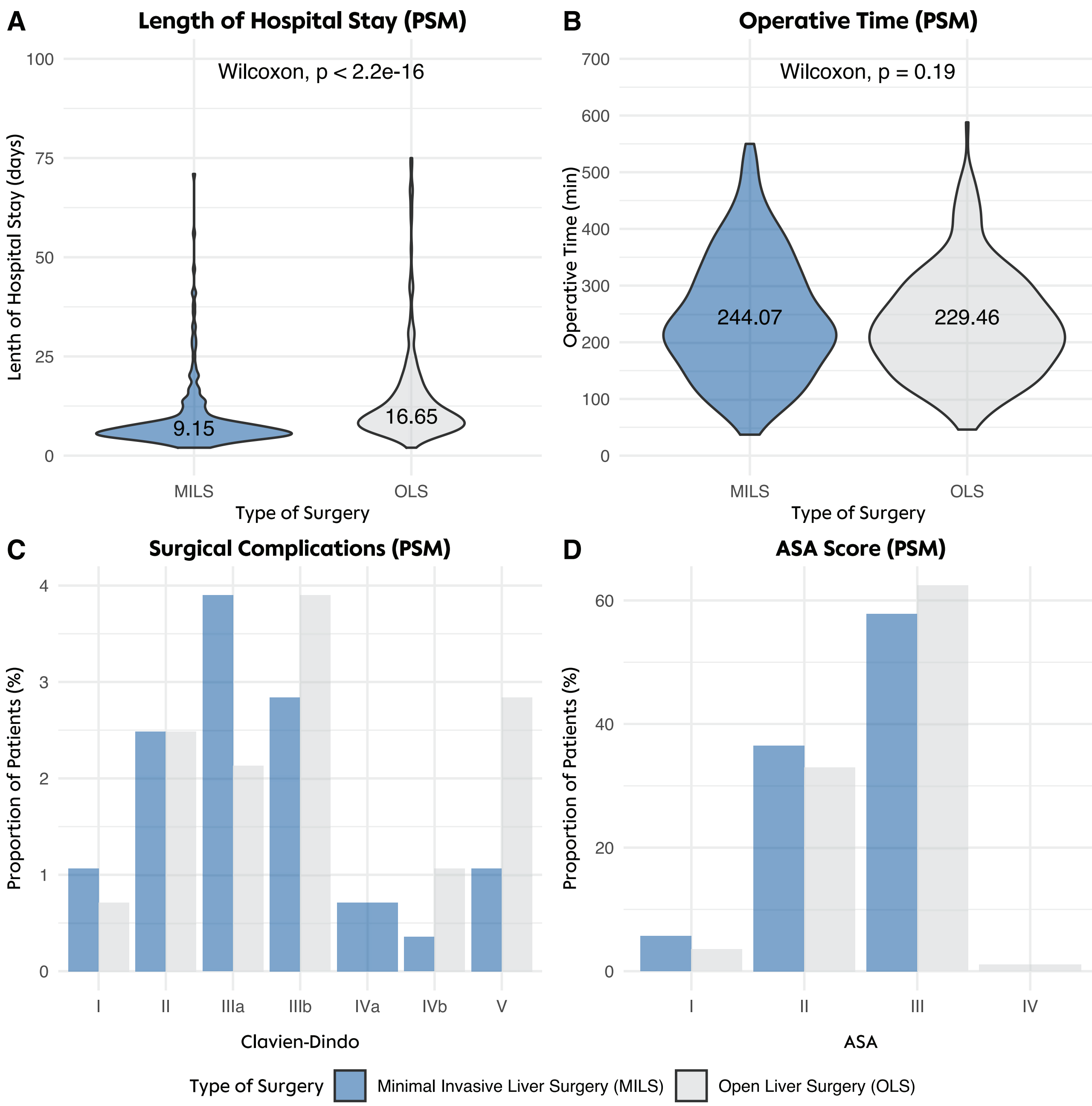

FIGURE 2. Comparison between MILS and OLS for colorectal liver metastases in the German Quality management registry for liver surgery after propensity-score matching (n = 564). Mean length of hospital stay was significantly longer in OLS (A) and surgery duration was the same (B). There were no significant differences in surgical complications classified after Clavien-Dindo (C) or patient health prior to surgery as estimated by the ASA score (D). ASA, American Society of Anesthesiologists; MILS, minimal invasive liver; OLS, open liver surgery.

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