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ORIGINAL ARTICLE

Implementation and outcome of minor and major minimally invasive liver surgery in the Netherlands

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Abstract

Background: While most of the evidence on minimally invasive liver surgery (MILS) is derived from expert centers, nationwide outcomes remain underreported. This study aimed to evaluate the implementation and outcome of MILS on a nationwide scale.

Methods: Electronic patient files were reviewed in all Dutch liver surgery centers and all patients undergoing MILS between 2011 and 2016 were selected. Operative outcomes were stratified based on extent of the resection and annual MILS volume.

Results: Overall, 6951 liver resections were included, with a median annual volume of 50 resections per center. The overall use of MILS was 13% (n = 916), which varied from 3% to 36% (P < 0.001) between centers. The nationwide use of MILS increased from 6% in 2011 to 23% in 2016 (P < 0.001). Outcomes of minor MILS were comparable with international studies (conversion 0–13%, mortality <1%). In centers which performed ≥20 MILS annually, major MILS was associated with less conversions (14 (11%) versus 41 (30%), P < 0.001), shorter operating time (184 (117–239) versus 200 (139–308) minutes, P = 0.010), and less overall complications (37 (30%) versus 58 (42%), P = 0.040).

Conclusion: The nationwide use of MILS is increasing, although large variation remains between centers. Outcomes of major MILS are better in centers with higher volumes.

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Introduction

Minimally invasive liver surgery (MILS) has been adopted slowly since its introduction in the early 1990s, especially compared to other procedures in gastrointestinal surgery. The widespread implementation of MILS was hampered by concerns about a learning curve effect combined with the low volume of liver surgery in most centres.[1]

In recent years, the pioneering work of several expert surgeons from very high-volume centers has confirmed the potential advantage of MILS as compared to open surgery.[1–3] These advantages include decreased intraoperative blood loss, fewer postoperative complications, less need for analgesics, faster functional recovery, shorter postoperative hospital stay, decreased risk of wound infections, better cosmetics and lower risk of incisional hernia.[1–3] These promising results boosted the interest in MILS worldwide and eventually resulted in three subsequent guideline meetings on MILS.[4–6] Based on these meetings, MILS is now considered the standard approach for minor liver resections (i.e. resection of less than three liver segments).[5,6] According to the most recent Southampton guidelines, implementation of both anatomically and technically major MILS (i.e. resection of three or more segments or resection from posterior segments, respectively[4]) should be handled in a stepwise fashion and combined with structured training in centers who have completed the learning curve for minor MILS.[6]

The remaining question is whether the promising results for minor and major MILS can be reproduced on a nationwide scale. Population based studies with data on both implementation and outcome of MILS are scarce and, if available, lack stratification for minor and major MILS.[7,8] Previous studies also did not investigate the impact of volume on the outcome of MILS. This study aimed to determine both the implementation and outcome of minor and major MILS on a nationwide level and to assess the impact of volume on overall outcome of major MILS.

Methods

This study was performed within the Dutch Liver Collaborative Group (DLCG) in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[9] It describes the outcomes and implementation rates of MILS in all 27 Dutch centers performing liver surgery. All centers perform at least 20 liver resections per year, which is the national annual volume requirement for liver surgery in the Netherlands. MILS included total laparoscopic, hand-assisted, and robot-assisted procedures. The ethics committee of the Amsterdam UMC, location AMC (Amsterdam, the Netherlands), waived the need for informed consent.

Design and patients

Patients were selected from center specific, prospectively collected liver surgery databases or from surgery schedules listing all liver resections. All patients who had undergone a MILS procedure between January 2011 and December 2016 were eligible. Patients were excluded when insufficient data were available, when they had previously objected to have their information gathered from their patient files for research purposes, when no resection was performed (e.g. fenestration/deroofing of cysts, biopsies, diagnostic laparoscopy) or in case of emergency surgery. A flowchart illustrating the patient selection process is provided in Appendix A.

Selection criteria for the minimally invasive approach were not standardized, so a comprehensive selection of MILS was included, regardless of the indication. All patients were discussed in a multidisciplinary team meeting with hepato-pancreato-biliary (HPB) surgeons, gastroenterologists, medical oncologists, radiologists and pathologists. The surgical indication was established before and independently of the decision regarding the surgical approach, which was made based on tumor characteristics such as size and location, patient performance status and the surgeon's experience and skill. An absolute contraindication for a minimally invasive approach in all centers was the need for vascular or biliary reconstruction and anatomically major liver resection combined with a colorectal resection. Enhanced recovery after surgery (ERAS) protocols were established in all centers.

Definitions and data collection

Major MILS was defined according to consensus agreements[4] and categorized based on evidence of a difference in outcome[10] as any resection of three or more segments (anatomically major) or any resection from the posteriorly located segments 7, 8, 4a and 1 (technically major), respectively. Intraoperative incidents were scored according to the Oslo Classification.[11] Postoperative complications were graded according to the modified Accordion Classification.[12] Resection margins were defined as R0 (1 mm or more tumor free margin), R1 (less than 1 mm tumor free margin) or R2 (macroscopic tumor involvement at the margin).

Four authors (MJvdP, RSF, BG, CNN) collected individual patient data from electronic patient files with daily notes in all centers. Baseline characteristics included patient demographics, body mass index (BMI, kg/m^2), American Society of Anesthesiologists (ASA) grade, abdominal surgery history, indication for surgery (benign/malignant), number of lesions on preoperative imaging, size of the largest lesion on preoperative imaging, neoadjuvant chemotherapy, minimally invasive approach (total laparoscopic, hand-assisted or robot-assisted), extent of resection (minor/anatomically major/technically major), type of resection, simultaneous colorectal procedure and the use of intraoperative ultrasound. Operative outcomes included operating time, intraoperative blood loss, conversion (both strategic and reactive), intraoperative adverse events, 30-day or in hospital postoperative complications (defined according to the Accordion Classification, severe complications were defined as Accordion grade three or higher), 30-day or in hospital re-intervention, 30-day re-admission, postoperative hospital stay, resection margins of malignant lesions, pathology report, 90-day or in hospital mortality and occurrence of incisional hernia within 1 year of follow up, either on imaging or requiring surgery. The total annual volume of liver resections performed per center during the study period was collected in order to determine the implementation rate of MILS.

Surgical technique

Surgical techniques were not standardized. In general, patients were placed in a supine position and, depending on the type of resection, 3–5 trocars were placed. In some cases, patients were placed in a lateral position. An intra-abdominal pressure of 12–15 mmHg was applied. Laparoscopic ultrasound was used to determine the parenchymal transection plane and for identification of additional lesions. The Pringle maneuver was used selectively. Different devices were used for the parenchymal transection phase. For minor resections the most frequently used devices were an ultrasonic dissector (n = 10 centers), vessel sealing device (n = 7), cavitron ultrasonic surgical aspirator (CUSA, n = 4) or clamp-crush with bipolar forceps (n = 2). For major resections again the ultrasonic dissector was most frequently used (n = 6 centers), followed by CUSA (n = 4), vessel sealing device (n = 3) and water-jet dissector (n = 2). Specimens were extracted in a plastic endoscopic bag through a Pfannenstiel incision or, in case of small lesions, through a widened trocar incision. For all robot-assisted procedures the da Vinci® Si Robotic Surgical System (Intuitive Surgical®, Inc., Sunnyvale, CA, USA) was used and devices used during parenchymal transection included the bipolar forceps and the vessel sealer.

Survey

To obtain baseline characteristics per center, a 50-question, online survey was sent to all centers in March 2017 (Appendix B). Surgeons were asked to describe their personal and institutional experience with MILS, including what form of training they had received prior to starting with MILS and whether they would be interested to participate in a nationwide, structured training program in major MILS. Non-responders received a maximum of three email reminders and one phone call.

Statistical analysis

Data analyses were performed using IBM SPSS Statistics for Windows version 24.0 (IBM corp., Armonk, NY, USA). Analysis was performed according to intention-to-treat principles, hence conversions to laparotomy were included in the MILS cohort. Continuous, parametric variables were reported as mean with standard deviation (SD). In case values were not normally distributed, continuous variables were reported as median with interquartile range (IQR). A Mann Whitney *U* test or independent-samples T test was used for the comparison of non-parametric and parametric continuous variables, respectively. Categorical variables were reported as proportions and compared using a chi-square or Fisher's exact test, as appropriate. A two-tailed P value of <0.05 was considered statistically significant.

Sensitivity analysis was performed to rule out any disproportional impact of simultaneous liver and colorectal resections and robot-assisted resections on MILS outcomes.

Two different subgroup analyses were performed comparing operative outcomes in high- and low-volume centers. In the first, high-volume was defined as an average annual volume of ≥20 MILS procedures over the entire study period. The low-volume comparison centers were all other centers, thus those centers with an average of <20 MILS procedures performed between 2011 and 2016. In the second subgroup analysis, the high volume group consisted of all patients that were operated in a year that the respective center performed ≥20 MILS procedures and compared to a low volume group with all patients operated in the other years.

Results

Of the 27 centers that were approached, data were gathered from 20 centers. The seven non-participating centers reported to have minimal experience with MILS. Eight out of 20 centers were university medical centers. A total of 49 surgeons performed MILS in these 20 centers with a median of 2 surgeons (2–3) per center. During the 6-year study period, a total of 6951 liver resections were performed, of which 916 were MILS (13%). There were no exclusions of patients objecting to the use of their data for research purposes. Of these 916 resections, 878 (96%) were totally laparoscopic, 31 (3%) were robot-assisted and 7 (1%) were hand-assisted. A flowchart of patient selection is given in Appendix A. Per year, the use of MILS increased from 6% of all liver resections in 2011 to 23% in 2016 ($P < 0.001$, Fig. 1). The overall use of MILS per center (all years combined) varied largely, from 3% to 36% ($P < 0.001$). Only one center performed more than 20 MILS procedures on average per year during the entire study period. When only assessing 2016, six centers performed more than 20 MILS procedures. Figs 2 and 3 show the overall

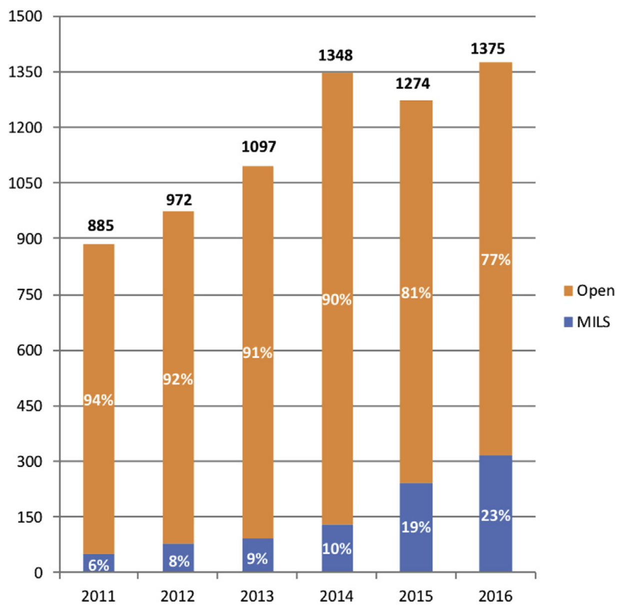

Figure 1 Proportion MILS of total annual volume of liver resections in the Netherlands (2011–2016)

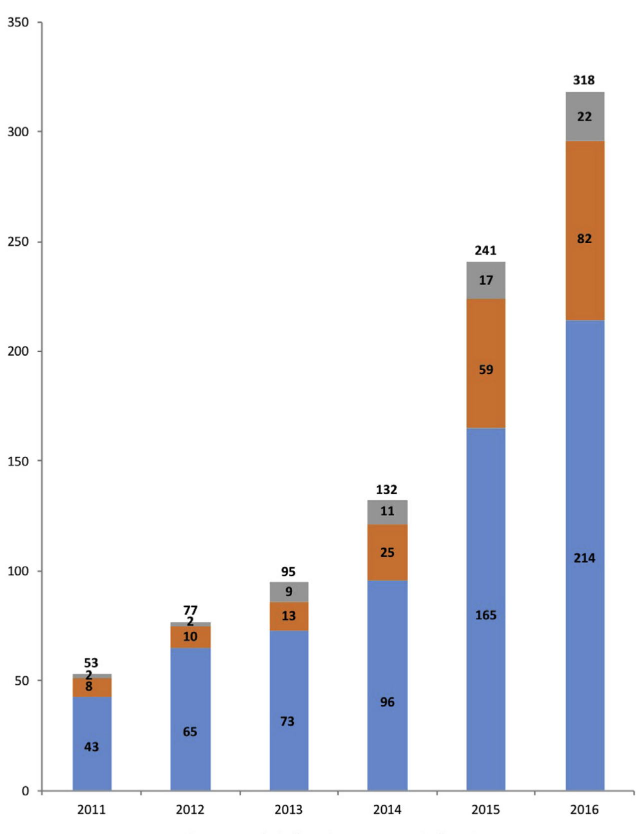

Figure 2 Annual use of minor and major MILS in the Netherlands (2011–2016)

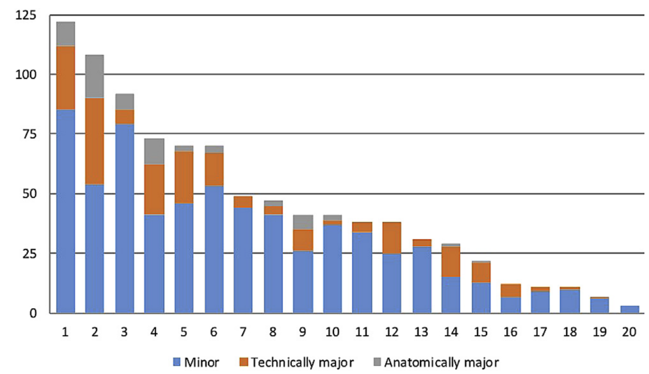

Figure 3 Total volume of MILS in 20 centers in the period 2011–2016

implementation of MILS and the annual volume of MILS per center categorized by the extent of resection, respectively.

Patient and procedure characteristics

The cohort consisted of 473 males (52%) and 443 (48%) females with a median age of 64 years (51–71). A total of 656 minor resections (72%), 63 anatomically major resections (7%) and 197 technically major resections (22%) were performed. All patient and procedure characteristics are presented in Table 1.

Operative outcomes

Operative outcomes were stratified for minor, anatomically major, and technically major resections (Table 2). Conversion rates were 10%, 21% and 21%, respectively. Reasons for conversion were difficulty to reach lesions (n = 47), bleeding (n = 28), concern about radicality (n = 15), adhesions (n = 11), open colorectal resection (n = 3), complications other than bleeding (n = 3), no laparoscopic ultrasound available to identify lesions (n = 3), equipment failure (n = 2) and other (n = 3). Intraoperative incidents occurred in 131 patients in total, mostly Grade 1 (54 (6%)) and Grade 2 (73 (8%)). In four patients (0.4%) a Grade 3 incident occurred which required operative re-intervention. There were no intraoperative deaths. Re-interventions included ultrasound guided drainage (n = 23), laparotomy (n = 21), re-laparoscopy (14), CT-guided drainage (n = 8) and ERCP with stent placement (n = 6). In four of the nine (44%) post-operative deaths within 90 days a multivisceral resection had been performed. This included two colorectal procedures that were complicated by eventually fatal anastomotic leakage, one distal pancreatectomy with splenectomy that was complicated by an eventually fatal intestinal perforation and one gastrojejunostomy. Other causes of death were respiratory insufficiency (n = 1) and disease progression (n = 5).

Sensitivity analysis

Both fatal simultaneous liver and colorectal resections were minor liver resections. Excluding these from the mortality analyses resulted in a 90-day mortality rate of 0.6% for minor MILS procedures. Other outcomes did not change when simultaneous

Table 1 Baseline characteristics

	Minor MILS (A) n = 656	Technically major MILS (B) n = 197	Anatomically major MILS (C) n = 63	*P* (A vs B)	*P* (A vs C)	*P* (B vs C)
Sex, male	325 (50)	117 (59)	31 (49)	0.015	0.959	0.155
Age, years, median (IQR)	63 (49–72)	65 (57–71)	63 (49–71)	0.052	0.673	0.137
BMI, kg/m^2, median (IQR)	25.6 (23–29)	25.5 (22.8–28.9)	21.1 (23–29.5)	0.850	0.561	0.513
American Society of Anesthesiology grade				0.041	0.728	0.038
ASA 1	129 (20)	24 (12)	16 (25)			
ASA 2	392 (60)	137 (70)	36 (57)			
ASA 3	116 (18)	34 (17)	10 (16)			
ASA 4	4 (1)	0	0			
Previous abdominal surgery	381 (58)	153 (78)	42 (67)	<0.001	0.186	0.079
Cancer as indication	461 (70)	170 (86)	47 (75)	<0.001	0.471	0.030
CRLM	328 (71)	139 (81)	38 (81)			
HCC	92 (14)	14 (8)	3 (6)			
Cholangiocarcinoma	11 (2)	3 (2)	2 (4)			
Other	30 (7)	14 (8)	4 (9)			
Number of lesions, median (IQR)	1 (1–1)	1 (1–2)	2 (1–2)	<0.001	<0.001	0.008
Size of largest tumor, mm, median (IQR)	27 (17–50)	23 (17–34)	44 (27–71)	0.004	<0.001	<0.001
Neoadjuvant chemotherapy	72 (11)	34 (17)	11 (17)	0.019	0.124	0.971
MILS approach				0.011	0.392	0.042
Total laparoscopic	638 (97)	184 (93)	63 (100)			
Robot-assisted	18 (3)	13 (7)	0			
Type of resection				<0.001	<0.001	<0.001
Wedge/non-anatomical resection	331 (50)	141 (72)	0			
Segmentectomy	78 (12)	21 (11)	0			
Bisegmentectomy	247 (38)	35 (18)	0			
Trisegmentectomy	0	0	11 (17)			
Hemihepatectomy	0	0	47 (75)			
○ Left	0	0	10 (16)			
○ Right	0	0	37 (59)			
Other major hepatectomy	0	0	5 (8)			
Simultaneous colorectal resection	70 (11)	21 (11)	0	0.997	0.006	0.007
Intraoperative ultrasound	467 (71)	178 (90)	58 (92)	<0.001	<0.001	0.241

All values in parentheses are proportions unless mentioned otherwise. Percentages may not add up due to rounding and missing data. MILS = minimally invasive liver surgery, IQR = inter quartile range, BMI = body mass index, CRLM = colorectal liver metastasis, HCC = hepatocellular carcinoma, MILS = minimally invasive liver surgery.

liver and colorectal resections and robot-assisted resections were excluded from analyses (data not shown). Baseline characteristics and operative outcome of simultaneous colorectal and liver resections and robot-assisted resections can be found in the supplementary material (Appendix C and D).

Subgroup analyses

Only one center averaged 20 or more MILS procedures annually during the entire study period. No significant differences were found for operating time, blood loss, conversion, morbidity, postoperative stay and mortality between this center and the other centers.

Six centers performed 20 or more minimally invasive resections in 2016, with a corresponding number of five centers in 2015 and 1 center in 2014. Comparing the outcomes of MILS procedures performed during these high-volume years to the rest showed higher implementation of major MILS (123 (38%) vs 137 (23%), $P < 0.001$) and less conversions (30 (9%) vs 88 (15%), $P = 0.02$) in the high-volume years. During these high-volume years, major MILS was associated with less conversions (14 (11%) vs 41 (30%), $P < 0.001$), a shorter operating time (184 (117–239) vs 200 (139–308) minutes, $P = 0.01$), and less overall complications (37 (30%) vs 58 (42%), $P = 0.04$) compared to the other years. The 90-day or

Table 2 Operative outcome

	Minor MILS (A) n = 656	Technically major MILS (B) n = 197	Anatomically major MILS (C) n = 63	*P* (A vs B)	*P* (A vs C)	*P* (B vs C)
Operative time, minutes, median (IQR)	127 (94–178)	176 (124–226)	304 (190–424)	<0.001	<0.001	<0.001
Blood loss, ml, median (IQR)	100 (50–300)	400 (113–975)	525 (363–938)	<0.001	<0.001	0.040
Conversion to laparotomy	63 (10)	42 (21)	13 (21)	<0.001	<0.001	0.368
Intraoperative incidents	66 (10)	51 (25)	14 (22)	<0.001	0.003	0.559
Postoperative complications						
Overall	136 (21)	64 (32)	31 (49)	<0.001	<0.001	0.016
Grade 3–6, severe	48 (7)	40 (20)	9 (14)	0.032	0.051	0.662
Reintervention	43 (6)	19 (9)	7 (11)	0.143	0.190	0.736
Relaparoscopy	7 (1)	6 (3)	1 (2)			
Relaparotomy	13 (2)	3 (2)	1 (2)			
CT-guided drainage	7 (1)	1 (1)	0			
US-guided drainage	8 (1)	7 (4)	3 (5)			
ERCP with stenting	3 (1)	1 (1)	2 (3)			
Other	5 (1)	1 (1)	0			
Readmission	33 (5)	12 (6)	9 (14)	0.548	0.008	0.040
Postoperative hospital stay, days, median (IQR)	5 (4–6)	6 (4–8)	7 (6–10)	<0.001	<0.001	<0.001
Resection margins for malignant lesions, R0	426/461 (92)	145/170 (85)	35/47 (74)	0.005	0.001	0.184
90-day/in hospital mortality	6 (0.9)	1 (0.5)	2 (3)	>0.999	0.150	0.147
1-year incisional hernia	13 (2)	8 (4)	3 (5)	0.184	0.297	0.768

All values in parentheses are proportions unless mentioned otherwise. Percentages may not add up due to rounding or missing data. IQR = inter quartile range.

in-hospital mortality was similar (2 (2%) vs 2 (1%), $P > 0.99$) (Tables 3 and 4).

Survey

Twenty-nine surgeons from 22 centers responded to the survey (center response rate 81%). Open liver surgery, including both minor and major resections, was performed in all centers, with a median of 11.3 years of experience (6.3–17.6) per surgeon. All but seven surgeons had an experience of ≥50 major open resections. The median experience with MILS was 6.3 years (4.3–9.3) per surgeon. Ten of 12 (83%) surgeons not yet performing major MILS indicated that they were willing to participate in a nationwide training program. When asked why they had not yet performed major MILS, the most noted reason was a lack of experience (n = 9). Other reasons were not enough patients to select appropriate candidates (n = 3), doubts about the advantages of laparoscopy (n = 2), problems acquiring required equipment (n = 2), switch to robotic surgery (n = 1) and no time in the OR schedule (n = 1).

The learning curve of MILS was approached differently between surgeons. Out of 29 surgeons performing MILS, 15 (52%) had completed an HPB fellowship with varying exposure to MILS, 13 (45%) were proctored (median of 4 (2–7) sessions), 17 (59%) had followed hands-on courses and 4 (14%) indicated they did not complete any training and skills were purely self-taught. Many surgeons (n = 16 (55%)) pursued combinations of different forms of training. Among 17 surgeons performing major MILS, 3 (18%) had completed a fellowship, 5 (29%) were proctored (median of 3 (3-3) sessions), 5 (29%) had followed hands-on courses and 4 (24%) were self-taught. Combinations of different forms of training in major MILS was less frequent (n = 3 (18%)).

Discussion

In this nationwide study, the overall implementation of MILS increased from 6% to 23%, with large variation between centers. Implementation of both technically and anatomically major MILS was low with a high conversion rate of 21%, and relatively high complication rates. Outcomes of major MILS (i.e. conversion, operating time, complications) were better when centers performed ≥20 MILS procedures per year, which suggests a benefit of centralization of major MILS.

Comprehensive data on implementation and outcome of MILS on a nationwide scale are scarce. Studies from France[7] and Italy[8,13] addressed the implementation of MILS but neither study reported on the impact of volume on outcome. Farges *et al.*[7] reported on 5527 MILS procedures from 270 French centers. They concluded that even in France, traditionally a pioneering country in minimally invasive surgery, MILS is still underused

Table 3 Baseline characteristics of major MILS procedures performed in low volume compared to high volume centers

	Low volume centers N = 137	High volume centers N = 123	*P*
Sex, male	72 (53)	76 (62)	0.133
Age, years, median (IQR)	64 (55–71)	66 (54–72)	0.274
BMI, kg/m^2, median (IQR)	25.7 (22.7–29.5)	25.8 (23.1–29.1)	0.914
American Society of Anesthesiology grade			0.158
- ASA 1	24 (18)	16 (13)	
- ASA 2	83 (61)	90 (73)	
- ASA 3	27 (20)	17 (14)	
Previous abdominal surgery	97 (71)	98 (80)	0.099
Cancer as indication	111 (81)	106 (86)	0.264
- CRLM	84 (61)	93 (76)	
- HCC	12 (9)	5 (4)	
- Cholangiocarcinoma	2 (1)	3 (2)	
- Other	13 (9)	5 (4)	
Number of lesions, median (IQR)	1 (1–2)	2 (1–2)	0.011
Size of largest tumor, mm, median (IQR)	26.5 (19–43.8)	26 (17–39.3)	0.529
Neoadjuvant chemotherapy	20 (15)	25 (20)	0.223
MILS approach			<0.001
- Total laparoscopic	124 (91)	123 (100)	
- Robot-assisted	13 (9)	0	
Type of resection			0.861
- Wedge/non-anatomical resection	76 (55)	65 (53)	
- Segmentectomy	11 (8)	10 (8)	
- Bisegmentectomy	20 (15)	15 (12)	
- Trisegmentectomy	4 (3)	7 (6)	
- Hemihepatectomy	24 (18)	23 (19)	
- Other major hepatectomy	2 (1)	3 (2)	
Simultaneous colorectal resection	10 (7)	11 (9)	0.672
Intraoperative ultrasound	120 (88)	116 (94)	0.129

All values in parentheses are proportions unless mentioned otherwise. Percentages may not add up due to rounding and missing data. MILS = minimally invasive liver surgery, IQR = inter quartile range, BMI = body mass index, CRLM = colorectal liver metastasis, HCC = hepatocellular carcinoma, MILS = minimally invasive liver surgery.

with only 14% of the total number of liver resections in the period 2007–2012. The Italian I GO MILS program by Aldrighetti *et al.*[13] performed a nationwide survey among 39 centers and reported a 10.3% implementation rate of MILS in the period 1995–2012. This same group also performed a national registry based analysis on 1678 MILS performed in 48 centres between 2014 and 2017.[8] With 7.1% major resections, a conversion rate of 10.1%, overall morbidity of 22.3% and mortality of 0.3%, their results are comparable to the current study. However, unlike the current study, they did not stratify outcomes for minor and major MILS. Others also evaluated their nationwide practice in MILS using surveys and questionnaires,[14–16] but none stratified outcomes for minor and major MILS or assessed the impact of volume on outcome. These reported implementation rates of MILS in nationwide studies, including the current study, are surprisingly low and clearly suggests that guidelines statements have not yet been fully implemented outside expert centers.

The Southampton guidelines stated that the implementation of MILS should be pursued in a stepwise fashion: starting with minor resections, before expanding to more difficult major resections.[6] The steady increase of the proportion of minimally invasive technically major and anatomically major resections over the years (Fig. 2) may suggest an overall good adherence to this concept. The gradual adoption of technically major resections in almost all centers suggests that these resections are considered an easier next step in the learning curve than larger resections such as hemihepactectomies or other anatomically major resections. Still, it remains difficult to define when a surgeon or center is ready for the next step in this

Table 4 Operative outcome of major MILS procedures performed in low volume compared to high volume centers

	Low volume centers N = 137	High volume centers N = 123	*P*
Operative time, minutes, median (IQR)	200 (139–308)	184 (117–239)	0.010
Blood loss, ml, median (IQR)	400 (150–900)	525 (198–1000)	0.190
Conversion to laparotomy	41 (30)	14 (11)	<0.001
Intraoperative incidents	36 (26)	21 (17)	0.616
Postoperative complications			
- Overall	58 (42)	37 (30)	0.040
- Grade 3–6, severe	20 (15)	13 (11)	0.330
Reintervention	12 (9)	14 (11)	0.482
- Relaparoscopy	2 (1)	5 (4)	
- Relaparotomy	1 (1)	3 (2)	
- CT-guided drainage	0	1 (1)	
- US-guided drainage	6 (4)	4 (3)	
- ERCP with stenting	2 (1)	1 (1)	
- Other	1 (1)	0	
Readmission	11 (8)	10 (8)	0.996
Postoperative hospital stay, days, median (IQR)	7 (5–9)	6 (5–8)	0.426
Resection margins for malignant lesions, R0	101/111 (91)	77/106 (73)	0.001
90-day/in hospital mortality	2 (1)	1 (1)	>0.999
1-year incisional hernia	4 (3)	7 (6)	0.461

All values in parentheses are proportions unless mentioned otherwise. Percentages may not add up due to rounding or missing data. IQR = inter quartile range.

implementation process. Many authors have previously reported the learning curve of minor and major MILS as a specific number of resections[17–22] but the applicability of these numbers in real-life clinical practice, especially in a nationwide pool of surgeons, is questionable. Differences in experience in open liver resection, differences in training in MILS and overall surgical skills all play an important role. In addition, logistical aspects and the annual volume of liver surgery patients whom to select minimally invasive candidates from are crucial for the decision to take a next step towards more advanced MILS procedures. Whether these recommendations also apply to the robot-assisted procedures is currently unknown. The relatively high percentage of technically major robot-assisted resections (42%) in this early phase might be attributed to the increased dexterity and accelerated learning curve with the robotic console. However, the proportion of robot-assisted liver resections is rather small (3%) as these procedures were only introduced in the Netherlands in 2014 and are currently performed in only three centres.[23] The potential advantages of the robotic approach over laparoscopy remains to be determined.[24]

The Southampton guideline also stated that a stepwise approach should always be combined with structured training[6] as was recently validated.[25] However, pursuing training can be difficult in daily clinical practice and the actual content of structured training remains unspecified. Dedicated laparoscopic HPB fellowships have been developed,[26,27] but pose a logistical challenge for many surgeons. Hands-on-courses are easier to organize, but lack the guided follow-up required to implement MILS safely. Setting up nationwide structured training programs that combine the best aspects of these different forms of training has proven to be feasible in the Netherlands for minimally invasive pancreatic surgery.[28,29] In order to standardize and guide the stepwise implementation and structured training of MILS in the Netherlands, a similar program (LAELIVE) has now been established for MILS and is currently ongoing.

Regardless of how MILS has been implemented so far, the outcome of minor MILS in this study are comparable to the results from selected international high-volume centers, as included in a large meta-analysis.[2] This meta-analysis showed the superiority of laparoscopy versus the open approach for minor liver resections in terms of intraoperative blood loss, operating time, postoperative hospital stay and postoperative morbidity. However, the overall results of major MILS in the Netherlands clearly show the complexity of these procedures. Although blood loss and operating time were slightly lower compared to the meta-analysis by Ciria *et al.*[2] (500 vs 620 ml and 185 vs 235 min, respectively), the conversion rate of 21% with a complication rate of 37%, respectively, are higher than previously reported for major MILS. Furthermore, the annual volume of MILS seems related to outcome. When centers performed 20 or more MILS procedures annually, outcome for major MILS was superior, with fewer conversions, a shorter operating time and less overall postoperative complications. The observed low R0 resection rate in high volume centers remains unexplained but could also reflect the residual selection bias, with more complex procedures being performed in these centers. Whether this outcome influences long term survival should be further investigated.

These subgroup analyses seem to suggest a benefit of a minimal volume for MILS, but should be interpreted carefully as they were not adjusted for confounding factors and the implementation of MILS is still ongoing. It is however clear that a certain annual total volume of liver resections is required to be able to select patients suitable for major MILS as well as a certain annual volume of MILS procedures. The current minimal annual volume for liver surgery in the Netherlands is set at 20 but does not take MILS into account. A comparison of the current data with highly centralized centers with large patient numbers could be very important to make a case for centralization of (major) MILS.

The current study has several limitations. First, the retrospective design introduces an inevitable risk of selection and information bias. For example, the actual use of intraoperative ultrasound might be higher as it might not have always been reported in operative reports. Second, since data were only gathered from those centers that responded to the survey, there is a possibility that some resections were missed. However, available information from the non-participating centers and surgeons suggests that the number of missed resections is negligible. The volume-outcome relationship could potentially have been further strengthened if these data would have been available. Third, difficulty scores[30–32] were not calculated since the focus was on the differentiation between minor and (technically) major as made in current guidelines. Furthermore, it is suggested that current difficulty scores still do not incorporate all the factors that are believed to influence difficulty.[33] Fourth, the current study only focused on MILS and excluded other minimally invasive techniques such as radiofrequency and microwave ablation that could possibly prove to be even less invasive.

In conclusion, the current study provides an overview of the implementation and outcome of minor and major MILS on a nationwide scale. Whereas the use of minor MILS is clearly increasing with outcomes comparable to international reports, the implementation of major MILS is slow and the observed volume-outcome relationship confirms its complexity and the need for a structured training program in centers with sufficient volume.

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Conflicts of interest
None declared.

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Appendix A. Supplementary data

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