University of Groningen

Comparing practice and outcome of laparoscopic liver resection between high-volume expert centres and nationwide low-to-medium volume centres

Dutch Liver Collaborative Grp; Gorgec, B.; Fichtinger, R. S.; Ratti, F.; Aghayan, D.; Van der Poel, M. J.; Al-Jarrah, R.; Armstrong, T.; Cipriani, F.; Fretland, A. A.

Published in:
British Journal of Surgery

DOI:
[10.1093/bjs/znab096](https://doi.org/10.1093/bjs/znab096)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2021

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Dutch Liver Collaborative Grp, Gorgec, B., Fichtinger, R. S., Ratti, F., Aghayan, D., Van der Poel, M. J., Al-Jarrah, R., Armstrong, T., Cipriani, F., Fretland, A. A., Suhool, A., Bemelmans, M., Bosscha, K., Braat, A. E., De Boer, M. T., Dejong, C. H. C., Doornebosch, P. G., Draaisma, W. A., Gerhards, M. F., ... Besselink, M. G. (2021). Comparing practice and outcome of laparoscopic liver resection between high-volume expert centres and nationwide low-to-medium volume centres. *British Journal of Surgery*, 108(8), 983-990. <https://doi.org/10.1093/bjs/znab096>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Comparing practice and outcome of laparoscopic liver resection between high-volume expert centres and nationwide low-to-medium volume centres

B. Görges^{1,2,3,†}, R. S. Fichtinger^{4,†}, F. Ratti^{5,‡}, D. Aghayan^{6,7,8,‡}, M. J. Van der Poel^{1,†}, R. Al-Jarrah², T. Armstrong², F. Cipriani⁵, Å. A. Fretland^{6,7}, A. Suhoor², M. Bemelmans⁴, K. Bosscha⁹, A. E. Braat¹⁰, M. T. De Boer¹¹, C. H. C. Dejong⁴, P. G. Doornebosch¹², W. A. Draaisma¹³, M. F. Gerhards¹⁴, P. D. Gobardhan¹⁵, J. Hagendoorn¹⁶, G. Kazemier¹⁷, J. Klaase^{11,18}, W. K. G. Leclercq¹⁹, M. S. Liem¹⁸, D. J. Lips^{9,18}, H. A. Marsman¹⁴, J. S. D. Mieog¹⁰, Q. I. Molenaar¹⁶, V. B. Nieuwenhuijs²⁰, C. L. Nota¹⁶, G. A. Patijn²⁰, A. M. Rijken¹⁵, G. D. Slooter¹⁹, M. W. J. Stommel²¹, R. J. Swijnenburg^{1,10}, P. J. Tanis¹, W. W. Te Riele²², T. Terkivatan²³, P. M. P. Van den Tol¹⁷, P. B. Van den Boezem²¹, J. A. Van der Hoeven²⁴, M. Vermaas¹², B. Edwin^{6,7,8,§}, L. A. Aldrighetti^{5,§}, R. M. Van Dam^{4,25,26,§}, M. Abu Hilal^{2,3,§}, M. G. Besselink^{1,§,*} for the Dutch Liver Collaborative Group

¹Department of Surgery, Cancer Centre Amsterdam, Amsterdam UMC, University of Amsterdam, the Netherlands

²Department of Surgery, University Hospital Southampton NHS Foundation Trust, Southampton, UK

³Department of Surgery, Fondazione Poliambulanza - Istituto Ospedaliero, Brescia, Italy

⁴Department of Surgery, Maastricht University Medical Centre+, Maastricht, the Netherlands and RWTH Aachen, Germany

⁵Hepatobiliary Surgery Division, IRCCS San Raffaele Hospital, Milan, Italy

⁶Department of Hepato-Pancreato-Biliary Surgery, Oslo University Hospital, Oslo, Norway

⁷The Intervention Centre, Oslo University Hospital - Rikshospitalet, Oslo, Norway

⁸Institute of Clinical Medicine, Medical Faculty, University of Oslo, Norway

⁹Department of Surgery, Jeroen Bosch Hospital, 's-Hertogenbosch, the Netherlands

¹⁰Department of Surgery, Leiden University Medical Centre, Leiden, the Netherlands

¹¹Department of Surgery, University Medical Centre Groningen, Groningen, the Netherlands

¹²Department of Surgery, IJsselland Hospital, Capelle aan den IJssel, the Netherlands

¹³Department of Surgery, Meander Medical Centre, Amersfoort, the Netherlands

¹⁴Department of Surgery, OLVG, Amsterdam, the Netherlands

¹⁵Department of Surgery, Amphia Hospital, Breda, the Netherlands

¹⁶Department of Surgery, University Medical Centre Utrecht, Utrecht, the Netherlands

¹⁷Department of Surgery, Cancer Centre Amsterdam, Amsterdam UMC, Vrije Universiteit Amsterdam, the Netherlands

¹⁸Department of Surgery, Medical Spectrum Twente, Enschede, the Netherlands

¹⁹Department of Surgery, Máxima Medical Centre, Veldhoven, the Netherlands

²⁰Department of Surgery, Isala, Zwolle, the Netherlands

²¹Department of Surgery, Radboud University Medical Centre, Nijmegen, the Netherlands

²²Department of Surgery, St. Antonius Hospital, Nieuwegein, the Netherlands

²³Department of Surgery, Erasmus Medical Centre, Rotterdam, the Netherlands

²⁴Department of Surgery, Albert Schweitzer Hospital, Dordrecht, the Netherlands

²⁵GROW - School for Oncology & Developmental Biology, Maastricht University, Maastricht, The Netherlands

²⁶Department of General and Visceral Surgery, University Hospital Aachen, Aachen, Germany

*Correspondence to: Department of Surgery, Cancer Centre Amsterdam, Amsterdam UMC, University of Amsterdam, Meibergdreef 9, 1105 AZ, Amsterdam, the Netherlands (e-mail: m.g.besselink@amsterdamumc.nl)

[†]Shared first authorship

[‡]Shared second authorship

[§]Shared senior authorship

Abstract

Background: Based on excellent outcomes from high-volume centres, laparoscopic liver resection is increasingly being adopted into nationwide practice which typically includes low-medium volume centres. It is unknown how the use and outcome of laparoscopic liver resection compare between high-volume centres and low-medium volume centres. This study aimed to compare use and outcome of laparoscopic liver resection in three leading European high-volume centres and nationwide practice in the Netherlands.

Method: An international, retrospective multicentre cohort study including data from three European high-volume centres (Oslo, Southampton and Milan) and all 20 centres in the Netherlands performing laparoscopic liver resection (low-medium volume practice) from January 2011 to December 2016. A high-volume centre is defined as a centre performing >50 laparoscopic liver resections per year. Patients were retrospectively stratified into low, moderate- and high-risk Southampton difficulty score groups.

Results: A total of 2425 patients were included (1540 high-volume; 885 low-medium volume). The median annual proportion of laparoscopic liver resection was 42.9 per cent in high-volume centres and 7.2 per cent in low-medium volume centres. Patients in the

high-volume centres had a lower conversion rate (7.4 versus 13.1 per cent; $P < 0.001$) with less intraoperative incidents (9.3 versus 14.6 per cent; $P = 0.002$) as compared to low-medium volume centres. Whereas postoperative morbidity and mortality rates were similar in the two groups, a lower reintervention rate (5.1 versus 7.2 per cent; $P = 0.034$) and a shorter postoperative hospital stay (3 versus 5 days; $P < 0.001$) were observed in the high-volume centres as compared to the low-medium volume centres. In each Southampton difficulty score group, the conversion rate was lower and hospital stay shorter in high-volume centres. The rate of intraoperative incidents did not differ in the low-risk group, whilst in the moderate-risk and high-risk groups this rate was lower in high-volume centres (absolute difference 6.7 and 14.2 per cent; all $P < 0.004$).

Conclusion: High-volume expert centres had a sixfold higher use of laparoscopic liver resection, less conversions, and shorter hospital stay, as compared to a nationwide low-medium volume practice. Stratification into Southampton difficulty score risk groups identified some differences but largely outcomes appeared better for high-volume centres in each risk group.

Introduction

Over the last three decades, numerous studies^{1–3} from leading high-volume centres reported excellent outcomes of laparoscopic liver resection. According to the most recent international Southampton guidelines⁴, laparoscopy is now seen as the standard for minor liver resections. Also, major laparoscopic liver resections are now considered feasible, safe and effective^{4–9}.

In recent years, based on these promising findings, laparoscopic liver resection is increasingly being implemented into nationwide practice which typically includes low-medium volume centres. This requires overcoming the learning curve for laparoscopic liver resection but also the need to maintain expertise and skills which requires sufficient annual surgical volume. The number of patients and laparoscopic liver resection complexity were recently shown to vary considerably among Dutch centres for liver surgery¹⁰. This variation in annual surgical volume between centres is seen in many countries worldwide. Furthermore, case selection is of paramount importance to make sure that the laparoscopic liver resection difficulty is compatible with surgical expertise and experience. The Southampton difficulty score¹¹ may be instrumental by objectively determining the difficulty of a laparoscopic liver resection.

While operative outcomes in low-medium volume practice have been studied for open liver surgery^{12–17}, limited data¹⁷ are available for laparoscopic liver resection. This is particularly relevant since current guidelines⁴ have almost exclusively based their advice on outcomes from high-volume centres. The aim of this study was therefore to compare outcomes of laparoscopic liver resection between three high-volume centres to a nationwide low-medium volume practice.

Methods

The current study has been conducted in line with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations¹⁸. All data have been stored anonymously and were approved to be used for research purposes. Three high-volume centres participated: the Oslo University Hospital in Norway, the University Hospital Southampton in the United Kingdom, and the San Raffaele Hospital in Milan, Italy and twenty low-medium volume centres in the Netherlands.

Study design and patient selection

A retrospective review of the prospectively collected surgical databases of the three high-volume centres and all laparoscopic liver resections performed in the twenty centres in the Netherlands was performed. Procedures were performed between January 2011 and December 2016.

Consecutive patients undergoing elective laparoscopic liver resection for all liver diseases were included. Patients were excluded when hand-assisted laparoscopy was planned preoperatively, no formal resection was planned (i.e. in the case of cyst fenestration/deroofing, biopsies, diagnostic laparoscopy), living donor liver resection was indicated, or when emergency hepatic surgery was performed.

The Southampton difficulty score¹¹ was calculated per patient in retrospect. Based on the Southampton difficulty score, patients were divided into the low- (0–2 points), moderate- (3–5 points), high- (6–9 points) and extremely high-risk (10–15 points) groups.

Definitions and data collection

A high-volume centre is defined as a centre performing >50 laparoscopic liver resections per year. The twenty centres in the Netherlands, including eight university medical centres, performed ≤50 laparoscopic liver resections per centre per year during the study period. Annual laparoscopic liver resection volume was defined as the number of laparoscopic liver resections performed in each centre during a specific year. This means that patients per centre could be included in multiple groups, depending on the volumes in a specific year. Annual laparoscopic liver resection proportion was defined as the rate of laparoscopic liver resections divided by the annual total volume of liver resections in each centre. More definitions, data collection and surgical technique are provided in detail in the [supplementary material](#).

Statistical analysis

All data analyses were performed using IBM SPSS Statistics for Macintosh version 26.0.0 (IBM corp., Armonk, NY, USA). Continuous variables are reported as median with interquartile range (i.q.r.). Categorical variables are presented as numbers and proportions. Comparisons have been performed with Mann-Whitney U-tests and Kruskal–Wallis test for continuous variables and Chi-Square tests or Fisher's exact tests for categorical variables. Laparoscopic liver resections that were converted to open surgery were included in the current analyses and were grouped as per initial laparoscopic procedure, according to intention-to-treat principles. Operative outcomes were subsequently analysed using paired tests. Two-tailed $P < 0.050$ was considered statistically significant. Bonferroni correction that narrowed the alpha border to 0.017 (0.05 divided by 3) was applied for multiple testing.

Two sensitivity analyses were performed. First, by excluding patients with colorectal liver metastases who received a simultaneous colorectal resection. Second, operative outcomes were reported separately for low-volume centres (<20 laparoscopic liver resections per centre annually) and medium-volume centres (20–50 laparoscopic liver resections per centre annually).

Results

Centre characteristics

The overall median annual volume of liver resections (including both open and laparoscopic resections) was 220.5 in the high-volume centres and 50.8 (i.q.r. 48.5–56.4) in nationwide low-medium volume practice. There were no high-volume centres in the Netherlands during the study period. The overall median annual laparoscopic liver resection volume was 79.5 in the high-volume centres and 6.5 (i.q.r. 5.3–10.0) in nationwide low-medium volume practice. The overall median annual laparoscopic liver resection proportion was 42.9 per cent (i.q.r. 38.0–50.6 per cent) in the high-volume centres and 7.2 per cent (i.q.r. 6.3–14.1 per cent) in nationwide low-medium volume practice ($P = 0.004$). In Oslo, resections were performed by 6 surgeons, and in Southampton and Milan by 5 surgeons each. A total of 49 surgeons performed the resections in the Netherlands with a median of 2 (2–3) surgeons per centre.

Patient and procedure characteristics

A total of 2425 patients were included: 563 from Oslo, 522 from Milan, 455 from Southampton, and 885 from the Netherlands (low-medium volume practice) (Fig. 1). Overall patient and procedure characteristics of the two groups are displayed in Table 1. The median Southampton difficulty score in the high-volume centres was significantly higher as compared with the nationwide low-medium volume practice (5 (i.q.r. 3–7) versus 3 (i.q.r. 2–4.5), $P < 0.001$). High-volume centres had relatively less patients in the low- (16.6 versus 38.9 per cent; $P < 0.001$), almost similar proportion of patients in the moderate- (45.3 versus 46.7 per cent; $P = 0.578$), and a higher proportion in the high- (34.3 versus 14.1 per cent; $P < 0.001$) and extremely high-risk (3.7 versus 0.2 per cent; $P < 0.001$) groups.

Operative outcomes

Table 2 shows operative outcomes of patients in high-volume centres and low-medium volume practice. Patients in the high-volume centres had a lower conversion rate (7.4 versus 13.1 per cent; $P < 0.001$) with less intraoperative incidents of all grades (9.3 versus 14.6 per cent; $P = 0.002$) as compared to low-medium volume centres. Whereas postoperative morbidity and mortality rates were similar in the two groups, a lower reintervention rate (5.1 versus 7.2%; $P = 0.034$) and a shorter postoperative hospital stay (3 versus 5 days; $P < 0.001$) were observed in the high-volume centres as compared to the low-medium volume centres.

Operative outcomes after stratification of patients into low-, moderate- and high-risk Southampton difficulty score groups are shown in Table 3 and Fig. 2. Conversion rate was lower in all risk groups in high-volume centres (1.2 versus 9.8 per cent in low, 6.1 versus 12.1 per cent in moderate and 11.1 versus 21.7 per cent in

high risk; all $P < 0.001$) and postoperative hospital stay shorter in high-volume centres (3 versus 5 days in low, 3 versus 5 days in moderate and 4 versus 7 days in high risk; all $P < 0.001$) as compared to low-medium volume centres. Among the low-risk groups of high-volume and low-medium volume centres, the rate of intraoperative incidents did not differ significantly, whilst this outcome was significantly better in high-volume centres for high-risk laparoscopic liver resections (13.2 versus 27.8 per cent; $P = 0.004$). The intraoperative incidents mainly consisted of intraoperative excessive bleeding and injury to the surrounding organs such as small bowel perforation during surgical manipulations and diaphragmatic injury during liver mobilization, all with further consequences. Severe postoperative complications and 90-day/in-hospital mortality did not differ between high-volume centres and low-medium volume practice in any of the risk groups. After excluding patients with colorectal liver metastases who received a simultaneous colorectal resection, the operative outcomes did not change considerably from the outcomes of the former analysis (Table S1).

Operative outcomes according to volume subgroups

Volume-based stratification resulted in 1540 patients in the high-volume group (>50 laparoscopic liver resections per centre annually), 313 patients in the medium-volume group (20–50 laparoscopic liver resections per centre annually) and 572 patients in the low-volume group (<20 laparoscopic liver resections per centre annually) (Table S2). There were less conversions, a lower rate of overall intraoperative incidents, less reinterventions, less readmissions and a shorter postoperative hospital stay in high-volume centres as compared to both low- and medium-volume groups. While an increasing hospital volume was associated with a decreasing conversion rate, there was no hospital volume-outcome correlation for postoperative morbidity and mortality.

Discussion

This international multicentre cohort study comparing the use and outcomes of laparoscopic liver resection between three international high-volume centres and nationwide low-medium volume practice in a single country found a sixfold higher use of laparoscopic liver resection in high-volume centres, especially in patients with higher Southampton difficulty scores. Whereas postoperative morbidity and mortality rates were similar between high-volume and nationwide low-medium volume centres, a lower conversion rate, less intraoperative incidents of all grades, lower reintervention rate and a shorter postoperative hospital stay were observed in the high-volume centres as compared to the low-medium volume centres. Stratification into

Fig. 1 Flowchart showing total cohort of patients who received laparoscopic liver resection in three high-volume expert centres and nationwide low-medium volume practice (20 Dutch centres) (1). Stratification into Southampton difficulty score risk groups (2) has been performed to compare operative outcomes between high-volume centres and nationwide low-medium volume practice. An additional subgroup analysis compared operative outcomes stratified for hospital volume (3).

Table 1 Patient and procedure characteristics

	High-volume centres (3 centres) n = 1540	Nationwide low-medium volume practice (20 centres) n = 885	P	SMD
Age (years)*	66 (56–74)	64 (52–71)	≤0.001 [#]	0.253
Sex (male)	792 (52)	457 (51.6)	0.850	0.008
BMI (kg/m ²)*	25 (23–28)	25.6 (23–29)	0.030 [§]	0.126
ASA grade			<0.001	0.285
ASA 1	111 (7.7)	166 (19.1)		
ASA 2	988 (68.4)	542 (62.4)		
ASA 3	342 (23.7)	157 (18.1)		
ASA 4	3 (0.2)	4 (0.5)		
Cirrhosis	14 (3.1)	59 (6.7)	0.006	0.176
Previous abdominal surgery	928 (60.3)	558 (63.1)	0.174	0.058
Southampton Difficulty score ^{11*}	5 (3–7)	3 (2–4.5)	<0.001 [#]	0.664
Preoperative chemotherapy	472 (30.8)	112 (12.7)	<0.001	0.432
Previous open liver surgery	82 (5.4)	19 (2.1)	<0.001	0.165
Malignancy	1305 (84.9)	655 (74)	<0.001	0.280
Size of lesions			<0.001	0.088
<3 cm	677 (45.3)	441 (54.2)		
3–5 cm	528 (35.4)	198 (24.4)		
>5 cm	288 (19.3)	174 (21.4)		
Extent of resection			<0.001	0.519
Minor	738 (47.9)	638 (72.1)		
Technically major	490 (31.8)	184 (20.8)		
Anatomically major	312 (20.3)	63 (7.1)		
Southampton difficulty risk group ¹¹				
Low-risk	245 (16.6)	316 (38.9)	<0.001	0.534
Moderate-risk	669 (45.3)	380 (46.7)	0.515	0.028
High-risk	507 (34.3)	115 (14.1)	<0.001	0.467
Extremely high-risk	55 (3.7)	2 (0.2)	<0.001	0.229
Pathology			<0.001	0.158
Colorectal liver metastasis	679 (44.1)	490 (55.5)		
Hepatocellular carcinoma	252 (16.4)	104 (11.8)		
Cholangiocarcinoma	92 (6.0)	15 (1.7)		
Benign tumour	121 (7.8)	142 (16.1)		
Other	361 (23.4)	132 (14.9)		
Number of lesions*	1 (1–2)	1 (1–2)	0.838 [§]	0.099
Size of largest lesion (mm)*	30 (18–47)	27 (17–47)	0.056 [§]	0.051
Type of resection			<0.001	0.534
Minor				
Wedge / non-anatomical	411 (55.8)	324 (50.8)		
Segmentectomy	120 (15.3)	75 (11.8)		
Bisegmentectomy	206 (28)	239 (37.5)		
Technically major				
Wedge / non-anatomical	307 (62.7)	132 (71.7)		
Segmentectomy	88 (18)	18 (9.8)		
Bisegmentectomy	95 (19.4)	34 (18.5)		
Anatomically major				
Trisegmentectomy	22 (7.1)	11 (17.5)		
Hemihepatectomy	286 (91.7)	47 (74.6)		
Other major hepatectomy	4 (1.3)	5 (7.9)		
Simultaneous colorectal resection	41 (2.7)	88 (9.9)	<0.001	0.325

Values in parentheses are percentages unless mentioned otherwise. * Values are median (i.q.r.). BMI, body mass index. ASA, American Society of Anesthesiology. All tests are χ^2 tests, unless mentioned otherwise. [#] Independent T-test. [§] Mann-Whitney U-test. [†] Fisher's exact test.

Southampton difficulty score risk groups showed that in all risk groups, outcomes in high-volume centres appeared largely better than in low-medium volume centres with an increasing difference in outcomes in the higher risk groups in favour of the high-volume centres. Collaborating regional networks of liver centres may be an effective structural strategy with each centre focusing on and aiming for high volume laparoscopic liver resection in a specific risk group.

Since this is the first study comparing high-volume centres with nationwide outcomes, we can only compare our findings to registry studies. Recently, a nationwide Italian registry study¹⁹ investigated the impact of volume of laparoscopic liver resection on operative outcomes. In accordance with the present study, a significant volume-outcome association for laparoscopic liver resection was reported, especially when more complex resections

were performed. However, unlike the current study, results were stratified according to the classification proposed by Kawaguchi et al.²⁰ due to limited data available in the national registry. A second nationwide population-based study²¹ performed a volume-based comparison of outcomes for open and minimally invasive liver resections. As the analyses remained within-groups (open compared with minimally invasive liver resections) without a subgroup-analysis focusing on outcomes of minimally invasive liver resections in different hospital volumes and different patient risk groups, their conclusions are difficult to extrapolate.

According to the recent Southampton guidelines⁴, laparoscopic liver resection is considered safe and feasible and should be implemented in a stepwise fashion in all liver centres with at least 2 surgeons proficient in laparoscopic liver resection. Of note, the technical complexity of laparoscopic liver resections

Table 2 Operative outcomes

	High-volume centres (3 centres) n = 1540	Nationwide low-medium volume practice (20 centres) n = 885	p [§]
Operative time (minutes)*	184 (116–274)	144 (100–201)	<0.001 [¶]
Blood loss (mL)*	200 (100–450)	200 (50–500)	0.024 [¶]
Conversion to laparotomy	113 (7.4)	115 (13.0)	<0.001
Intraoperative incidents	83 (9.3)	129 (14.6)	0.002
Grade 1	40 (4.5)	53 (6.0)	
Grade 2	43 (4.8)	72 (8.1)	
Grade 3	0 (0)	4 (0.5)	
Postoperative complications	278 (18.3)	157 (17.7)	0.736
Severe, grade 3–6	99 (8.0)	76 (8.6)	0.632
Reintervention	78 (5.1)	64 (7.2)	0.034
Readmission	44 (2.9)	51 (5.8)	<0.001
Postoperative hospital stay (days)*	3 (2–5)	5 (4–7)	<0.001 [¶]
R1 resection margin	113 (8.0)	94 (10.6)	<0.001
90-day / in-hospital mortality	12 (0.8)	9 (1.0)	0.543

Values in parentheses are percentages unless mentioned otherwise; * values are median (i.q.r.). [§] χ^2 , except [¶] Mann-Whitney U test.

Table 3 Operative outcomes, stratified for low-, moderate- and high-risk Southampton difficulty risk groups

	Low risk		Moderate risk		High risk	
	High-volume centres n = 245	Nationwide low-medium volume practice n = 316	High-volume centres n = 669	Nationwide low-medium volume practice n = 380	High-volume centres n = 507	Nationwide low-medium volume practice n = 115
Operative time (minutes)*	120 (75–191)	120 (90–176)	162 (95–240)	146 (109–194)	249 (180–330)	204.5 (148–334)
Blood loss (mL)*	50 (30–200)	100 (50–300)	200 (50–400)	150 (50–500)	330 (200–500)	500 (200–973)
Conversion to laparotomy	3 (1.2)	31 (9.8)	41 (6.1)	46 (12.1)	56 (11.1)	25 (21.7)
Intraoperative incidents	5 (4.1)	31 (9.8)	25 (7.2)	53 (13.9)	48 (13.2)	32 (27.8)
Grade 1	2 (1.7)	11 (3.5)	12 (3.5)	24 (6.3)	25 (6.8)	14 (12.2)
Grade 2	3 (2.5)	19 (6.0)	13 (3.8)	28 (7.4)	23 (6.3)	16 (13.9)
Grade 3	0	1 (0.3)	0	1 (0.3)	0	2 (1.7)
Postoperative complications	35 (14.6)	52 (16.5)	97 (14.6)	62 (16.3)	127 (25.1)	29 (25.2)
Severe, grade 3–6	11 (6.6)	25 (7.9)	33 (5.9)	31 (8.2)	43 (10.1)	13 (11.3)
Reintervention	10 (4.2)	20 (6.3)	29 (4.4)	26 (6.8)	31 (6.1)	9 (7.8)
Readmission	3 (1.2)	21 (6.7)	17 (2.5)	13 (3.4)	22 (4.3)	9 (7.9)
Postoperative hospital stay (days)*	3 (2–4)	5 (4–7)	3 (2–5)	5 (4–7)	4 (3–6)	7 (5–9)
R1 resection margin	20 (9.8)	28 (8.9)	48 (7.6)	35 (9.2)	40 (8.2)	20 (17.5)
90-day / in-hospital mortality	0	4 (1.3)	2 (0.3)	2 (0.5)	7 (1.4)	3 (2.6)

Values in parentheses are percentages unless mentioned otherwise; * values are median (i.q.r.); Values in bold are considered statistically significant ($P < 0.017$) after Bonferroni correction.

varies from peripheral wedge to major liver resections. Increased operative time, blood loss and postoperative complications have been acknowledged for complex and difficult laparoscopic liver resections^{22–27}, and therefore, a great emphasize should be put on careful preoperative assessment of the difficulty of a laparoscopic liver resection according to a surgeon's skills and experience. In the current study, the Southampton difficulty scoring system¹¹ has been used to determine the difficulty of a laparoscopic liver resection. This difficulty scoring system estimates the risk of intraoperative complications during laparoscopic liver resection and has been internally validated¹¹ on a large European multicenter cohort including seven tertiary referral centers. Recently, an external validation²⁸ has been performed showing the accuracy of the Southampton difficulty score to estimate the risk of intra- and postoperative complications. The latter may confirm that the Southampton difficulty score is a valid difficulty scoring system to use within our daily clinical practice.

In the Netherlands, 20 of the 27 liver centres have a laparoscopic liver resection program, demonstrating that the laparoscopic approach is being implemented. The current study found that increasing complexity of the laparoscopic liver resections is

related to an increasing difference in postoperative hospital stay and rates of intraoperative incidents between high-volume and nationwide low-medium volume practice in favour of the high-volume centres. In addition, stratifying low-medium volume practice into low- and medium-volume centres showed superior operative outcomes in high-volume centres as compared to both low- and medium-volume groups. Many Dutch centres, especially centres defined as low-volume centres, could still be in their learning curve for laparoscopic liver resections during the study period and therefore experience more difficulty with the complex laparoscopic liver resections. Interestingly, patients in medium-volume centres had worse outcomes as compared to low-volume centres. This might be explained by the fact that low-volume centres in the Netherlands performed less difficult and complex procedures, whereas medium-volume centres in the Netherlands had to deal with the more difficult and complex cases. This may be confirmed by our previously published nationwide study¹⁰, demonstrating that centres performed more than 20 laparoscopic liver resections annually (i.e. medium-volume centres) had better outcomes for major laparoscopic liver resections than low-volume centres.

Fig. 2 Operative outcomes, stratified for low-, moderate- and high-risk Southampton difficulty risk groups.

It is without doubt that annual laparoscopic liver resection volume is highly relevant for adequate patient outcome. Centralization has been proposed as an effective structural intervention to improve operative outcomes after complex surgery^{29–31}. However, despite the clear benefits of centralization, its application is still poor due to opposition from local and regional

health care organizations, medical staff and patients^{31,32}. Intensified collaboration between high- and low-volume liver surgery centres in regional networks could provide an alternative strategy to further disseminate the use of laparoscopic liver resection and improve outcomes. Ravaiola et al.³² demonstrated a partnership model in which tutor surgeons from two

high-volume hospitals were involved in the perioperative course of hepatobiliary patients at a low-volume hospital. Due to this collaborative effort, the number of hepatobiliary surgical procedures at the low-volume centre increased, while the complication and mortality rates fell to rates that were similar to the high-volume centres. Regional networks of liver centres could also include one high-volume and multiple lower-volume centres each focusing on laparoscopic liver resection in a specific risk group. The high-volume centre could perform laparoscopic liver resection in the moderate and high-risk groups and the lower-volume centres in the low-risk groups. In this manner, operative volumes would be sufficient in all centres with good outcomes and the number of patients who could profit from the benefits of laparoscopic liver resection would be maximized.

All centres in such networks could also participate in tailored and structured training programs^{33,34}. Two nationwide training programs in the Netherlands for minimally invasive pancreatic surgery^{35,36} were shown to be feasible. A similar program (LAELIVE) has been established for laparoscopic liver resections in the Netherlands and has recently been completed.

Several limitations of the current study should be acknowledged. First, the retrospective design introduces an inevitable risk of selection and information bias. However, with the realization of prospective nationwide and international liver surgery audit databases (e.g. the European Registry of Minimally Invasive Liver Surgery), update and replication of the current results in other countries should be possible. Second, the choice of the high-volume centres could be subject to selection bias. For this reason, three high-volume centres, with pioneering and highly established surgeons, who were generally comparable in surgical practice were chosen from three different countries. The Dutch cohort is far less likely to be subject to selection bias, as all centres that performed laparoscopic liver resections were included. Third, although the Southampton difficulty scoring system is believed to be a reliable model, there are still factors not incorporated in this model that are believed to influence difficulty. Fourth, this study focused on comparing outcomes of laparoscopic liver resection in high-volume and nationwide low-medium volume practice, without specifically considering the effect of surgeon and hospital related factors, such as preoperative patient assessment, surgeon experience and training, anaesthetic care and perioperative management. It is important to register the experience for each surgeon performing the laparoscopic liver resection procedures and to assess the impact of this experience on surgical outcome. Information about these variables is currently missing and may be valuable to improve laparoscopic liver resection outcomes. In addition, the current study focused on annual laparoscopic liver resection volume and didn't consider cumulative laparoscopic liver resection volume, which might be important in emphasizing more the differences between high-volume and low-medium volume centres. However, all laparoscopic liver resection data were not collected and therefore calculating cumulative laparoscopic liver resection volumes was not feasible.

Acknowledgements

We thank the following collaborators: Babs Zonderhuis (Amsterdam UMC), Inne B. Rinkes (University Medical Centre Utrecht), Christiaan Hoff (Medical Centre Leeuwarden), and Steven Oosterling (Spaarne Gasthuis Hospital).

Conflicts of Interest and Source of Funding

M.J. van der Poel and M.G. Besselink received an educational grant from Johnson & Johnson Medical B.V. and Integra LifeSciences and an Innovation grant from the Dutch Digestive Foundation for a nationwide training program in major minimally invasive liver surgery. For the remaining authors none were declared.

Supplementary material

Supplementary material is available at *BJS* online.

References

1. Fretland ÅA, Dagenborg VJ, Bjørnelv GMW, Kazaryan AM, Kristiansen R, Fagerland MW, et al. Laparoscopic versus open resection for colorectal liver metastases. *Ann Surg* 2018;**267**: 199–207.
2. Martínez-Cecilia D, Cipriani F, Vishal S, Ratti F, Tranchart H, Barkhatov L, et al. Laparoscopic versus open liver resection for colorectal metastases in elderly and octogenarian patients. *Ann Surg* 2017; **265**: 1192–1200.
3. Ratti F, Fiorentini G, Cipriani F, Catena M, Paganelli M, Aldrighetti L. Laparoscopic vs open surgery for colorectal liver metastases. *JAMA Surg* 2018;**153**:1028–1035.
4. Abu Hilal M, Aldrighetti L, Dagher I, Edwin B, Troisi RI, Alikhanov R, et al. The southampton consensus guidelines for laparoscopic liver surgery: from indication to implementation. *Ann Surg* 2018;**268**:11–18.
5. Ciria R, Cherqui D, Geller DA, Briceno J, Wakabayashi G. Comparative short-term benefits of laparoscopic liver resection: 9000 cases and climbing. *Ann Surg* 2016;**263**:761–777.
6. Takahara T, Wakabayashi G, Konno H, Gotoh M, Yamaue H, Yanaga K, et al. Comparison of laparoscopic major hepatectomy with propensity score matched open cases from the National Clinical Database in Japan. *J Hepatobiliary Pancreat Sci* 2016;**23**: 721–734.
7. Abu Hilal M, Di Fabio F, Teng MJ, Lykoudis P, Primrose JN, Pearce NW. Single-centre comparative study of laparoscopic versus open right hepatectomy. *J Gastrointest Surg* 2011;**15**: 818–823.
8. Kasai M, Cipriani F, Gayet B, Aldrighetti L, Ratti F, Sarmiento JM, et al. Laparoscopic versus open major hepatectomy: a systematic review and meta-analysis of individual patient data. *Surgery* 2018;**163**:985–995.
9. Cipriani F, Ratti F, Cardella A, Catena M, Paganelli M, Aldrighetti L. Laparoscopic versus open major hepatectomy: analysis of clinical outcomes and cost effectiveness in a high-volume center. *J Gastrointest Surg* 2019;**23**:2163–2173.
10. Van der Poel MJ, Fichtinger RS, Bemelmans M, Bosscha K, Braat AE, de Boer MT, et al. Implementation and outcome of minor and major minimally invasive liver surgery in the Netherlands. *HPB* 2019;**21**:1734–1743.
11. Halls MC, Berardi G, Cipriani F, Barkhatov L, Lainas P, Harris S, et al. Development and validation of a difficulty score to predict intraoperative complications during laparoscopic liver resection. *Br J Surg* 2018;**105**:1182–1191.
12. Garcea G, Breukink SO, Marlow NE, Maddern GJ, Barraclough B, Collier NA, et al. A systematic review of the impact of volume of hepatic surgery on patient outcome. *Surgery* 2009;**145**: 467–475.

13. Richardson AJ, Pang TCY, Johnston E, Hollands MJ, Lam VWT, Pleass HCC. The volume effect in liver surgery—a systematic review and meta-analysis. *J Gastrointest Surg* 2013;**17**:1984–1996.
14. Schneider EB, Ejaz A, Spolverato G, Hirose K, Makary MA, Wolfgang CL, et al. Hospital volume and patient outcomes in hepato-pancreatico-biliary surgery: is assessing differences in mortality enough? *J Gastrointest Surg* 2014;**18**:2105–2115.
15. Vallance AE, vanderMeulen J, Kuryba A, Botterill ID, Hill J, Jayne DG, et al. Impact of hepatobiliary service centralization on treatment and outcomes in patients with colorectal cancer and liver metastases. *Br J Surg* 2017;**104**:918–925.
16. Gilg S, Sparrelid E, Isaksson B, Lundell L, Nowak G, Strömberg C. Mortality-related risk factors and long-term survival after 4460 liver resections in Sweden—a population-based study. *Langenbecks Arch Surg* 2017; **402**: 105–113.
17. Lassen K, Nymo LS, Olsen F, Brudvik KW, Fretland ÅA, Søreide K. Contemporary practice and short-term outcomes after liver resections in a complete national cohort. *Langenbecks Arch Surg* 2019;**404**:11–19.
18. Vandenbroucke JP, von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, et al. Strengthening the reporting of observational studies in epidemiology (STROBE): explanation and elaboration. *Int J Surg* 2014;**12**:1500–1524.
19. Viganò L, Cimino M, Aldrighetti L, Ferrero A, Cillo U, Guglielmi A, et al. Multicentre evaluation of case volume in minimally invasive hepatectomy. *Br J Surg* 2020;**107**:443–451.
20. Kawaguchi Y, Fuks D, Kokudo N, Gayet B. Difficulty of laparoscopic liver resection. *Ann Surg* 2018;**267**:13–17.
21. Varley PR, Tohme ST, Chidi AP, Goswami J, van der Windt D, Geller DA, et al. Dissemination of minimally invasive liver resection for primary malignancy: reevaluating effectiveness. *Ann Surg Oncol* 2018;**25**:808–817.
22. van der Poel MJ, Barkhatov L, Fuks D, Berardi G, Cipriani F, Aljaiuossi A, et al. Multicentre propensity score-matched study of laparoscopic versus open repeat liver resection for colorectal liver metastases. *Br J Surg* 2019;**106**:783–789.
23. Sa Cunha A, Laurent C, Rault A, Couderc P, Rullier E, Saric J. A second liver resection due to recurrent colorectal liver metastases. *Arch Surg* 2007;**142**:1144–1149.
24. Cipriani F, Shelat VG, Rawashdeh M, Franccone E, Aldrighetti L, Takhar A, et al. Laparoscopic parenchymal-sparing resections for nonperipheral liver lesions, the diamond technique: technical aspects, clinical outcomes, and oncologic efficiency. *J Am Coll Surg* 2015;**221**:265–272.
25. Abu Hilal M, Tschuor C, Kuemmerli C, López-Ben S, Lesurtel M, Rotellar F. Laparoscopic posterior segmental resections: How I do it: Tips and pitfalls. *Int J Surg* 2020;**82**:178–186.
26. Ulas M, Ozer I, Bostanci EB, Karaman K, Dalgic T, Polat E, et al. Giant hemangiomas: Effects of size and type of surgical procedure on postoperative outcome. *Hepatogastroenterology* 2014;**61**: 1297–1301.
27. Levi Sandri GB, Spoleitini G, Vennarecci G, Franccone E, Abu Hilal M, Ettorre GM. Laparoscopic liver resection for large HCC: short- and long-term outcomes in relation to tumor size. *Surg Endosc* 2018;**32**:4772–4779.
28. Ivanecz A, Plahuta I, Magdalenic T, Mencinger M, Peruš I, Potrč S, et al. The external validation of a difficulty scoring system for predicting the risk of intraoperative complications during laparoscopic liver resection. *BMC Surg* 2019;**19**:179.
29. Chowdhury MM, Dagash H, Pierro A. A systematic review of the impact of volume of surgery and specialization on patient outcome. *Br J Surg* 2007;**94**:145–161.
30. Pieper D, Mathes T, Neugebauer E, Eikermann M. State of evidence on the relationship between high-volume hospitals and outcomes in surgery: a systematic review of systematic reviews. *J Am Coll Surg* 2013; **216**: 1015–1025. e18.
31. Vonlanthen R, Lodge P, Barkun JS, Farges O, Rogiers X, Soreide K, et al. Toward a consensus on centralization in surgery. *Ann Surg* 2018;**268**:712–724.
32. Ravaioli M, Pinna AD, Francioni G, Montorsi M, Veneroni L, Grazi GL, et al. A partnership model between high- and low-volume hospitals to improve results in hepatobiliary pancreatic surgery. *Ann Surg* 2014;**260**:871–877.
33. Subhas G, Mittal VK. Training minimal invasive approaches in hepatopancreatobiliary fellowship: The current status. *HPB* 2011;**13**:149–152.
34. Gumbs AA, Gayet B. The medical and surgical department of digestive diseases and minimally invasive HPB fellowship at IMM. *HPB* 2007;**9**:470–471.
35. De Rooij T, Van Hilst J, Boerma D, Bonsing BA, Daams F, Van Dam RM, et al. Impact of a nationwide training program in minimally invasive distal pancreatectomy (LAELAPS). *Ann Surg* 2016; **264**:754–762.
36. De Rooij T, van Hilst J, Topal B, Bosscha K, Brinkman DJ, Gerhards MF, et al. Outcomes of a multicenter training program in laparoscopic pancreatoduodenectomy (LAELAPS-2). *Ann Surg* 2019;**269**:344–350.