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Is Minimally-Invasive Surgery of Lesions in the Right Superior Segments of the Liver Justified? A Multi-Institutional Study of 245 Patients

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Abstract

Background: Controversy exists regarding the safety and feasibility of minimally invasive resection for lesions in segments 7 or 8. We compare outcomes of MIS and Open parenchymal sparing liver resections at two high-volume centers.

Methods: From 2003 to 2016 we identified patients who underwent MIS or Open resections for lesions in segments 7 or 8 at two institutions (MSKCC and SGH). Outcomes were compared using univariate and multivariate analyses.

Results: Two-hundred and forty-five patients underwent resection of lesions in segments 7 or 8 (MIS 30%, Open 70%). Compared to the Open group, the MIS group had longer operative time (223 ± 88 min vs. 188 ± 72 min, $P = 0.003$), lower blood loss (297 ± 287 mL vs. 448 ± 670 mL, $P = 0.03$), and shorter mean length of stay (5.2 ± 7.4 days vs. 8.3 ± 11.7 days, $P < 0.001$), which

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Conflicts of interest
The authors declare that there are no conflicts of interest.

Data availability statement
The data used in this article contain protected health information and therefore cannot be shared.

remained significant on multivariate analysis. No differences in Pringle time, rate of postoperative complications, or R0 resections were detected.

Conclusions: With appropriately selected patients treated by experienced MIS HPB surgeons, MIS resection of segments 7 or 8 is safe with similar rates of complications and R0 resections, with significantly less blood loss and shorter length of stay.

Keywords

Laparoscopic liver resection; Minimally Invasive Surgery (MIS) liver resection; parenchymal sparing liver resection; Liver segments 7/8; Posterior-superior liver segments

Introduction

The prevalence of minimally invasive surgery (MIS) for liver resections including laparoscopic, robotic, and hybrid procedures, is increasing worldwide.[1] Since the initial descriptions of laparoscopic and robotic liver resections in 1992[2] and 2003[3], respectively, the minimally invasive approach for liver resection has been increasing, [4,5] and an MIS approach has been used for benign and malignant liver lesions, even with success in higher risk patients with cirrhosis and resultant portal hypertension.[6] With improved techniques and increased surgeon experience, laparoscopy is now the recommended approach for resection of lesions in the left lateral section.[7,8] In 2008[7], then expanded in 2014[8], an international group of experts concluded that laparoscopic liver surgery is safe in the hands of experienced laparoscopic and hepatobiliary surgeons, though the field is still in an exploratory and learning phase. Since that time, the literature would suggest that resection of any liver segment can be performed using an MIS approach, with appropriate patient selection and surgeon experience.[7–14] Authors reporting a benefit for MIS approach note decreases in length of hospital stay, postoperative pain, blood loss, and wound complications compared to an open approach, while maintaining non-inferior oncologic outcomes in liver surgery.[6,8,15,16] In cases of resection for known or potential malignancies, those decreases in lengths of stay and recovery time can translate into earlier initiation and increased rates of adjuvant therapies, which may ultimately improve long-term oncologic outcomes.[17]

A unique challenge in liver surgery has been resection of segments 7 or 8 due to their anatomic location and technical complexity. Given these technical difficulties, arduous bleeding control, and challenges due to the anatomic location of segment 7 and 8, it is controversial whether MIS resections are a safe and reasonable alternative to an open approach. Prior reports have described the safety of an MIS approach to the postero-superior segments[18–20], but these conclusions are drawn from smaller patient cohorts and include segments 1, 4a, 7, and 8. Additionally, a recent multi-institutional report on MIS liver surgery suggests that resections of postero-superior segments are associated with increased rates of conversion to open surgery and result in worse outcomes.[21] Therefore, the aim of this study was to compare outcomes of MIS and open (“Open”) parenchymal sparing liver resections of lesions in segments 7 or 8 at two high-volume centers.

Materials and Methods:

Between 2003 and 2016, patients who underwent MIS or Open resections of lesions in segment 7 or 8 were retrospectively identified from prospective databases at two institutions – Memorial Sloan Kettering Cancer Center (MSKCC) or Singapore General Hospital (SGH). MIS was defined as a complete laparoscopic or robotic approach without utilization of a hand port (cases utilizing a "hybrid" approach were excluded from analysis). Patients requiring resection of additional liver segments were excluded from analysis. Those patients requiring conversion from MIS to open surgery were analyzed in the MIS cohort. Demographic information, pre-operative clinical characteristics, intra-operative variables (operative time, Pringle time, blood loss), length of stay, and 30-day postoperative morbidity and mortality were collected for analysis. Patient factors including age at the time of surgery, gender, body mass index (BMI, kg/m^2), tumor histology (benign, primary liver/bile duct, colorectal metastasis, and other metastasis), tumor surgical margin (R0, R1, N/A), tumor size (cm), and any prior abdominal surgery were collected and analyzed from the medical records. Cases with combined resection of additional organs (such as colectomy, oophorectomy) were excluded from analysis of operative time. Complications were identified as any Clavien-Dindo grade I-V complication.[22] Selection of patients for MIS approach was surgeon dependent and heterogeneous. For some surgeons in the study the only contraindication for MIS approach is need for vascular reconstruction or involvement (e.g. IVC involvement). For others only superficial tumors were approached in segment VII or VII or tumors in these segments were only considered for open resection. In addition, technical approaches were heterogeneous, with combinations of CUSA (Integra LifeSciences), Sonosurg (Olympus Medical), Thunderbeat (Olympus Medical), and bipolar cautery used for liver dissection.

Statistical analysis

Univariate and multivariate analyses were conducted to evaluate outcome differences between the MIS and Open groups. Log transformations were used to investigate data that were highly skewed. Categorical variables were compared using Chi-square tests and unpaired two-tailed Student's t-test was used to compare log-transformed continuous variables. General linear regression models with log-transformed variables were adjusted for age at surgery, gender, BMI, tumor histology, and surgical margin to compare outcomes between MIS and Open groups. Differences in the outcomes were calculated as percent difference. Multivariate logistic regression was utilized to assess differences in the risk of a complication between MIS and Open surgery cohorts. Risk of complications are reported by odds ratio (OR) with 95% confidence interval (95% CI) and *P*-values. All tests were 2-sided and *P*-values <0.05 were considered statistically significant. Analyses were performed with SAS software, version 9.4 (SAS Institute, Cary, NC, USA).

Results

Patients

We identified 245 patients who underwent liver resection in segment 7 or 8 (MSKCC = 114 (46.5%), SGH = 131 (53.5%)) and were included in the analysis. As detailed in Table 1, 172 cases were Open (MSKCC = 78 (32% of total), SGH = 94 (38%) and 73 were MIS (MSKCC = 36 (15%), SGH = 37 (15%)). Of the MIS cases for analysis, n = 15 (21%) were robotic. Patients who underwent conversion from MIS to an open approach were included in the MIS analysis, and this occurred in 10 patients (10/73, 13.7%). Reasons for conversions included bleeding, proximity to vessels, inadequate margin assessment, and no clearly identifiable lesion based on imaging.

The characteristics of all patients and between the MIS and Open groups are detailed in Table 2. In comparing MIS to Open, there was no difference in age (58.4 ± 11.0 vs. 59.3 ± 12.8, $P = 0.52$) or gender (female 46.6% vs. 36.6%, $P = 0.14$), or BMI (25.1 ± 5.0 kg/m^2 vs. 25.9 ± 4.9 kg/m^2, $P = 0.19$). There was a difference in the distribution of histology types between the MIS and Open groups ($P = 0.03$), though most lesions were colorectal metastasis (43.8% vs. 44.8%), followed by primary liver or bile duct cancers (31.5% vs. 43.0%), benign lesions (16.4% vs. 5.2%), and other metastasis (8.2% vs. 7.0%). Between the MIS and Open groups there was a similar rate of R0 (n = 62 (87%) vs. n = 150 (87%)) and R1 (n = 4 (5.6%) vs. 13 (7.5%)) ($P = 0.32$) resections. Mean ± SD tumor size for the entire cohort was 3.3 ± 2.5 cm with a significant difference in the size between the MIS and Open groups (2.7 ± 1.6 cm vs. 3.5 ± 2.8 cm, $P = 0.01$). There was no difference in the rate of prior abdominal surgeries between the MIS or Open groups (35.4% vs. 36.6%, $P = 0.86$).

Surgical Outcomes

The MIS and Open groups were compared using univariate analysis and these results are detailed in Table 3. In comparing MIS to Open, mean ± SD operative time was significantly longer in the MIS group (223 ± 88 min vs. 188 ± 72 min, $P < 0.01$), though with similar mean Pringle times (15.5 ± 26.7 min vs. 21.0 ± 22.2 min, $P = 0.19$). The MIS group was also associated with decreases in estimated blood loss (297 ± 287 ml vs. 448 ± 670 ml, $P = 0.03$). Analysis of the immediate postoperative period indicates the MIS approach was associated with decreased mean length of stay (5.2 ± 7.4 days vs. 8.3 ± 11.7 days, $P < 0.001$), while thirty-day complications rates were comparable between the MIS and Open groups (9.7% vs. 15.1%, $P = 0.25$). In the MIS group, 7 patients experienced 12 unique complications, and in the Open group, 26 patients experienced 34 unique complications. While the rates of complications were not statistically different between the two groups, a broader range of complications occurred among the Open group. These complications were primarily related gastrointestinal and genitourinary issues and a listing of individual complications is shown in Table 4.

The MIS and Open groups were then compared using multivariate analysis (Table 5). After adjusting for differences in age, gender, BMI, tumor size, and histology, operative time, decreased blood loss, and decreased length of stay remained significant. Operative time was approximately 20% longer in the MIS compared to Open group ($P < 0.001$), though the MIS approach had a 35% decrease in blood loss ($P = 0.01$). The MIS group experienced a 39% decrease in hospital length of stay ($P < 0.001$). This was achieved without increasing odds of complications (OR 0.55, 0.22 – 1.40).

Discussion

This retrospective analysis of patients undergoing MIS versus open liver resections of segments 7 or 8 at two high volume specialty centers highlights the safety and benefits of an MIS approach when performed on well selected patients. Specifically, the MIS approach was associated with decreased blood loss and a shorter length of stay with comparable 30-day complication and R0 resection rates.

The initial reports of laparoscopic liver surgery date back to 1992[2], but have lagged behind in its widespread adoption of the MIS techniques due to the inherent risks of liver surgery, technical difficulty of the resection, potential for significant blood loss, complexity of the reconstruction, and lack of dedicated training. Indications for laparoscopic liver resections based on the Louisville consensus statement are patients with solitary liver lesions ≤ 5 cm located in segment 2–6.[7] Historically, resection of liver lesions in the right posteriosuperior segments (7 and 8) was mostly reserved for open procedures. The difficulty in resection of lesions in segment 7 and/or 8 is considered to be comparable to that of major hepatectomies.[23–25] In 2010, Yoon et al. demonstrated longer postoperative hospital stay, longer operative time, and a higher conversion rate to an open approach in patients who underwent laparoscopic liver resections for hepatocellular carcinoma located in the PS segments.[26] This perception was confirmed by a validated difficulty scoring system for laparoscopic liver resection that placed segment 7 and 8 resections more frequently into “high difficulty” on a three-level scoring system (low, intermediate, high).[27,28] Resections with a high difficulty score were significantly associated with increased operative time, intraoperative blood loss, conversion rate to open or hand-assisted, and postoperative complications.[28] A recent, large multi-institutional study confirmed this observation in detailing the higher rate of conversion for laparoscopic resection of PS segments.[21] Our results presented here indicate that an MIS approach to segments 7 or 8 is associated with increased operative time, but without increases in estimated blood loss or postoperative complications. Our conversion rate was approximately 13.7% and is consistent with the 10.7% conversion rate of the postero-superior segments from a large, multi-institutional study.[21] Interestingly, all conversions occurred in the laparoscopic subgroup, and none were identified in the robotic subgroup, a potential confounding variable that warrants further investigation on additional studies, as it is unclear if the robotic platform offers an advantage over laparoscopy for these challenging operations.

Well-described technical obstacles for MIS liver resection in PS segments include poor visualization, limited degree of freedom of the laparoscopic instruments, and difficulty in obtaining vascular and hemorrhage control.[10,29,30] Technical modifications have been implemented to overcome these challenges in MIS resections of segments 7 or 8, including, but not limited to patient positioning techniques, the caudal approach, and placement of intercostal port(s).[31–33] The introduction of the robotic platform has also opened avenues for a more widespread implementation of the MIS approach given its three-dimensional, high-definition and magnified view, in addition to increased articulation of wristed instruments.

The first major adaptation of MIS techniques in gastrointestinal oncology was after publication of the first clinical trial for colon cancer, which showed equivalent oncologic outcomes between laparoscopic and open colectomy.[34] Prior to this study, there was significant concern that minimally-invasive colectomy would not result in equivalent oncologic outcomes due to the challenges of laparoscopic surgery. The results presented here offer further evidence that the MIS approach to segment 7 or 8 is safe and does not immediately compromise oncologic outcome by reducing R0 resection rates. In a smaller study evaluating outcomes for MIS resection of PS segments, there was comparable median recurrence-free survival in the MIS and open cohorts.[20] While these results are promising, our data also show that the Open group had significantly larger masses compared to the MIS group. As tumor size is correlated with conversion rates[21], this represents a potential selection bias in our data, given surgeons may select an open approach with larger tumors. Further data on tumor location and relationship to vascular structures is warranted to delineate these potential differences.

We also detected additional benefits of an MIS approach, including decreased blood loss and shorter length of stay. These results are consistent with a prior report describing outcomes of 104 patients undergoing MIS or open resection of segments 7 or 8 for hepatocellular carcinomas (MIS, n = 46 vs. Open, n = 58).[35] Similar to our results, the authors also detected decreased blood loss and shorter length of stay in the MIS group. Regarding intra-operative blood loss, Maehara et al. and Man et al. described the benefits of implementing the Pringle maneuver in minimizing the amount of blood loss during laparoscopic hepatectomies.[36,37] Consequently, they detected decreased volume of transfused blood products and reduced time to complete the parenchymal transection secondary to application of the laparoscopic Pringle maneuver.[36,37] Similarly, our current study shows significantly lower estimated blood loss in the MIS group compared to Open, but without significant difference in mean Pringle time, suggesting that other factors and variables may be influencing this observation.

The benefit of a shorter hospital length of stay after laparoscopic operations is well described in the literature.[38–40] In a retrospective cohort of 318 patients (MIS=148, Open=170) who underwent resection of the PS segments, Scuderi et al, described the shorter hospital length of stay in the MIS group when compared to open.[41] They further showed decrease need for postoperative analgesia, longer operative time in the MIS group, higher complication rate in the open group, and similar oncological outcome in both groups.[41] Similarly, the current results corroborate these findings and demonstrate shorter mean length of stay in the MIS group when compared to the Open group by 3 days (5 days vs. 8 days, $P < 0.001$). Though not examined in this study, the decreased length of stay in the MIS group may decrease certain complications and decrease hospital and societal costs associated with complex medical care.

A key limitation of our study is the patient and provider selection bias inherent to the non-randomized, retrospective nature of the study design performed at our two institutions. Though this is a limitation of the results presented here, the analysis of large patient cohorts at two high volume institutions treated by several surgeons may help decrease the effects of our biases.

Although the multi-institutional nature is a strength of the study, it also poses other confounding factors such as length of stay in the cultural context of how these patients are treated at the respective institutions.[42] And although these cultural differences exist, there was no difference in length of stay between MSKCC and SGH within groups (MIS or Open). Another component of any oncologic research must be long-term clinical outcomes and cancer-specific events. However, this is beyond the scope of the current study, given this is a mix of histologies with different predicted outcomes. Nevertheless, a well-established surrogate of oncologic outcomes, resection margin status, was utilized and found to be similar between the two groups.

In conclusion, our study shows that well selected MIS parenchymal preserving resection of liver lesions in segment 7 or 8 is safe and feasible with comparable outcomes to open resections when performed at high volume centers. This study is one of the few multi-institutional studies with the specific emphasis on MIS resection of segment 7 or 8 lesions with a sample size of more than 200 patients, including broad tumor pathologies. In addition to analysis of long-term disease-free and overall survival, further studies expanding on the benefits of an MIS approach may help inform patient selection and resource allocation moving forward.

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Synopsis:

The authors present an analysis of patients undergoing minimally invasive or open resection of liver segments 7 or 8. The MIS approach was associated with longer operative time, but decreased blood loss and length of stay in this retrospective cohort.

Table 1.

Patients undergoing MIS vs Open resection of liver segments 7 or 8 identified at each institution from 2003–2016.

	All Patients	MIS	Open
All Cases	245	73 (29.8)	172 (73.2)
Institution			
MSKCC	114 (46.5)	36 (49.3)	78 (45.3)
SGH	131 (53.5)	37 (50.7)	94 (54.7)

MSKCC, Memorial Sloan Kettering Cancer Center; SGH, Singapore General Hospital.

Table 2.

Characteristics of patients undergoing resection of liver segments 7 or 8 from 2003–2016.

		Type of Procedure		
	All patients N=245	**MIS 73 (29.8%)**	**Open 172 (73.2%)**	***P*-value**
Age in years				0.52
mean (SD)	59.0 (12.3)	58.4 (11.0)	59.3 (12.8)	
Sex, N (%)				0.15
female	97 (39.6)	34 (46.6)	63 (36.6)	
male	148 (60.4)	39 (53.4)	109 (63.4)	
Body mass index (BMI)				0.19
mean (SD)	25.6 (4.9)	25.1 (5.0)	25.9 (4.9)	
Histology				0.03
benign	21 (8.6)	12 (16.4)	9 (5.2)	
primary liver/bile duct	97 (39.6)	23 (31.5)	74 (43.0)	
colorectal	109 (44.5)	32 (43.8)	77 (44.8)	
other mets	18 (7.4)	6 (8.2)	12 (7.0)	
Surgical margin				0.32
R0	212 (88.7)	62 (87.2)	150 (87.2)	
R1	17 (7.1)	4 (5.6)	13 (7.5)	
NA	10 (4.2)	7 (7.0)	5 (3.0)	
missing			4 (2.3)	
Tumor size, cm				0.01
mean (SD)	3.3 (2.5)	2.7 (1.6)	3.5 (2.8)	
Abdominal surgery *				0.86
yes	86 (36.3)	23 (35.4)	63 (36.6)	
no	151 (63.7)	42 (64.6)	109 (63.4)	

SD: Standard Deviation, IQR: Interquartile Range.

*missing data on abdominal surgery for 7 patients.

Table 3.

Univariate analysis comparing perioperative outcomes between MIS and Open groups.

	MIS N=73 (29.8%)	Open N=172 (70.2%)	*P*-value
Operative time, minutes			
mean (SD)	222.7 (87.7)	188.3 (71.8)	<0.01
Pringle time, minutes			
mean (SD)	15.5 (26.7)	21.0 (22.2)	0.19
Blood loss, mL			
mean (SD)	296.7 (287)	447.7 (669.5)	0.03
Length of stay, days			
mean (SD)	5.2 (7.4)	8.3 (11.7)	<0.001
Complication, N (%)	7 (9.7)	26 (15.1)	0.25

Table 4.

30-day postoperative complications identified within the MIS and Open groups.

MIS			Open		
Complication	**Frequency**	**Percent**	**Complication**	**Frequency**	**Percent**
Pulmonary			**Pulmonary**		
Aspiration	1	8.3	Apnea	1	2.9
Hypoxemia	1	8.3	Pleural effusion	1	2.9
Pneumothorax	1	8.3	Pneumonitis	1	2.9
Cardiovascular			Pneumothorax	3	8.8
Decompensation	1	8.3	Pulmonary embolus	2	5.9
DVT	1	8.3	**Cardiovascular**		
Infectious			DVT	2	5.9
Sepsis	1	8.3	MI	1	2.9
UTI	2	17	CVA	2	5.9
Unspecified	3	25	**Infectious**		
Miscellaneous *	1	8.3	Abscess	2	5.9
			Fever	1	2.9
			UTI	1	2.9
			Wound Infection	5	15
			Catheter-related	1	2.9
			Gastrointestinal		
			Ileus	1	2.9
			Pancreatic leak	1	2.9
			Genitourinary		
			Acute renal failure	2	5.9
			Hematuria	1	2.9
			Miscellaneous **	**6**	18

* Hypophosphatemia

** Includes anemia, delirium, wound breakdown

Table 5.

Percent difference between MIS and Open group from multivariable model adjusted for age, gender, BMI, tumor size, and histology.

	Percent difference MIS and Open	*P*-value
Operation Time, minutes	20.6	<0.001
Pringle Time, minutes	−25.8	0.10
Blood Loss, (mL)	−34.7	0.01
Length of Stay, days	−39.3	<0.001
Complication *	0.55 (0.22, 1.40)	0.21

*Odds Ratio (OR), 95% confidence interval (CI) estimates from logistic regression.