A multi-institutional analysis of minimally invasive liver resections

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Background: As minimally invasive liver resection (MILR) gains acceptance, techniques, and outcomes must be analyzed in multi-institution series comparing both laparoscopic and robotic approaches to open liver resections (OLRs). The objective of this study was to describe the experience with MILR at three high volume centers.

Methods: Retrospective tri-institutions analysis of MILR from 2000 to 2016. Patient demographics, tumor characteristics, and outcomes were analyzed for statistical significance compared to OLR.

Results: A total of 1,323 patients were included with 746 OLR (56.4%) and 577 MILR (530 laparoscopic, 40.1%, and 47 robotic liver resections, 3.6%). MILRs increased during the study period (0.5%, year 2000, *vs.* 40.5%, year 2016, P<0.001). Compared to OLR, MILR had significantly decreased estimated blood loss (634.2±33.4 *vs.* 275.9±18.4 mL, P<0.0001), post-operative complications (35.5% *vs.* 16.1%, P<0.0001), hospital length of stay (8.7±0.3 *vs.* 4.2±0.2 days, P<0.0001), and re-admissions (10.2% *vs.* 4.0% P<0.0001) with no increase in bile leak (P=0.42) or re-operation P=0.20). There was no difference in 90-day patient mortality (OLR, 2.4% *vs.* MILR, 1.0%, P=0.09).

Conclusions: The current study evaluates the steady adoption of MILR in high volume centers. This data confirms MILR, whether performed laparoscopically or robotically, confers significant patient benefits.

Keywords: Liver resection; minimally invasive; complications; laparoscopic; robotic

Received: 29 May 2018; Accepted: 29 June 2018; Published: 26 July 2018.
doi: 10.21037/ls.2018.07.01
View this article at: http://dx.doi.org/10.21037/ls.2018.07.01

Introduction

Hepatobiliary surgeons continue to struggle over the optimal role for minimally invasive liver surgery in the management of hepatic tumors (1-3). The laparoscopic approach has slowly replaced a segment of open liver resection (OLR). Despite great enthusiasm, some centers have less than a 10% adoption rate while others report an aggressive 80% incidence of minimally invasive liver resections (MILR). This rate of laparoscopic adoption has varied significantly across the international spectrum as well, varying from 43% in select groups within the European Union to less than 20% in the Americas (4). Since the earliest reports of MILR in the early 1990s, multiple authors have advocated numerous approaches, techniques and surgical devices (5-7). Subsequently, there have been three significant international consensus meetings held to evaluate, define, and recommend standardize guidelines for approaches in MILR (1-3).

As the minimally invasive approach gains greater adoption and acceptance, techniques and outcomes must be critically analyzed through multi-institutional clinical trials and large propensity case series comparing open, laparoscopic and robotic approaches to liver resections (8-10). Initial reports, series and clinical trials have confirmed innumerable valuable improvements to patient outcomes

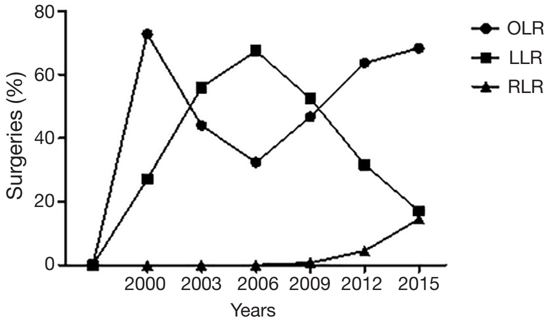

Figure 1 Trends of liver resections from 2000 to 2016 at three academic institutions compared to open liver resections (OLR), laparoscopic liver resection (LLR) and robotic liver resections (RLR).

while maintaining the oncologic integrity of the operation (1-3). The most recent innovation in liver surgery has been the introduction of robotic liver surgery, where there is a paucity of published literature (11-13). The objective of this study was to evaluate the operative experience of three senior high volume hepatobiliary surgeons over a 16-year study period. The primary endpoint of the study was major complications, operating time, blood loss, and 90-day mortality.

Methods

A retrospective chart review from three high volume surgeons of all consecutive liver resections was performed. Each institution maintained a prospective database of MILR from 2000 to 2016. The study received approval from the Institutional Board Review Committee of Tulane University (No. 351684-OTH) with a waiver of written informed consent. MILR was defined as laparoscopic and robotic-assisted resections. OLR were recorded. Exclusion criteria were patients less than 18 years of age. Patient demographics including race, age, gender, tumor characteristics were recorded. Intra-operative characteristics including surgeon, operative time, and estimated blood loss (EBL) were also obtained. Major liver resections were identified as right or left lobectomies or tri-segmentectomies. The primary endpoint of the study was to evaluate 90-day patient mortality. Other patient outcomes measured included hospital length of stay (HLOS) and patient re-admission. Major complications (bile leak, takeback operation, post-op bleeding, post-operative infection, wound dehiscence, respiratory difficulty, myocardial infarction, and renal dysfunction) were also measured and compared between the two groups.

Data from all three institutions were pooled for analysis. Univariate analysis for statistical significance was performed using Student's t test for continuous variables and Fisher's exact test for categorical variables. Kaplan-Meier survival curves were generated to compare 90-day patient mortality between MILR and OLR patients. A binary logistic regression was used to evaluate several variables (type of surgical procedure, major liver resection, patient age, gender, malignancy, EBL) on patient mortality. Data were analyzed using GraphPad software (version 5, La Jolla, CA) for univariate analysis and SPSS IBM software for multivariate analysis (version 24, Armonk, NY).

Results

Study population

A cohort of 1,323 patients were included with 746 OLR (56.4%) and 577 MILR [530 laparoscopic, 40.1% and 47 robotic liver resections (RLRs), 3.6%]. The number of MILRs increased significantly during the study period (0.5%, year 2000, *vs.* 40.5%, year 2016, P<0.001) as shown in *Figure 1*.

Surgical procedures

Data was obtained from three different hepatobiliary surgeons with a significant amount of MILR had significantly decreased EBL (634.2±33.4 *vs.* 275.9±18.4 mL, P<0.0001). The average case length for MILR liver resections was less compared to OLR (258.3±2.9 *vs.* 288.3±4.2 min, P<0.001). These results are shown in *Table 1*.

Patient outcomes

The average hospital length of stay was higher in the OLR group (8.7±0.3 *vs.* 4.2±0.2 days, P<0.001). The incidence of post-op re-admissions was also significantly higher in the OLR group compared to MILR (10.2% *vs.* 4.0%, P<0.0001).

Complications

The overall incidence of post-operative complications was significantly higher in the OLR cohort (35.5% *vs.* 16.1%, P<0.0001). Post-operative infections were higher in the

Table 1 Patient demographics for 1,323 patients with open (OLR) or minimally invasive (MILR) liver resection from three surgeons

Demographics	Total (n=1,323)	OLR (n=746)	MILR (n=577)	P value
Age, mean (SEM), years	56.8 (0.4)	58.2 (0.5)	54.9 (0.6)	<0.0001
Male gender, n (%)	604 (45.7)	375 (50.3)	229 (39.7)	0.0002
Race, n (%)				
Caucasian	955 (72.2)	537 (72.0)	418 (72.4)	0.90
African American	240 (18.1)	106 (14.2)	134 (23.2)	<0.0001
Asian	71 (5.4)	59 (7.9)	12 (2.1)	<0.0001
Other races	57 (4.3)	44 (5.9)	13 (2.3)	0.0010
Operative details				
Oncologic resection, n (%)	932 (70.4)	644 (86.3)	288 (49.9)	<0.0001
Major resection, n (%)	526 (39.8)	354 (47.5)	172 (29.8)	<0.0001
EBL, mean (SEM), mL	477.1 (21.0)	634.2 (33.4)	275.9 (12.1)	<0.0001
Operation time, mean (SEM), min	276.9 (3.1)	288.3 (4.2)	258.3 (2.9)	<0.0001

SEM, standard error of mean; EBL, estimated blood loss.

Table 2 Study outcomes and complications for 1,323 patients with open (OLR) or minimally invasive (MILR) liver resection from 2000 to 2016

Outcome	Total (n=1,323)	OLR (n=746)	MILR (n=577)	P value
Hospital LOS, mean (SEM), days	6.9 (0.2)	8.7 (0.3)	4.2 (0.2)	<0.0001
Readmission, n (%)	99 (7.5)	76 (10.2)	23 (4.0)	<0.0001
Take back surgery, n (%)	15 (1.1)	11 (1.5)	4 (0.7)	0.20
Bile leak, n (%)	41 (3.1)	26 (3.5)	15 (2.6)	0.42
Post-operative infection, n (%)	68 (5.1)	60 (8.0)	8 (1.4)	<0.0001
Major post-operative complication, n (%)	358 (27.1)	265 (35.5)	93 (16.1)	<0.0001
Post-operative bleed, n (%)	33 (2.5)	24 (3.2)	9 (1.6)	0.07
90-day mortality, n (%)	24 (1.8)	18 (2.4)	6 (1.0)	0.09

SEM, standard error of mean; LOS, length of stay.

OLR group (8.0% *vs.* 1.4%, P<0.0001). No difference in bile leak (P=0.42) or take back to the operating room (P=0.29) was found between the techniques. The incidence of the 5-year disease recurrence was found to be significantly higher in the open group (42.5% *vs.* 27.9%, P<0.001). Results are presented in *Table 2*.

Patient survival

Overall patient survival for the study cohort was 75.6% with an average follow-up length of 1.7±0.1 years. When comparing 90-day patient mortality between the groups, there was no significant difference between the OLR and MILR (2.4% *vs.* 1.0%, P=0.09). Kaplan-Meier 90-day survival curve was generated for OLR and MILR and is shown in *Figure 2*. Log rank test did not show a significant difference in 90-day mortality between the groups [hazard ratio (HR) 0.55; 95% CI, 0.2–1.6, P=0.54].

Multivariate analysis for mortality

MILR as a risk factor for 90-day death was analyzed using a binary logistic regression to control for possible cofounders (*Table 3*). MILR was not found to increase the risk of 90-day

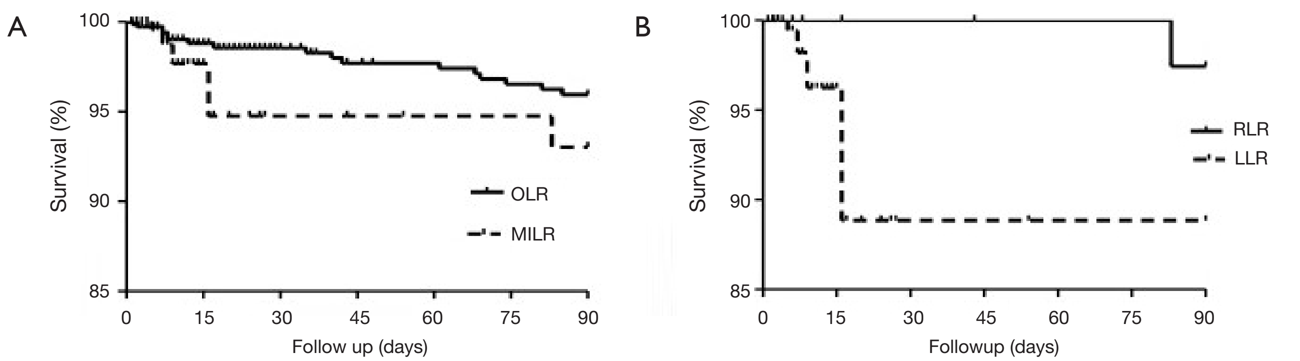

Figure 2 Ninety-day patient survival following liver resection. (A) Kaplan-Meier survival curve for open (OLR) *vs.* minimally invasive (MILR) liver resections (HR 0.55; 95% CI, 0.2–1.6, P=0.54); (B) Kaplan-Meier survival curve for laparoscopic (LLR) *vs.* robotic (RLR) liver resections (HR 0.23; 95% CI, 0.04–1.26, P=0.10).

Table 3 Multivariate analysis for risk factors for 90-day mortality

Independent variable	Odds ratio	95% CI	P value
MILR	0.6	0.2–1.6	0.300
Age	1.000	1.000–1.048	0.384
EBL	1.000	1.000–1.001	0.247
Male gender	1.3	0.6–3.1	0.500
Oncologic resection	1.8	0.5–6.7	0.400
Major resection	0.9	0.4–2.2	0.900

MILR, minimally invasive liver resection; EBL, estimated blood loss.

mortality [odds ratio (OR) 0.6; 95% CI, 0.2–1.6, P=0.3].

RLR

A sub-group analysis was performed on RLRs, which represented 3.6% (n=47/1,323) of total resections performed. The first RLR for this data set was performed in 2009 with increasing numbers observed 2014–2016 (23.4%, 34.0%, and 25.5%, respectively). Univariate analysis of RLRs compared to the large pool of laparoscopic liver resections (LLRs) did not find any significant differences in patient outcomes or complications compared to LLRs (*Table 4*). Interestingly, RLR was performed for a higher percentage of oncologic resections compared to LLR (80.9% *vs.* 47.2%, P<0.0001). Kaplan-Meier survival curve for RLR *vs.* LLR is shown in *Figure 2B* (HR 0.23; 95% CI, 0.04–1.26, P=0.10).

Discussion

MILR continues to gain wide acceptance amongst hepatobiliary surgeons and patients alike. A decade of studies confirmed the benefits of MILR though the benefits of RLR have not been as clear to date. The current study provides further evidence in the hands of early adopters of MILR for the continued proliferation of laparoscopic and RLR in high volume academic specialty centers. Several robotic series have indicated the benefit of robotic platforms including 3D high definition visualization, stable platforms, fourth arm retraction, arm articulation for suturing and newly deployed monopolar devices as well as inline stapling (14,15). Recent upgrade to the Da Vinci Xi platform (Sunnyvale, CA, USA) allows a new approach to targeting and robot placement to minimize robotic arm interference.

A recent study by the French Hepatectomy Study Group analyzed 44,240 liver resections performed in France between 2007 and 2012 (16). The laparoscopic cohort was comprised of 7,881 patients or 17.8% of cases. In this study, the incidence of LLR increased more than open resection (7.0% *vs.* 1.3%) but most procedures were relegated to minor resections (61.1% *vs.* 28.9%; P<0.001).

Table 4 Sub-group analysis of minimally invasive liver resections comparing robotic to laparoscopic liver resections

Variables	Robotic (n=47)	Laparoscopic (n=530)	P value
Age, mean (SEM), years	59.6 (1.8)	54.6 (0.6)	0.02
Male gender, n (%)	23 (48.9)	209 (39.4)	0.22
Caucasian, n (%)	33 (70.2)	392 (74.0)	0.61
Cancer resection, n (%)	38 (80.9)	250 (47.2)	<0.0001
Hospital LOS, mean (SEM), days	4.3 (0.5)	4.2 (0.2)	0.88
EBL, mean (SEM), mL	200.6 (31.0)	281.4 (19.6)	0.22
Bile leak, n (%)	0	15 (2.8)	0.62
Post-operative infection, n (%)	1 (2.1)	7 (1.3)	0.50
Major post-operative complication, n (%)	7 (14.9)	88 (16.6)	1.00
Post-operative bleed, n (%)	2 (4.3)	8 (1.5)	0.19
Overall mortality, n (%)	4 (8.5)	53 (10.0)	1.00
90-day mortality, n (%)	1 (2.1)	5 (0.9)	0.40

SEM, standard error of mean; LOS, length of stay; EBL, estimated blood loss.

This result is in contrast to 15% of major resections undergoing laparoscopic procedures in only 19.5% of hospitals that performed liver resections. The proportion of cases performed laparoscopically was directly inverse to the annual caseload.

In contrast, a group of European Specialized Centers including Ghent, Oslo, Southampton, and Milan did 43% of cases laparoscopically (4). This observation confirms laparoscopic liver surgery is still in the phase of early and interim phase adoption. Clearly, as is documented in our series from three early adopters, a 40–60% utilization of MILR is feasible, but is most reasonably achievable at high volume specialty centers.

The current robotic platform and surgical devices for the performance of MILR resection have significantly evolved over the last decade. The current literature has been limited to lower volume series but each confirming the safety and efficacy of the operation. Several of these series have identified equivalent patient and disease-free survival when deployed for cancer (17,18). Our analysis of the current series confirms that the robotic platform is now robust enough to approach not only minor but major resections with assurance of safety and oncologic integrity. The proliferation of robotic liver surgery like any other early adoption of MILR should proceed first in high-volume centers with experienced hepatobiliary surgeons.

As previously described by several authors, our study did not identify a higher tumor recurrence or an inferior oncologic operation using the MILR approach. A recent review by the Hong Kong group identified an overall patient survival advantage in a laparoscopic resection cohort compared to the open approach for hepatocellular cancer (5-year survival: 83.7% *vs.* 52.2%) (19). A meta-analysis by Cheng *et al.* demonstrated similar 5-year patient and disease free survival for MILR compared to open resection to manage metastatic colon cancer to the liver (20). This study further identified an increased R0 rate in the MILR group (OR =0.43, P=0.03). Araki and colleagues then addressed the use of MILR in difficult to access cases including the right posterosuperior segments (VII/VIII) and the caudate (I) confirming an equivalent low R1 rate for these resections (21).

Our study had several limitations. The first limitation was the retrospective nature of the study design. This may have resulted in introduction of possible patient selection bias. In addition, the results presented are the work of three aggressive early adopters of MILR with significant prior hepatobiliary experience. As observed by the French and the European studies, this fact may limit the widespread applicability of these results to other surgeons, especially to low volume centers with less experienced surgeons or even in large volume centers where senior surgeons may be late adopters. In this situation with senior surgeons, robotics may play a more significant role. As was observed in urologic and pelvic surgery, senior surgeons were more apt to adopt minimally invasive approaches using robotic platforms than pure laparoscopic techniques. Finally, more detailed information on the specific anatomic locations and techniques of laparoscopic liver transection and operative outcomes would provide more useful insight into the particular challenges that could be encountered with different types of liver resections.

In conclusion, this large multi-institutional retrospective study of MILR demonstrates that whether laparoscopic or robotic, significant patient benefits including less blood loss, complications, length of stay, readmissions were observed in both groups. Furthermore, no evidence of increased bile leak, re-operation, 90-day mortality or decreased oncologic integrity were apparent. This study provides a snapshot of three large volume centers of experience with the growth of MILR over the past two decades. Future studies are further needed to help solidify the long-term outcomes of MILR, especially in the era of RLRs.

Acknowledgments

Funding: None.

Footnote

Conflicts of Interest: The authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/ls.2018.07.01). JFB serves as an unpaid editorial board member of *Laparoscopic Surgery* from January 2018 to December 2020. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the manuscript in ensuring that questions related to the accuracy or integrity of any part of the manuscript are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study received approval from the Institutional Board Review Committee of Tulane University (No. 351684-OTH) with a waiver of written informed consent.

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doi: 10.21037/ls.2018.07.01

Cite this article as: Smith A, Konstantinidis IT, Fong Y, Martinie J, Iannitti D, Buell JF. A multi-institutional analysis of minimally invasive liver resections. Laparosc Surg 2018;2:35.