Published in final edited form as:

J Am Coll Surg. 2017 May ; 224(5): 851–861. doi:10.1016/j.jamcollsurg.2017.01.051.

Comparative Effectiveness of Minimally Invasive Surgery and Conventional Approaches to Major or Challenging Hepatectomy

Lucas W Thornblade, MD¹, Xu Shi, MS², Alex Ruiz, BS¹, David R Flum, MD, MPH, FACS¹, and James O Park, MD, FACS¹

¹Department of Surgery, University of Washington, Seattle, WA

²Department of Biostatistics, University of Washington, Seattle, WA

Abstract

Background—The benefits of minimally invasive surgery (MIS) for low-risk or minor liver resection are well established. There is growing interest in MIS for major hepatectomy (MH) and other challenging resections, but there remain unanswered questions of safety that prevent broad adoption of this technique.

Study Design—Retrospective cohort study of patients undergoing hepatectomy at 65 hospitals participating in the NSQIP Hepatopancreatobiliary Collaborative in 2014. We assessed serious morbidity or mortality (SMM, including organ-space infection and organ failure). Secondary outcomes included transfusion, bile leak, liver failure, reoperation or intervention, and 30-day readmission. We also measured factors considered to make resection more challenging (large tumors, cirrhosis, 3 concurrent resections, prior neoadjuvant chemotherapy, or morbid obesity).

Results—2819 patients underwent hepatectomy (age 58±14 years, 53% female; 25% MIS). After adjusting for clinical and operative factors, the odds of SMM (OR=0.57, 95%CI: 0.34–0.96, p=0.03) and reoperation or intervention (OR=0.52 (0.29–0.93), p=0.03) were significantly lower for patients undergoing MIS compared with open. In the MH group (n=1,015; 13% MIS), there was no difference in the odds of SMM after MIS (OR=0.37, (0.13–1.11), p=0.08) however MIS MH met criteria for non-inferiority. There were no differences in liver-specific complications or readmission between the groups. Odds of SMM were significantly lower following MIS among patients who had received neoadjuvant chemotherapy (OR 0.33 (0.15–0.70), p=0.004).

Conclusion—In this large study of minimally invasive major hepatectomy, we demonstrate safety outcomes that are equivalent or superior to conventional open surgery. While the decision to

Correspondence Address: Lucas W Thornblade, MD, Surgical Outcomes Research Center, Department of Surgery, University of Washington, 1107 NE 45th Street, Suite 502, Seattle, WA 98105, Telephone: 206-616-5536, Fax: 206-616-9032, lucaswt@uw.edu.

Disclosure Information: Nothing to disclose.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Presented at the American College of Surgeons 102nd Annual Clinical Congress, Washington, DC, October 2016

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

offer MIS may be influenced by factors not included in this evaluation, (e.g. surgeon experience and other patient factors), these findings support its current use in major hepatectomies.

INTRODUCTION

Laparoscopy has well-established benefits over the conventional, open approach to abdominal surgery including reduced pain, fewer wound complications, and shorter hospital stays.^{1–3} As surgical resection for benign and malignant tumors of the liver has become safer and more common, so has the use of minimally invasive surgery (MIS) in liver resection.^{4,5} Numerous studies support the use of MIS in liver resection, reporting less intraoperative blood loss, lower rates of bile leak, as well as fewer complications.^{6–12} Data to support MIS hepatectomy, however, are derived predominantly from studies of patients undergoing non-anatomic or minor resections of the liver (two or fewer contiguous Couinaud segments) and most studies of MIS have not included high-risk resections.^{13–16} According to the recent 2nd International Consensus on Laparoscopic Liver Resection, MIS minor liver resection is now considered standard of care but major hepatectomy (MH) (3 or more Couinaud segments) performed via MIS remains an innovative procedure.^{17,18} As surgeons gain more experience with MIS techniques, there is growing interest in applying MIS in major liver resections.^{19–22} The comparative effectiveness, including oncologic, safety and cost outcomes of MIS major hepatectomy, however, has not been established.

Prevention and control of significant hemorrhage remains the most important intra-operative goal during MH, which can sometimes be challenging in MIS.¹⁹ A primary reason for choice of open approach over MIS is the perceived difficulty of resection.^{23,24} A number of known technical, anatomic, and patient factors contribute to the difficulty of resection including tumor location (particularly right-posterior lesions), large tumor size and extent of resection, proximity to major vessels, underlying liver function and parenchymal texture.^{25,26} The fibrosis and resulting portal hypertension of cirrhosis increases the risk of hemorrhage during parenchymal transection and there is a paucity of data on the safety of MIS hepatectomy in patients with cirrhosis.^{27,28} Similarly, the friable and steatotic liver parenchyma which results from chemotherapy or obesity may makes hemostasis more difficult and be associated with adverse outcomes.^{29–32} Patient habitus may also add to the difficulty of liver resection although this has not been extensively studied. Liver resection in patients with morbid obesity require significantly longer operative times which may be due to difficulty of exposure and fatty infiltration of the liver parenchyma.³³ Although these patient factors influence the choice of surgical approach in liver resection, it is unknown whether MIS resection under challenging conditions is associated with worse outcomes. In this study, we aimed to measure the comparative effectiveness of MIS approaches to hepatectomy among the less well-studied groups of MH and patients with features of a challenging resection.

The National Surgical Quality Improvement Program (NSQIP) was developed by the American College of Surgeons for the purposes of measuring surgical outcomes, improving quality and safety of surgical care, and providing validated calculations of surgical risk.^{34,35} Procedure-targeted modules within NSQIP allow hospitals to collect organ specific data on over 30 high-risk procedures within nine subspecialty areas.³⁶ Beginning in 2014, NSQIP

formed the Hepatopancreatobiliary (HPB) collaborative and began collecting data on patient comorbidities, surgical factors and 30-day adverse events specifically related to liver resection. This data source presents an opportunity to perform large-scale evaluation of outcomes after major or challenging hepatectomy. By leveraging the NSQIP HPB collaborative procedure-targeted data, we aimed to measure serious morbidity and mortality as well as liver-related outcomes after MIS and open surgery among patients undergoing liver resection. We hypothesized that the MIS approach to both major and challenging hepatectomies among trained surgeons is as safe as the standard open approach.

METHODS

Cohort selection

We performed a retrospective analysis of all adult patients undergoing elective hepatectomy at 65 high-volume medical centers participating in the NSQIP HPB Collaborative in 2014. All patients included in the HPB collaborative dataset were linked to the NSQIP Public Use File, which includes preoperative laboratory, comorbidity, and demographic data as well as 30-day in-hospital and post-discharge adverse events. In order to exclusively capture liver resection cases, we excluded patients who required biliary reconstruction, which involves bowel anastomosis. We identified and reported all cases that had a concomitant colon resection because these cases may have a higher risk of early post-operative complications. Demographic and historical data were obtained on patients prior to surgery including laboratory values (e.g. hepatic panel, etc.), medical comorbidities (e.g. diabetes, etc.) and other conditions existing at the time of surgery including infection or sepsis. Following surgery, patients were followed for 30 days for complications, reoperation or intervention, readmission, and death. Due to the de-identified nature of the data, this research was not considered human subjects research and did not require approval by the University of Washington's Human Subjects Division Institutional Review Board.

Comparison groups

We report outcomes from all hepatectomies, major hepatectomies (resection of 3 consecutive Couinaud segments, Current Procedural Terminology (CPT) numbers 47122: trisegmentectomy, 47125: left lobectomy, 47130: right lobectomy), and five subgroups indicating a challenging resection among all (major and minor) hepatectomies: large tumors, cirrhosis, 3 concurrent resections, patients with a prior history of neoadjuvant chemotherapy, and morbid obesity. Large tumors were defined as >5cm (for benign tumors) or tumor stages III and IV (for malignant tumors) (American Joint Committee on Cancer 7th edition, Cancer Staging System). Cirrhosis was identified either on preoperative imaging or by the surgeon at the time of operation based upon liver texture. Cases were identified in which the surgeon performed at least two concurrent resections (e.g. wedge, subsegmental, or segmental resections) in addition to the primary resection (either major or minor hepatectomy). NSQIP abstractors recorded any history of neoadjuvant chemotherapy from the patients' preoperative charts. Finally, morbid obesity was defined as a preoperative body mass index (BMI) ≥ 40 kg/cm².

Case definition

Cases were defined as MIS if it was documented that the resection was performed by laparoscopy or robotic assistance including any cases with open assistance. Surgical approach was defined as MIS by intention to treat, and therefore, any case that began by a minimally invasive approach but required open conversion was included in the MIS group. We excluded any cases described as hybrid approach (laparoscopic mobilization of the liver followed by open parenchymal transection, which is typically used in hepatectomy for living liver donation).

Outcomes

The primary outcome in this study was serious morbidity or mortality (SMM). NSQIP defines serious morbidity as any of the following events occurring during the 30-day period following surgery: organ space surgical site infection, surgical wound dehiscence, stroke, myocardial infarction, cardiac arrest requiring cardiopulmonary resuscitation, pulmonary embolism, respiratory failure requiring mechanical ventilation >48 hours after surgery, postoperative acute renal failure, sepsis, or septic shock.³⁵ Bleeding and subsequent transfusion is a component of SMM, however, as a common event after liver surgery that may not represent serious morbidity, we report transfusions separately as a secondary outcome.

There were five secondary outcomes including three liver-specific outcomes. First, we measured all patients who required transfusion of red blood cells. Second, we recorded any postoperative bile leak which is classified as persistent drainage of bilious fluid with three times the serum concentration of bilirubin. Third, we reported any patients who developed grade A, B, or C post-hepatectomy liver failure as defined by the International Study Group of Liver Surgery.^{37,38} Fourth, we reported any patients requiring reoperation or invasive intervention including drainage or aspiration of a fluid collection, biliary stent placement, or angiography or embolization for bleeding. Finally, we reported all patients requiring hospital readmission within 30 days.

Analysis

We performed univariate analysis of relevant clinical variables using chi-squared and Fischer's exact tests (categorical variables) and two-tailed unpaired Student's t-tests (continuous variables). In order to control for known differences between patients undergoing MIS and open hepatectomy, we performed an adjusted analysis of patients in each group. Using logistic regression, we controlled for clinically relevant covariates including American Society of Anesthesia (ASA) Class, history of viral hepatitis, primary tumor pathology, presence of challenging resection types (including cirrhosis), presence of major hepatectomy, and operation-specific variables, including use of Pringle maneuver and use of concurrent tumor ablation. An additional factor included in the regression model was the NSQIP morbidity probability which is a value derived from a validated prediction model based upon 19 comorbidities including patient age, wound classification, preoperative albumin, and tests of coagulation factors.^{34,35} Regression models reported in this study included only those covariates that were significantly different between groups by univariate analysis with an alpha-level of 20%. Comparative assessment of outcomes between MIS

and open surgery were performed for all hepatectomies, major hepatectomies, and each of the five challenging subgroups.

Because this study compares an established procedure (open MH) with an innovative procedure (MIS MH), we performed a *post-hoc* non-inferiority analysis for primary outcomes (i.e. SMM). We selected a non-inferiority margin of 5%, which represents the tolerated increase in adverse event rates for the novel procedure. We calculated the odds ratio (OR) corresponding to a 5% increase in rates of SMM in the open group. Using the regression model, we calculated one-sided 95% confidence intervals.

All statistical analyses were performed using commercially available software (Stata, version 14; StataCorp, College Station, TX; R-software, version 3.1.3). All statistical tests were considered significant if $p < 0.05$.

RESULTS

All hepatectomies

Between January 1 and December 31, 2014, 2,819 patients (mean age 58 $\pm$ 14 years, 53% female) underwent liver resection (36% major hepatectomy) at 65 medical centers. Including both laparoscopy and robotic approaches, 706 cases (25%) were performed via MIS, and 109 of these required conversion to open (15.4%). The rate of SMM was 6% among MIS cases and 13% among open cases ($p < 0.001$). Unadjusted rates of transfusion (9% vs. 19%), bile leak (3% vs. 7%), post-operative liver failure (1% vs. 5%), and reoperation or intervention (5% vs. 10%), were also significantly lower in the MIS group compared with the open group, respectively (all $p < 0.001$). The 30-day readmission rate was similar (8% vs. 10%, $p = 0.09$) (Table 1). After adjusting for clinically relevant covariates listed in Table 1, MIS among all hepatectomies was associated with significantly lower odds of SMM compared with open resection (OR 0.57, 95% CI: 0.34–0.96, $p = 0.03$). MIS was also associated with significantly lower odds of transfusion (OR: 0.60, 95% CI: 0.40–0.92, $p = 0.02$), and postoperative reoperation or invasive intervention (OR 0.52, 95% CI: 0.29–0.93, $p = 0.03$) (Table 2). Among all hepatectomies, MIS reached non-inferiority for SMM when compared with open resection.

Major hepatectomies

A total of 1,015 patients underwent major hepatectomy (MH) (mean age 57.0 $\pm$ 14 years, 52% female, 13% MIS). Right hemi-hepatectomy was a greater proportion of the open MH group (55%) versus the MIS MH group (42%, $p = 0.002$). Among MH, MIS patients had lower unadjusted rates of serious morbidity and mortality than open resection (6% vs. 16%, $p = 0.004$), as well as lower rates of post-operative liver failure (2% vs. 8%, $p = 0.03$). There were no significant differences in rates of transfusion, bile leak, reoperation or intervention, or readmission (Table 3). After adjusted analysis, there was no significant difference in odds of SMM after MIS MH vs. open (OR: 0.37, 95% CI: 0.13–1.11, $p = 0.08$), however MIS for MH did reach non-inferiority when compared with open resection (one-sided 95% CI: < 0.93). There were no significant differences in odds of transfusion, bile leak, liver failure, reoperation or intervention, or readmission (Table 4). Because we anticipated that there are

differences in difficulty even among major resections, we also measured outcomes for right hemi-hepatectomies (n=544, 10% MIS) and observed lower rates of SMM after MIS (5%) than after open (16%). After adjusted analysis, odds of SMM were significantly lower for MIS right hemi-hepatectomies (OR: 0.25, 95% CI: 0.07–0.87, p=0.03).

Challenging hepatectomy subgroups

From the entire cohort, 693 patients had large tumors (23% MIS), 285 patients had documented cirrhosis (33% MIS), 720 patients required ≥3 concurrent resections (20% MIS), 138 patients were morbidly obese (36% MIS), and 880 patients had a history of neoadjuvant chemotherapy (19% MIS). For patients undergoing ≥3 concurrent resections, median number of resections was two among both patients undergoing open (Interquartile Range (IQR): 2–4) and MIS resection (IQR: 2–3, p=0.052). Mean BMI among morbidly obese patients was similar among open (45.2 kg/m²) and MIS resections (45.4 kg/m², p=0.86). Unadjusted rates of SMM were lower after MIS in patients with large tumors (6% vs. 14%, p=0.005), and patients with a history of neoadjuvant chemotherapy (5% vs. 16%, p<0.001). Patients with large tumors also had lower unadjusted rates of post-operative liver failure after MIS (1%) compared with open resection (6%, p=0.008). The distribution of outcomes by challenging subgroup is listed in Table 2.

After adjusted analysis, including adjustment for major resection, MIS resection for patients with history of neoadjuvant chemotherapy was associated with 67% lower odds of SMM compared with open resection (OR: 0.33, 95% CI: 0.15–0.70, p=0.004). There was no significant difference in odds of adverse outcomes between MIS and open resection among patients with large tumors, cirrhosis, those requiring ≥3 concurrent resections, or patients with morbid obesity. MIS hepatectomy reached non-inferiority compared with open hepatectomy for patients with large tumors (one-sided 95% CI<1.02) or with a history of neoadjuvant chemotherapy (one-sided 95% CI<0.62). There was insufficient evidence, however, to indicate that MIS was non-inferior to open hepatectomies for patients with cirrhosis, those requiring ≥3 concurrent resections and for patients with morbid obesity.

DISCUSSION

In this study, minimally invasive (MIS) hepatectomy was associated with a significant reduction in the risk of serious morbidity or mortality (SMM) including organ-space infection and organ failure. MIS was also associated with a significant reduction in odds of transfusion and post-operative reoperation or invasive intervention compared with open resection. For major hepatectomy (MH), resection of large tumors, or for patients with a history of neoadjuvant chemotherapy, MIS was found to be “non-inferior” to open resection. While the preponderance of major and challenging hepatectomies are performed via an open approach, reflecting the preference of many practicing surgeons, our findings suggest that short-term outcomes after MIS major hepatectomy are at least equivalent to and for some challenging subgroups may be superior to open resection.

By leveraging the newly formed NSQIP HPB collaborative, we are reporting the largest-to-date multi-institutional comparison of outcomes after major hepatectomy. There are a number of previously published studies on short-term outcomes after MIS hepatectomy, but

most do not include any major hepatectomies.^{39–41} Other studies have reported both major and minor hepatectomies but did not compare to open controls.^{42–47} Five recent studies report both single and multi-institutional comparisons of MIS and open hepatectomies, but each reports fewer than 15 MIS major hepatectomies.^{13,48–51} In 2013, Lin *et al.* reviewed four studies which report MIS major hepatectomy matched with open cases.⁵² These data indicate that for major hepatectomies, MIS was significantly associated with less blood loss (3 of 4 studies), fewer transfusions (1 of 4 studies), fewer complications (2 of 4 studies) and shorter length of stay (3 of 4 studies).^{53–56} Case-matched studies provide important data on outcomes of two different interventions; however, matching methods may not completely account for confounding by indication. By utilizing the standardized perioperative data collected through the NSQIP HPB collaborative, we were able to control for important differences between patients who undergo MIS or open resections in each of the comparisons. Logistic regression modeling was used to minimize the impact of confounding by indication on our estimates of outcome.

Our findings build upon those in recent analysis of the NSQIP HPB data by Bagante *et al.*, which reported lower postoperative morbidity and shorter length of stay after MIS hepatectomy.¹¹ In our study we aimed primarily to address the knowledge gap for major hepatectomies, a procedure that is considered by consensus opinion to be innovative and which has not been described previously from the nationwide NSQIP HPB collaborative.¹⁷ Bagante *et al.* found that MIS was favored in eight of 24 separate outcomes. Our study adds to this evidence by reporting a single primary outcome allowing direct comparison of composite adverse events. Lastly, while Bagante *et al.* showed that if a hepatectomy is completed laparoscopically, then the outcomes may be favorable to open by including cases converted to open in the MIS group (intention-to-treat), our analysis adds evidence on the safety of this procedure.¹¹

Research to date demonstrates agreement for MIS as the standard of care for minor hepatectomies, especially in liver segments with easy exposure and those not proximate to hilar structures, e.g. left lateral sectionectomy¹⁷. Standardized approaches to MIS major hepatectomy have not been widely adopted.⁵⁷ and for malignant disease, resection with negative margins remains a concern in MIS approaches. Despite this, there is a growing interest in use of MIS for larger resections. Across North America, Europe and East Asia, no more than half of surveyed surgeons employ MIS approach to major hepatectomies.⁵⁸ The 2nd International Consensus Conference on Laparoscopic Liver Resection reported an analysis of the current literature on minimally invasive major hepatectomy and concluded that this procedure remains innovative. The consensus jury made a call for larger scale studies of outcomes after this high-risk surgery.¹⁷ Our study provides important data that addresses this knowledge gap.

While safety of innovative approaches is principally important, equivalent oncologic outcomes must also be demonstrated for MIS approaches to become standard of care. Oncologic outcomes after MIS hepatectomy are still questioned and while there are several studies reporting long-term outcomes,^{13,59,60} to date no randomized studies have been completed in this area. There are two ongoing randomized trials of MIS for liver disease which, once published, may help inform the choice of approach in MIS liver resections. The

Oslo-CoMet trial (Clinicaltrials.gov identifier NCT01516710) is currently enrolling patients with colorectal liver metastases for randomization to open or laparoscopic resection.⁶¹ This study includes some major hepatectomies, however these findings will need to be applied with caution to patients with primary tumors of the liver, which are, by design, not included in the trial. The ORANGE II trial (Clinicaltrials.gov identifier: NCT00874224) is randomizing patients for left lateral sectionectomy within a framework of Enhanced Recovery After Surgery to either laparoscopic or open resection.⁶² This study is limited to minor resections but will provide data generalizable to both primary and secondary liver tumors. The addition of the upcoming ORANGE II PLUS trial (Clinicaltrials.gov identifier: NCT01441856) from the same European research collaborative will add needed information on outcomes after major hepatectomy and may complement the findings of our study.

Central to the choice of surgical approach is the anticipated difficulty of resection. While extent of resection is an important factor in this decision (e.g. major versus minor), tumor features, location, proximity to vasculature, quality of the parenchyma, and ease of access to the targeted segment(s) are likely as important as volume of liver resected. Ban *et al.* highlight the difficulty of standardizing measurement of the difficulty of liver resection.²³ The interplay of patient and tumor factors against surgeon experience renders perceived difficulty of resection less suitable to measurement. There is agreement that billing codes (e.g. CPT) do not adequately capture the differences among types of liver resections, and CPT codes are used in the NSQIP HPB module. Nevertheless, these data allow us to examine the challenging features of liver resection in a novel way. Similar to major hepatectomy, our data suggest that safety of MIS in resection of large tumors, patients with cirrhosis, and after neoadjuvant chemotherapy is at least equivalent to open resection. One explanation for this finding is that in patients with compromised parenchyma (cirrhosis or after chemotherapy), MIS approaches may be superior because of more limited parenchymal transection and preservation of collateral circulation.¹³ For patients with morbid obesity or those requiring 3 concurrent resections, however, there is not sufficient data in this analysis to support MIS liver resection.

This study does have several limitations. Studies that compare effectiveness of two surgical interventions are subject to confounding by indication, meaning there are important differences between treatment groups that may be associated with both the choice of treatment and outcomes. By controlling for known patient- and surgery-related variables in a logistic regression model, we attempt to minimize any confounding. While propensity score matching is often applied in comparing two different interventions, the NSQIP database does not provide surgeon or hospital identifiers that would be important for estimating the propensity of patients to undergo either open or MIS resection. An important factor in the choice of surgical approach is the anatomic location of the tumor. Superior-posterior resections are notoriously challenging; however, the NSQIP dataset does not identify these more difficult areas of the liver, and we therefore were unable to assess outcomes based upon this critical feature. Another important measure of quality in surgery for cancer is attaining negative margins however the NSQIP does not capture this pathological data. There are also limitations to the precision of some NSQIP variables. For example, cirrhosis was reported by either preoperative imaging or intraoperative examination, both of which likely have lower sensitivity for this diagnosis than a standard liver biopsy. Nonetheless, the

macroscopic cirrhosis identified in this study is likely a subset of more advanced cases and therefore findings for these patients are conservative.

This study assesses only short-term postoperative outcomes and does not take into account the potentially favorable outcomes of MIS including shorter length of stay, reduced narcotic use, improved cosmesis, and rates of wound complications such as hernia. Quality of life may also play an important role in choice of surgery but at this stage in assessment, data do not exist to study these outcomes in liver resection. Finally, although we were unable to control for clustering of effects by surgeon or institution, the data for this study comes from specialty centers that employ surgeons with advanced training in laparoscopic liver resection. There is agreement that mastering MIS liver resection requires high case volume,^{63,64} and therefore the results of this study should be applied strictly to the practice of surgeons with a similar level of training as those in the NSQIP HPB Collaborative.

CONCLUSIONS

This study finds that a minimally invasive approach to hepatectomy, including major hepatectomy, is associated with short-term outcomes that are equal or even superior to open surgery. While data is lacking to support its use in patients with cirrhosis, those requiring multiple (≥ 3) concurrent resections or in patients with morbid obesity, minimally invasive surgery appears to be non-inferior to open surgery in several challenging resections including patients with large tumors and after neoadjuvant chemotherapy.

Acknowledgments

We would like to thank the surgeons, patients and institutions that contribute data to the NSQIP HPB Collaborative.

Support: This study was supported by a training grant from the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health under Award Number T32DK070555.

ABBREVIATIONS

NSQIP	National Surgical Quality Improvement Program
HPB	hepatopancreatobiliary
MIS	minimally invasive surgery
MH	major hepatectomy
SMM	serious morbidity and mortality
OR	odds ratio
CPT	Current Procedural Terminology
CI	confidence interval

References

1. Lacy AM, García-Valdecasas JC, Delgado S, et al. Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: A randomised trial. *Lancet*. 2002; 359(9325):2224–2229. DOI: 10.1016/S0140-6736(02)09290-5 [PubMed: 12103285]
2. Guillaou PJ, Quirke P, Thorpe H, et al. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre , randomised controlled trial. *Methods*. 2005:365.
3. Mohiuddin K, Swanson SJ. Maximizing the benefit of minimally invasive surgery. *J Surg Oncol*. 2013; 108(5):315–319. DOI: 10.1002/jso.23398 [PubMed: 24037974]
4. Dimick JB, Wainess RM, Cowan JA, et al. National trends in the use and outcomes of hepatic resection. *J Am Coll Surg*. 2004; 199(1):31–38. DOI: 10.1016/j.jamcollsurg.2004.03.005 [PubMed: 15217626]
5. Ejaz A, Sachs T, He J, et al. A comparison of open and minimally invasive surgery for hepatic and pancreatic resections using the nationwide inpatient sample. *Surg (United States)*. 2014; 156(3): 538–547. DOI: 10.1016/j.surg.2014.03.046
6. Luo L, Zou H, Yao Y, Huang X. Laparoscopic versus open hepatectomy for hepatocellular carcinoma: short- and long-term outcomes comparison. *Int J Clin Exp Med*. 2015; 8(10):18772–18778. <http://www.ncbi.nlm.nih.gov/pubmed/26770494>. [PubMed: 26770494]
7. Jackson NR, Hauch A, Hu T, et al. The safety and efficacy of approaches to liver resection: a meta-analysis. *JSLs*. 2015; 19(1):e2014.00186.doi: 10.4293/JSLs.2014.00186
8. Nguyen KT, Gamblin TC, Geller DA. World review of laparoscopic liver resection-2,804 patients. *Ann Surg*. 2009; 250(5):831–841. DOI: 10.1097/SLA.0b013e3181b0c4df [PubMed: 19801936]
9. Schiffman SC, Kim KH, Tsung A, et al. Laparoscopic versus open liver resection for metastatic colorectal cancer: A metaanalysis of 610 patients. *Surgery*. 2014; 157(2):1–12. DOI: 10.1016/j.surg.2014.08.036
10. Sham JG, Richards MK, Seo YD, et al. Efficacy and cost of robotic hepatectomy: is the robot cost-prohibitive? *J Robot Surg*. 2016; doi: 10.1007/s11701-016-0598-4
11. Bagante F, Spolverato G, Strasberg SM, et al. Minimally Invasive vs. Open Hepatectomy: a Comparative Analysis of the National Surgical Quality Improvement Program Database. *J Gastrointest Surg*. 2016; 20(9):1608–1617. DOI: 10.1007/s11605-016-3202-3 [PubMed: 27412321]
12. Rao A, Rao G, Ahmed I. Laparoscopic vs. open liver resection for malignant liver disease. A systematic review. *Surgeon*. 2012; 10(4):194–201. DOI: 10.1016/j.surge.2011.06.007 [PubMed: 22818276]
13. Tranchart H, Di Giuro G, Lainas P, et al. Laparoscopic resection for hepatocellular carcinoma: a matched-pair comparative study. *Surg Endosc*. 2010; 24(5):1170–1176. DOI: 10.1007/s00464-009-0745-3 [PubMed: 19915908]
14. Han DH, Choi SH, Park EJ, et al. Surgical outcomes after laparoscopic or robotic liver resection in hepatocellular carcinoma: a propensity-score matched analysis with conventional open liver resection. *Int J Med Robot*. 2015; doi: 10.1002/rcs.1714
15. Palanisamy S, Sabnis SC, Patel ND, et al. Laparoscopic Major Hepatectomy-Technique and Outcomes. *J Gastrointest Surg*. 2015; 19(12):2215–2222. DOI: 10.1007/s11605-015-2933-x [PubMed: 26361772]
16. Nachmany I, Pencovich N, Zohar N, et al. Laparoscopic versus open liver resection for metastatic colorectal cancer. *Eur J Surg Oncol*. 2015; 41(12):1615–1620. DOI: 10.1016/j.ejso.2015.09.014 [PubMed: 26454765]
17. Wakabayashi G, Cherqui D, Geller DA, et al. Recommendations for laparoscopic liver resection: a report from the second international consensus conference held in Morioka. *Ann Surg*. 2015; 261(4):619–629. DOI: 10.1097/SLA.0000000000001184 [PubMed: 25742461]
18. Coelho FF, Kruger JAP, Fonseca GM, et al. Laparoscopic liver resection: Experience based guidelines. *World J Gastrointest Surg*. 2016; 8(1):5–26. DOI: 10.4240/wjgs.v8.i1.5 [PubMed: 26843910]

19. Koffron AJ, Auffenberg G, Kung R, Abecassis M. Evaluation of 300 minimally invasive liver resections at a single institution: less is more. *Ann Surg.* 2007; 246(3):385, 392–394. DOI: 10.1097/SLA.0b013e318146996c [PubMed: 17717442]
20. Pearce NW, Di Fabio F, Teng MJ, et al. Laparoscopic right hepatectomy: a challenging, but feasible, safe and efficient procedure. *Am J Surg.* 2011; 202(5):e52–8. DOI: 10.1016/j.amjsurg.2010.08.032 [PubMed: 21861979]
21. Ocuin LM, Tsung A. Minimally Invasive Hepatic Surgery. *Surg Clin North Am.* 2016; 96(2):299–313. DOI: 10.1016/j.suc.2015.12.004 [PubMed: 27017866]
22. Cardinal JS, Reddy SK, Tsung A, Marsh JW, Geller DA. Laparoscopic major hepatectomy: Pure laparoscopic approach versus hand-assisted technique. *J Hepatobiliary Pancreat Sci.* 2013; 20(2): 114–119. DOI: 10.1007/s00534-012-0553-3 [PubMed: 23053353]
23. Ban D, Kudo A, Ito H, et al. The difficulty of laparoscopic liver resection. *Updat Surg.* 2015; 67(2):123–128. DOI: 10.1007/s13304-015-0302-7
24. Ban D, Tanabe M, Ito H, et al. A novel difficulty scoring system for laparoscopic liver resection. *J Hepatobiliary Pancreat Sci.* 2014; 21(10):745–753. DOI: 10.1002/jhbp.166 [PubMed: 25242563]
25. Lee MK, Gao F, Strasberg SM. Perceived complexity of various liver resections: Results of a survey of experts with development of a complexity score and classification. *J Am Coll Surg.* 2015; 220(1):64–69. DOI: 10.1016/j.jamcollsurg.2014.09.017 [PubMed: 25451665]
26. Shelat VG, Cipriani F, Basseres T, et al. Pure laparoscopic liver resection for large malignant tumors: does size matter? *Ann Surg Oncol.* 2015; 22(4):1288–1293. DOI: 10.1245/s10434-014-4107-6 [PubMed: 25256130]
27. Worhunsky DJ, Dua MM, Tran TB, et al. Laparoscopic hepatectomy in cirrhotics: safe if you adjust technique. *Surg Endosc.* 2016; doi: 10.1007/s00464-016-4748-6
28. Cai X, Liang X, Yu T, et al. Liver cirrhosis grading Child-Pugh class B: a Goliath to challenge in laparoscopic liver resection?-prior experience and matched comparisons. *Hepatobiliary Surg Nutr.* 2015; 4(6):391–397. DOI: 10.3978/j.issn.2304-3881.2015.09.02 [PubMed: 26734623]
29. Hewes JC, Dighe S, Morris RW, et al. Preoperative chemotherapy and the outcome of liver resection for colorectal metastases. *World J Surg.* 2007; 31(2):353–356. DOI: 10.1007/s00268-006-0103-8 [PubMed: 17219289]
30. Kneuert PJ, Maithel SK, Staley Ca, Kooby Da. Chemotherapy-associated liver injury: impact on surgical management of colorectal cancer liver metastases. *Ann Surg Oncol.* 2011; 18(1):181–190. DOI: 10.1245/s10434-010-1201-2 [PubMed: 20645011]
31. Aloia T, Sebagh M, Plasse M, et al. Liver histology and surgical outcomes after preoperative chemotherapy with fluorouracil plus oxaliplatin in colorectal cancer liver metastases. *J Clin Oncol.* 2006; 24(31):4983–4990. DOI: 10.1200/JCO.2006.05.8156 [PubMed: 17075116]
32. Vauthey JN, Pawlik TM, Ribero D, et al. Chemotherapy regimen predicts steatohepatitis and an increase in 90-day mortality after surgery for hepatic colorectal metastases. *J Clin Oncol.* 2006; 24(13):2065–2072. DOI: 10.1200/JCO.2005.05.3074 [PubMed: 16648507]
33. Gedaly R, McHugh PP, Johnston TD, et al. Obesity, diabetes, and smoking are important determinants of resource utilization in liver resection: a multicenter analysis of 1029 patients. *Ann Surg.* 2009; 249(3):414–419. DOI: 10.1097/SLA.0b013e31819a032d [PubMed: 19247028]
34. Bilimoria KY, Liu Y, Paruch JL, et al. Development and evaluation of the universal ACS NSQIP surgical risk calculator: A decision aid and informed consent tool for patients and surgeons. *J Am Coll Surg.* 2013; 217(5):833–842. e3. DOI: 10.1016/j.jamcollsurg.2013.07.385 [PubMed: 24055383]
35. Cohen ME, Bilimoria KY, Ko CY, Hall BL. Development of an American College of Surgeons National Surgery Quality Improvement Program: morbidity and mortality risk calculator for colorectal surgery. *J Am Coll Surg.* 2009; 208(6):1009–1016. DOI: 10.1016/j.jamcollsurg.2009.01.043 [PubMed: 19476884]
36. [Accessed September 29, 2016] ACS NSQIP Data Collection, Analysis, and Reporting. <https://www.facs.org/quality-programs/acs-nsqip/>
37. Ishii M, Mizuguchi T, Harada K, et al. Comprehensive review of post-liver resection surgical complications and a new universal classification and grading system. *World J Hepatol.* 2014; 6(10):745–751. DOI: 10.4254/wjh.v6.i10.745 [PubMed: 25349645]

38. Koch M, Garden OJ, Padbury R, et al. Bile leakage after hepatobiliary and pancreatic surgery: A definition and grading of severity by the International Study Group of Liver Surgery. *Surgery*. 2011; 149(5):680–688. DOI: 10.1016/j.surg.2010.12.002 [PubMed: 21316725]
39. Sasaki A, Nitta H, Otsuka K, et al. Ten-year experience of totally laparoscopic liver resection in a single institution. *Br J Surg*. 2009; 96(3):274–279. DOI: 10.1002/bjs.6472 [PubMed: 19224518]
40. Memeo R, de' Angelis N, Compagnon P, et al. Laparoscopic vs. open liver resection for hepatocellular carcinoma of cirrhotic liver: a case-control study. *World J Surg*. 2014; 38(11):2919–2926. DOI: 10.1007/s00268-014-2659-z [PubMed: 24912628]
41. Cheung TT, Poon RT-P, Yuen WK, et al. Long-Term Survival Analysis of Pure Laparoscopic Versus Open Hepatectomy for Hepatocellular Carcinoma in Patients With Cirrhosis: A Single-Center Experience. *Ann Surg*. 2013; 262(1):20–21. DOI: 10.1097/SLA.0000000000000443
42. Bryant R, Laurent A, Tayar C, Cherqui D. Laparoscopic liver resection-understanding its role in current practice: the Henri Mondor Hospital experience. *Ann Surg*. 2009; 250(1):103–111. DOI: 10.1097/SLA.0b013e3181ad6660 [PubMed: 19561476]
43. Belli G, Gayet B, Han HS, et al. Laparoscopic left hemihepatectomy a consideration for acceptance as standard of care. *Surg Endosc Other Interv Tech*. 2013; 27(8):2721–2726. DOI: 10.1007/s00464-013-2840-8
44. Dagher I, Gayet B, Tzanis D, et al. International experience for laparoscopic major liver resection. *J Hepatobiliary Pancreat Sci*. 2014; 21(10):732–736. DOI: 10.1002/jhbp.140 [PubMed: 25098667]
45. Soubrane O, Goumard C, Laurent A, et al. Laparoscopic resection of hepatocellular carcinoma: A French survey in 351 patients. *Hpb*. 2014; 16(4):357–365. DOI: 10.1111/hpb.12142 [PubMed: 23879788]
46. Dagher I, O'Rourke N, Geller DA, et al. Laparoscopic Major Hepatectomy. *Ann Surg*. 2009; 250(5):856–860. DOI: 10.1097/SLA.0b013e3181bcaf46 [PubMed: 19806057]
47. Di Fabio F, Samim M, Di Gioia P, et al. Laparoscopic major hepatectomies: clinical outcomes and classification. *World J Surg*. 2014; 38(12):3169–3174. DOI: 10.1007/s00268-014-2724-7 [PubMed: 25159116]
48. Abu Hilal M, Underwood T, Zuccaro M, et al. Short- And medium-term results of totally laparoscopic resection for colorectal liver metastases. *Br J Surg*. 2010; 97(6):927–933. DOI: 10.1002/bjs.7034 [PubMed: 20474003]
49. Nguyen KT. Comparative Benefits of Laparoscopic vs Open Hepatic Resection. *Arch Surg*. 2011; 146(3):348. doi: 10.1001/archsurg.2010.248 [PubMed: 21079109]
50. Cheung TT, Poon RTP, Yuen WK, et al. Outcome of laparoscopic versus open hepatectomy for colorectal liver metastases. *ANZ J Surg*. 2013; 83(11):847–852. DOI: 10.1111/j.1445-2197.2012.06270.x [PubMed: 23035809]
51. Cheung TT, Dai WC, Tsang SHY, et al. Pure Laparoscopic Hepatectomy Versus Open Hepatectomy for Hepatocellular Carcinoma in 110 Patients With Liver Cirrhosis. *Ann Surg*. 2016; XX(X):1. doi: 10.1097/SLA.0000000000001848
52. Lin N-C, Nitta H, Wakabayashi G. Laparoscopic Major Hepatectomy. *Ann Surg*. 2013; 257(2): 205–213. DOI: 10.1097/SLA.0b013e31827da7fe [PubMed: 23263192]
53. Martin RCG, Scoggins CR, McMasters KM. Laparoscopic Hepatic Lobectomy: Advantages of a Minimally Invasive Approach. *J Am Coll Surg*. 2010; 210(5):627–634. DOI: 10.1016/j.jamcollsurg.2009.12.022 [PubMed: 20421019]
54. Cai XJ, Wang YF, Liang YL, Yu H, Liang X. Laparoscopic left hemihepatectomy: a safety and feasibility study of 19 cases. *Surg Endosc*. 2009; 23(11):2556–2562. DOI: 10.1007/s00464-009-0454-y [PubMed: 19347401]
55. Dagher I, Di Giuro G, Dubrez J, et al. Laparoscopic versus open right hepatectomy: a comparative study. *Am J Surg*. 2009; 198(2):173–177. DOI: 10.1016/j.amjsurg.2008.09.015 [PubMed: 19268902]
56. Hilal MA, Di Fabio F, Teng MJ, et al. Single-Centre Comparative Study of Laparoscopic Versus Open Right Hepatectomy. *J Gastrointest Surg*. 2011; 15(5):818–823. DOI: 10.1007/s11605-011-1468-z [PubMed: 21380633]

57. Kluger MD, Vigano L, Barroso R, Cherqui D. The learning curve in laparoscopic major liver resection. *J Hepatobiliary Pancreat Sci.* 2013; 20(2):131–136. DOI: 10.1007/s00534-012-0571-1 [PubMed: 23064988]
58. Hibi T, Cherqui D, Geller DA, et al. International Survey on Technical Aspects of Laparoscopic Liver resection: A web-based study on the global diffusion of laparoscopic liver surgery prior to the 2nd International Consensus Conference on Laparoscopic Liver Resection in Iwate, Japan. *J Hepatobiliary Pancreat Sci.* 2014; 21(10):737–744. DOI: 10.1002/jhbp.141 [PubMed: 25088825]
59. Parks KR, Kuo Y, Davis JM, et al. Laparoscopic versus open liver resection: a meta-analysis of long-term outcome. *Hpb.* 2014; 16(2):109–118. DOI: 10.1111/hpb.12117 [PubMed: 23672270]
60. Castaing D, Vibert E, Ricca L, et al. Oncologic results of laparoscopic versus open hepatectomy for colorectal liver metastases in two specialized centers. *Ann Surg.* 2009; 250(5):849–855. DOI: 10.1097/SLA.0b013e3181bcaf63 [PubMed: 19801934]
61. Fretland ÅA, Kazaryan AM, Bjørnbeth BA, et al. Open versus laparoscopic liver resection for colorectal liver metastases (the Oslo-CoMet study): study protocol for a randomized controlled trial. *Trials.* 2015; 16(1):577.doi: 10.1186/s13063-015-0577-5 [PubMed: 26680020]
62. van Dam RM, Wong-Lun-Hing EM, van Breukelen GJP, et al. Open versus laparoscopic left lateral hepatic sectionectomy within an enhanced recovery ERAS® programme (ORANGE II-trial): study protocol for a randomised controlled trial. *Trials.* 2012; 13:54.doi: 10.1186/1745-6215-13-54 [PubMed: 22559239]
63. Vigano L, Laurent A, Tayar C, et al. The learning curve in laparoscopic liver resection: improved feasibility and reproducibility. *Ann Surg.* 2009; 250(5):772–782. DOI: 10.1097/SLA.0b013e3181bd93b2 [PubMed: 19801926]
64. Kluger MD, Vigano L, Barroso R, Cherqui D. The learning curve in laparoscopic major liver resection. *J Hepatobiliary Pancreat Sci.* 2013; 20(2):131–136. DOI: 10.1007/s00534-012-0571-1 [PubMed: 23064988]

Table 1

Patient Demographics, Treatment Characteristics, and Outcomes among Patients Undergoing Minimally Invasive or Open Hepatectomy.

Characteristic	MIS (n=706)	Open (n=2113)	All (n=2819)	p Value
Major, n (%)	132 (19)	883 (42)	1015 (36)	<0.001 *
Demographic				
Age, y, mean (SD)	59 (15)	58 (13)	58 (14)	0.65
Female, n (%)	414 (59)	1073 (51)	1487 (53)	<0.001 *
Non-white race, n (%)	107 (18)	276 (16)	383 (17)	0.43
BMI, mean (SD)	28.8 (7)	28.3 (6)	28.4 (6)	0.04 *
Concomitant colon resection, n (%)	31(4)	93 (4)	124 (4)	0.99
ASA Class, n (%)				0.002 *
I	7 (1)	68 (3)	75 (3)	
II	215 (30)	537 (25)	752 (27)	
III	445 (63)	1361 (64)	1806 (64)	
IV	39 (6)	144 (7)	183 (6)	
NSQIP morbidity probability,mean (SD)	0.16 (0.07)	0.19 (0.08)	0.18 (0.08)	<0.001 *
Challenging subgroup, n (%)				
Large tumor	157 (22)	536 (25)	693 (25)	0.11
Cirrhosis	93 (13)	192 (9)	285 (10)	0.005 *
3 concurrent resections	147 (21)	573 (27)	720 (26)	<0.001 *
Neoadjuvant	171 (24)	708 (34)	880 (31)	<0.001 *
Morbid obesity	49 (7)	89 (4)	138 (5)	0.005 *
Pathology, n (%)				<0.001 *
Primary hepatobiliary	161 (23)	551 (26)	712 (25)	
Secondary (metastatic)	308 (44)	1092 (52)	1401 (50)	
Benign	217 (31)	349 (17)	566 (20)	
Liver specific feature, n (%)				
Pringle maneuver	101 (14)	618 (29)	719 (25)	<0.001 *
Viral hepatitis	88 (14)	212 (11)	300 (12)	0.13
Concurrent ablation	82 (12)	320 (15)	402 (14)	0.02
Outcome, n (%)				
Serious morbidity or mortality	42 (6)	267 (13)	309 (11)	<0.001 *
Transfusion	67 (9)	398 (19)	465 (17)	<0.001 *
Bile Leak	23 (3)	158 (7)	181 (6)	<0.001 *
Liver Failure	8 (1)	100 (5)	108 (4)	<0.001 *
Postop reoperation or intervention	38 (5)	209 (10)	247 (9)	<0.001 *

Characteristic	MIS (n=706)	Open (n=2113)	All (n=2819)	p Value
30-day readmission	56 (8)	215 (10)	271 (10)	0.09

* indicates statistically significant differences (ie $p < 0.05$)

ASA, American Society of Anesthesiologists; MIS, minimally invasive surgery

Table 2

Outcomes among Patients Undergoing Both Minimally Invasive and Open Hepatectomy among Five Challenging Subgroups including Both Major and Minor Hepatectomies.

Outcome	MIS, n (%)	Open, n (%)	All, n (%)	p Value
Large tumor	157 (23)	536 (77)	693 (100)	-
Major hepatectomy	36 (23)	280 (52)	316 (46)	<0.001 *
Serious morbidity or mortality	27 (17)	190 (36)	217 (31)	<0.001 *
Transfusion	9 (6)	76 (14)	85 (12)	0.003 *
Bile leak	9 (6)	55 (10)	64 (9)	0.08
Postoperative liver failure	1 (1)	30 (6)	31 (5)	0.008 *
Postop reoperation or intervention	11 (7)	62 (12)	73 (11)	0.10
30-day readmission	12 (8)	58 (11)	70 (10)	0.24
Cirrhosis	93 (33)	192 (67)	285 (100)	-
Major hepatectomy	16 (17)	68 (35)	84 (30)	0.002 *
Serious morbidity or mortality	7 (8)	19 (10)	26 (9)	0.66
Transfusion	8 (9)	32 (17)	40 (14)	0.07 *
Bile leak	2 (2)	12 (6)	14 (5)	0.14
Postoperative liver failure	5 (5)	17 (9)	22 (8)	0.30
Postop reoperation or intervention	5 (5)	21 (11)	26 (9)	0.12
30-day readmission	8 (9)	18 (9)	26 (9)	0.77
3 concurrent resections	147 (20)	573 (80)	720 (100)	-
Major hepatectomy	30 (20)	196 (34)	226 (31)	0.001 *
Serious morbidity or mortality	16 (11)	72 (13)	88 (12)	0.58
Transfusion	15 (10)	78 (14)	93 (13)	0.27
Bile leak	9 (6)	40 (7)	49 (7)	0.69
Postoperative liver failure	3 (2)	22 (4)	25 (4)	0.29
Postop reoperation or intervention	12 (8)	48 (8)	60 (8)	0.92
30-day readmission	15 (10)	47 (8)	62 (9)	0.74
Neoadjuvant chemotherapy	171 (21)	708 (81)	879 (100)	-
Major hepatectomy	44 (26)	352 (50)	396 (45)	<0.001 *
Serious morbidity or mortality	9 (5)	110 (16)	119 (14)	<0.001 *
Transfusion	29 (17)	140 (20)	169 (19)	0.40
Bile leak	8 (5)	57 (8)	65 (8)	0.12
Postoperative liver failure	4 (2)	38 (5)	42 (5)	0.10
Postop reoperation or intervention	10 (6)	69 (10)	79 (9)	0.11
30-day readmission	13 (8)	83 (12)	96 (11)	0.29
Morbid obesity	49 (36)	89 (65)	138 (100)	-
Major hepatectomy	8 (16)	19 (21)	27 (20)	0.48

Outcome	MIS, n (%)	Open, n (%)	All, n (%)	p Value
Serious morbidity or mortality	4 (8)	11 (12)	15 (11)	0.84
Transfusion	11 (22)	16 (18)	27 (20)	0.53
Bile leak	0 (0)	4 (5)	4 (3)	0.13
Postoperative liver failure	0 (0)	2 (2)	2 (2)	0.29
Postop reoperation or intervention	5 (10)	8 (9)	13 (9)	0.82
30-day readmission	5 (10)	7 (8)	12 (9)	0.64

* indicates statistically significant differences (ie $p < 0.05$) MIS, minimally invasive surgery

Table 3

Patient Demographics, Treatment Characteristics, and Outcomes among Patients Undergoing Minimally Invasive or Open Major Hepatectomy

Characteristic	MIS (n=132)	Open (n=883)	All (n=1015)	p Value
Demographic				
Age, y, mean (SD)	57 (14)	57 (14)	57 (14)	0.95
Female, n (%)	73 (53)	451 (51)	524 (52)	0.37
Non-white race, n (%)	23 (20)	121 (18)	144 (18)	0.53
BMI, mean (SD)	28.2 (7)	27.6 (6)	27.7 (6)	0.23
Concomitant colon resection, n (%)	3 (2)	27 (3)	30 (3)	0.62
ASA Class, n (%)				0.47
I	2 (2)	43 (5)	45 (4)	
II	33 (25)	231 (26)	264 (26)	
III	87 (66)	551 (62)	638 (63)	
IV	10 (8)	57 (7)	67 (7)	
NSQIP morbidity probability, mean (SD)	0.23 (0.08)	(0.08)	0.24 (0.08)	0.31
Challenging subgroups, n (%)				
Large tumor	36 (27)	280 (32)	316 (31)	0.35
Cirrhosis	16 (12)	68 (8)	84 (8)	0.08
3 concurrent resections	30 (23)	196 (22)	226 (22)	1
Neoadjuvant	44 (33)	352 (40)	396 (39)	0.21
Morbid obesity	8 (6)	19 (2)	27 (2)	0.02 *
Pathology, n (%)				0.06
Primary hepatobiliary	34 (26)	242 (27)	276 (27)	
Secondary (metastatic)	65 (49)	454 (51)	519 (51)	
Benign	31 (23)	127 (14)	158 (16)	
Liver specific features, n (%)				
Pringle maneuver	29 (22)	209 (30)	298 (29)	0.06
Viral hepatitis	16 (14)	87 (11)	103 (11)	0.44
Concurrent ablation	16 (12)	83 (9)	99 (10)	0.41
Outcomes, n (%)				
Serious Morbidity or Mortality	8 (6)	136 (16)	145 (14)	0.003 *
Transfusion	23 (17)	216 (24)	239 (24)	0.08
Bile leak	9 (7)	94 (11)	103 (10)	0.22
Postoperative liver failure	3 (2)	72 (8)	75 (7)	0.03 *
Postop Reoperation or Intervention	12 (9)	111 (13)	123 (12)	0.34
30-day readmission	15 (11)	100 (11)	115 (11)	1

* indicates statistically significant differences (ie $p < 0.05$)

ASA, American Society of Anesthesiologists; MIS, minimally invasive surgery

Table 4

Odds Ratios of Primary and Secondary Outcomes Associated with Minimally Invasive Hepatectomy after Adjustment.

Characteristic	Outcome	OR (95% CI)	p Value
All patients, n=2819 (706 MIS)	Serious morbidity or mortality	0.57 (0.34–0.96)	0.03 *
	Transfusion	0.60 (0.40–0.92)	0.02 *
	Bile leak	0.77 (0.40–1.50)	0.44
	Post-hepatectomy liver failure	0.51 (0.22–1.18)	0.12
	Postop reoperation or intervention	0.52 (0.29–0.93)	0.03 *
	30-day readmission	0.71 (0.41–1.22)	0.21
Major hepatectomy, n=1015 (132 MIS)	Serious morbidity or mortality	0.37 (0.13–1.11)	0.08
	Transfusion	0.53 (0.24–1.18)	0.12
	Bile leak	0.57 (0.19–1.67)	0.30
	Post-hepatectomy liver failure	0.33 (0.07–1.45)	0.14
	Postop reoperation or intervention	0.80 (0.34–1.92)	0.62
	30-day readmission	0.94 (0.37–2.41)	0.90
Large tumor, n=693 (157 MIS)	Serious morbidity or mortality	0.54 (0.26–1.15)	0.11
	Transfusion	0.57 (0.34–0.97)	0.04 *
	Bile leak	0.65 (0.29–1.45)	0.29
	Post-hepatectomy liver failure	0.19 (0.03–1.49)	0.12
	Postop reoperation or intervention	0.60 (0.29–1.24)	0.17
	30-day readmission	0.79 (0.40–1.58)	0.51
Cirrhosis, n=285 (93 MIS)	Serious morbidity or mortality	0.97 (0.36–2.61)	0.96
	Transfusion	0.48 (0.20–1.14)	0.10
	Bile leak	0.59 (0.12–3.00)	0.53
	Post-hepatectomy liver failure	0.66 (0.22–1.99)	0.47
	Postop reoperation or intervention	0.66 (0.22–1.94)	0.45
	30-day readmission	1.25 (0.48–3.24)	0.65
3 concurrent resections n=720 (147 MIS)	Serious morbidity or mortality	1.04 (0.56–1.92)	0.90
	Transfusion	0.79 (0.42–1.47)	0.45
	Bile leak	0.96 (0.43–2.14)	0.92
	Post-hepatectomy liver failure	0.92 (0.26–3.46)	0.90
	Postop reoperation or intervention	1.04 (0.51–2.1)	0.92
	30-day readmission	1.49 (0.79–2.82)	0.22
Neoadjuvant chemotherapy, n=879 (171 MIS)	Serious morbidity or mortality	0.33 (0.15–0.70)	0.004 *
	Transfusion	1.07 (0.66–1.72)	0.78
	Bile leak	0.78 (0.35–1.72)	0.53
	Post-hepatectomy liver failure	0.71 (0.24–2.13)	0.54
	Postop reoperation or intervention	0.72 (0.35–1.47)	0.36

Characteristic	Outcome	OR (95% CI)	p Value
	30-day readmission	0.61 (0.32–1.18)	0.14
Morbid obesity, n=138 (49 MIS)	Serious morbidity or mortality	0.68 (0.17–2.63)	0.57
	Transfusion	1.66 (0.57–4.89)	0.78
	Bile leak	– [†]	–
	Post-hepatectomy liver failure	– [†]	–
	Postop reoperation or intervention	1.09 (0.28–4.24)	0.90
	30-day readmission	1.48 (0.36–6.14)	0.59

* indicates statistically significant differences (ie p<0.05)

[†] Model failed to converge due to low event rates

MIS, minimally invasive surgery; OR, odds ratio