EC CLINICAL AND MEDICAL CASE REPORTS
Research Article

Comparison of Outcomes in Major and Minor Hepatectomies Between Minimally Invasive Versus Open Surgical Techniques: NSQIP Database, 2015

Yana Puckett*, Theophilus Pham, Quang Nguyen, Catherine A Ronaghan and Edwin Onkendi

Department of Surgery, Texas Tech University Health Sciences Center, Lubbock, TX, USA

***Corresponding Author:** Yana Puckett, Department of Surgery, Texas Tech University Health Sciences Center, Lubbock, TX, USA.

Received: November 16, 2020; **Published:** January 27, 2021

Abstract

Introduction: Minimally invasive surgery (MIS) to treat liver disease has increased in prevalence over the past decade; however, little data exists comparing outcomes between MIS and open hepatectomies. We sought to compare preoperative and postoperative outcomes between MIS and open hepatectomies performed for hepatobiliary malignancies.

Methods: The National Surgical Quality Improvement Program (NSQIP) Database was used to analyze all patients who underwent hepatectomies between January 1 and December 31, 2015. Hepatectomies were divided into three groups (open, laparoscopic, robotic). Preoperative variables such as pringle maneuver usage, concurrent ablation, concurrent hepaticojejunostomy, whether neoadjuvant therapy was used were compared between MIS and open hepatectomies. Perioperative outcomes such as conversion from laparoscopic or robotic to open, bile leakage, drain placement, INR, bilirubin (drain and serum), number of days of drain removal after surgery, post-hepatectomy liver failure, need for invasive intervention postoperatively, and pathology results were are compared. Groups were further dichotomized into major (> 3 liver segments resected) versus minor (1 - 2 liver segments resected) liver hepatectomies.

Results: A total of 1,010 patients were analyzed. Hepatocellular carcinoma comprised 58.91% (Drain placement, peak postoperative bilirubin, need for invasive intervention postoperatively, bile leakage, post-hepatectomy liver failure were all significantly lower in MIS hepatectomies compared to open (< 0.0001).

Conclusion: Overall, MIS hepatectomies performed for hepatobiliary malignancies were found to have lower complication rate in both major and minor hepatic resections. When possible, MIS surgery should be attempted in all hepatectomy patients.

Keywords: *Minimally Invasive Surgery (MIS); National Surgical Quality Improvement Program (NSQIP); Open Surgical Techniques*

Introduction

Hepatectomies have many clinical indications. They are currently used for a wide variety of treatments such as liver abscesses, calculi in intrahepatic ducts, malignant tumors, benign tumors, many other liver diseases. However, even though advances in medical technology has decreased the complexity of the surgical procedure, post-operative management of hepatectomies remains a challenge. Post-operative morbidity and mortality remains a burden for hepatectomies and one of the deadliest post-operative complications is post-hepatectomy liver failure (PHLF).

In addition to PHLF, there are many other post-operative hepatectomy complications that should be considered. The complications include pleural effusions, incisional infection, sub-phrenic infections, venous catheter-related infection, pulmonary atelectasis or infection, gastrointestinal tract bleeding, biliary tract hemorrhage, coagulation disorders, and bile leakage [1]. These complications are even more prevalent in elderly patients receiving hepatectomies. In a study that was designed to analyze the risk factors associated with performing hepatectomies in elderly patients, they concluded that given the elderly's lower physiologic reserve, the elderly is at much greater risk for morbidities or mortalities after a hepatectomy. Surgeons looking to perform the procedure on the elderly need to balance the age of the patient, preoperative comorbidities, and the magnitude of the liver resection with the risk factors of performing the procedure [2].

There have been numerous studies regarding pre-operative evaluation of the patient. These studies aimed to reduce the incidence of post-hepatectomy complications by applying parameters of liver function. In a study conducted in 2010 they concluded that the most observed complication among their patients after undergoing hepatectomy is uncontrolled ascites and the second most observed complication was liver failure. After analyzing the data, they realized that preoperative evaluation of prothrombin activity, levels of hyaluronic acid, and LHL5 (hepatic uptake ratio of technetium-99m galactosyl human serum albumin) serves as good parameters for selecting candidates to reduce the incidence of hepatic complications after the surgery [3]. In addition, there are intraoperative complications that can increase the risk of postoperative morbidity and mortality. An example of such intraoperative complications is intraoperative blood loss more than 1200 ml and an operating time of more than 150 minutes [4]. A study performed in 2009 concluded that the benchmarks of mortality and morbidity of hepatic resections was 2.5% and 19.6% respectively. They also concluded that some of the causes of the post-operative complications can be associated with liver function, nutritional status, and the extent of the procedure [5].

However, one of the most studied and feared post-operative complication of hepatectomy is liver failure. A retrospective study done in 2012 found that after a hepatic resection, the most common complication in their group of 133 patients was liver failure [6]. Another study conducted in 2013 determined that PHLF remains an event that has a major impact on the 2-year survival of patients [7]. The International Study Group of Liver Surgery (ISGLS) proposed a standard definition and grading system for post-hepatectomy liver failure that aimed to allow comparison of results between different studies and institutions. Their definition of post-hepatectomy liver failure is the impaired ability of the liver to maintain its synthetic, excretory, and detoxifying functions, which are characterized by an increased international normalized ratio and contaminant hyperbilirubinemia on or after post-operative day five. In addition to the definition, ISGLS also proposed a grading system. Grade A requires no change in the patient's clinical management, grade B deviates from the regular course but does not require invasive therapy and grade C post hepatectomy liver failure requires invasive surgery [8]. Currently, the comprehensive therapy for liver failure includes supplementation of fresh blood transfusions, albumin, fibrinogen, prothrombin complex, and intravenous nutrition [1].

The major risk factors for PHLF are comorbid conditions, pre-existing liver disease, small remnant liver volume, excessive intra-operative blood loss, need for blood transfusion, malnutrition, advanced age and male gender [9-11]. Many studies have been conducted to predict the chances of liver failure by using preoperative techniques as well as predict the chances of liver failure post operatively. One technique used to evaluate the risk of PHLF is by the utilization of gadoxetic enhanced magnetic resonance (MR) to measure the relative liver enhancement (RLE) preoperatively. Patients that suffered PHLF have significantly lower RLE than those without liver failure. Therefore, the use of this imaging technique can help with the assessment of the risk of liver failure after a major liver resection [12,13]. A post-operative technique that has been utilized to predict the chances of liver failure in patients after undergoing hepatic resection is by measuring indocyanine green (ICG) elimination by pulse spectrophotometry. Patients who suffered PHLF have a significantly lower ICG elimination rate on postoperative day one than patients without liver failure [14,15].

PHLF is a feared complication following liver resection and one of the major causes of postoperative morbidity and mortality.

Aim of the Study

This study aims to add to the current research on PHLF by analyzing the quantitative risk association of perioperative factors with PHLF.

Methods

The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) Database, which was hepatectomy procedure targeted database, was used to analyze all patients who underwent hepatectomies between January 1 and December 31, 2015. This NSQIP database includes data prospectively collected from over 85 participating hospitals on variables such as demographics, comorbidities, indication, procedure details and morbidity and mortality.

Hepatectomies were divided into three groups (open, laparoscopic, robotic). Preoperative variables such as pringle maneuver use, concurrent ablation, concurrent hepaticojejunostomy, whether neoadjuvant therapy was used were compared between MIS and open hepatectomies. Perioperative outcomes such as conversion from laparoscopic or robotic to open, bile leakage, drain placement, INR, bilirubin (drain and serum), number of days of drain removal after surgery, post-hepatectomy liver failure, need for invasive intervention postoperatively, and pathology results were are compared. Groups were further dichotomized into major (> 3 liver segments resected) versus minor (1 - 2 liver segments resected) liver hepatectomies. Post-hepatectomy liver failure was graded according to International Study Group of Liver Surgery (ISGLS).

Statistical analysis was performed comparing three groups utilizing ANOVA and Chi-Square test statistics. A multiple logistic regression model was performed to identify predictors of post-hepatectomy liver failure.

Results

A total of 3,844 patients who underwent hepatectomy were analyzed. Major hepatectomies comprised 10.2% (391) of operations. Pringle maneuver was used in 24.7% (948). Drains were placed in 43.1% (1,658) of the operations. Surgery was converted from laparoscopic or robotic to open in 3.6% (138) (Table 1).

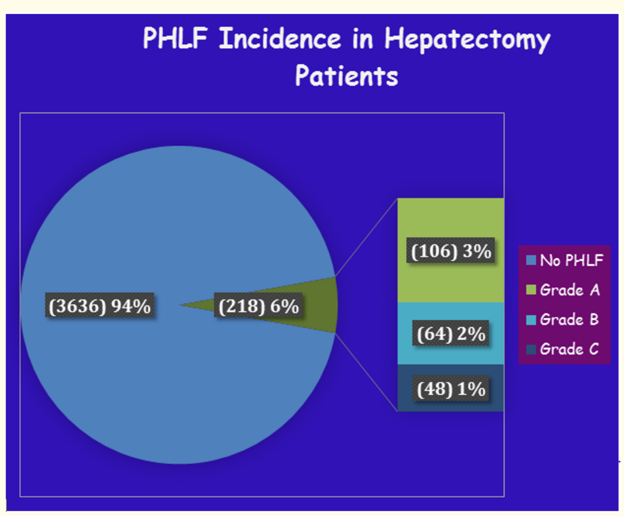
	Open (n = 2,905)	**Laparoscopic (n = 872)**	**Robotic (n = 67)**	**P-Value**
	% (n)	**% (n)**	**% (n)**	
Pringle Maneuver Used	29.36% (853)	10.32% (90)	7.46% (5)	< 0.0001
Concurrent Ablation	13.70% (398)	9.40% (82)	8.86% (6)	0.002
Concurrent Hepaticojejunostomy	8.06% (234)	1.95% (17)	1.49% (1)	< 0.0001
Neoadjuvant Therapy	33.15% (963)	24.89% (217)	20.90% (14)	< 0.0001
Viral Hepatitis				N/A
Hepatitis B	3.55% (103)	3.44% (30)	4.48% (3)	
Hepatitis B and C	0.38% (11)	0.92% (8)	0	
Hepatitis C	6.06% (176)	7.80% (68)	8.96 (6)	
None	80.21% (2330)	80.50% (702)	82.09% (55)	
Other	0.72% (21)	0.23% (2)	0	
Unknown	9.09% (264)	7.11% (62)	4.48% (3)	

Liver Texture				N/A
Cirrhotic	8.67% (252)	11.35% (99)	7.46% (5)	
Congested	2.07% (60)	1.15% (10)	0	
Fatty	12.60% (366)	13.65% (119)	16.42% (11)	
Normal	29.02% (843)	27.87% (243)	25.37% (17)	
Not Documented	47.64% (1384)	45.99% (401)	50.75% (34)	
Number of Concurrent Partial Resections				< 0.0001
> 3 (Major) (n = 391)	11.57% (336)	5.85% (51)	4.48% (3)	
< 3 (Minor) (n = 3,373)	86.02% (2499)	92.09% (803)	95.52% (64)	
Drain Placement	47.23% (1372)	31.31% (273)	19.40% (13)	< 0.0001
Conversion from Laparoscopic or Robotic to Open	N/A	15.48% (135)	4.48% (3)	0.001

Table 1: *Patient demographics (n = 3,844).*

Of the 3,853 patients, 218 (5.7%) patients had PHLF. Of the 218 patients with PHLF, 106 (48.6%) had ISGLS grade A PHLF, 64 (29.4%) grade B, and 48 (22%) grade C. Of all the factors analyzed, open hepatectomy, post-operative bile leak, liver cirrhosis and parenchymal congestion had the highest risk for developing PHLF. Open hepatectomy was associated with a 13-fold risk of developing PHLF compared to minimally invasive hepatectomy (p = 0.018), postoperative bile leak was associated with a 5-fold risk for developing PHLF (p < 0.0001), liver cirrhosis and parenchymal congestion was associated with a 2-fold risk for develop PHLF (p = 0.004 and 0.02). Increased INR and bilirubin was postoperative day five were associated with a slightly increased risk in PHLF (p < 0.0001 and p < 0.001).

The factors analyzed that had no association with PHLF were preoperative stenting, hepatitis B/C status, intraoperative ablation, major versus minor hepatectomy, duration of drain, and drain bilirubin level. In addition, the Pringle maneuver and hepatobiliary reconstruction were protective against PHLF.



	Open (n = 2,905)	Laparoscopic (n = 872)	Robotic (n = 67)	P-Value
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	
Postoperative Drain Billirubin on or after POD #3 (mg/dl)	28.7 (91.19)	50.31 (152.01)	2.07 (0.95)	0.416
Number of Days of Drain Removal after Surgery	7.48 (5.83)	5.20 (4.47)	6.00 (5.99)	< 0.0001
Peak Postoperative INR (on or after POD #5)	1.48 (1.57)	1.33 (0.96)	1.66 (0.31)	0.274
Peak Postoperative Billirubin (on or after POD #5)	6.95 (31.97)	3.52 (14.56)	2.10 (3.31)	0.062
	% (n)	**% (n)**	**% (n)**	
Need for Invasive Intervention Postoperatively Excluding Reoperation	11.19% (325)	4.36% (38)	5.97% (4)	< 0.0001
Bile Leakage				< 0.0001
Yes-clinical diagnosis, drain continued on or after POD3	1.10% (32)	0.23% (2)	0	
Yes-clinical diagnosis, percutaneous drainage performed	2.00% (58)	1.61% (14)	1.49% (1)	
Yes-clinical diagnosis, reoperation performed	0.65% (19)	0.11% (1)	0	
Yes-persistent drainage, drain continued on or after POD3	3.03% (88)	1.95% (17)	0	
Yes-persistent drainage, percutaneous drainage performed	1.41% (41)	0	0	
Yes-persistent drainage, reoperation performed	0.14% (4)	0.11% (1)	0	
Post Hepatectomy Liver Failure	6.85% (199)	1.95% (17)	2.99% (2)	< 0.0001
Grade A	3.24% (94)	1.38% (12)	0	
Grade B	2.03% (59)	0.46% (4)	1.49% (1)	
Grade C	1.58% (46)	0.11% (1)	1.49% (1)	
Pathology Results				
Benign	17.21% (500)	34.86% (304)	25.37% (17)	<0.0001
N/A	3.92% (114)	1.49% (13)	1.49% (1)	
Primary hepatobiliary cancer	28.95% (841)	23.62% (206)	19.40% (13)	
Secondary (metastatic) tumor	49.23% (1430)	39.33% (343)	52.24% (35)	
Unknown	0.69% (20)	0.69% (6)	1.49% (1)	
If Primary Hepatobilliary Cancer, Indicate Histologic Subtype				< 0.0001
Gallbladder cancer	3.06% (89)	0.57% (5)	1.49% (1)	
Hepatocellular carcinoma	14.77% (429)	18% (157)	13.43% (9)	
Hilar cholangiocarcinoma	2.07% (60)	0.34% (3)	0	
Intrahepatic cholangiocarcinoma	7.50% (218)	4.13% (36)	4.48% (3)	

T (tumor) Stage				< 0.0001
T0	0.14% (4)	0.23% (2)	0	
T1	8.78% (255)	11.81% (103)	4.48% (3)	
T2	10.98% (319)	6.77% (59)	13.43% (9)	
T3	5.06% (147)	2.18% (19)	0	
T4	1.24% (36)	0.34% (3)	0	
Tis	0.03% (1)	0	0	
Tx	0.21% (6)	0.11% (1)	0	
Unknown	2.00% (58)	2.18% (19)	0	
N (node) Stage				<0.0001
N0	9.60% (279)	3.90% (34)	5.97% (4)	
N1	3.82% (111)	1.03% (9)	0	
N2	0.10% (3)	0	0	
Nx	12.25% (356)	15.60% (136)	11.94% (8)	
Unknown	2.44% (71)	2.98% (26)	0	
M (metastases) Stage				0.03
M0/Mx	18% (523)	15.71% (137)	17.91% (12)	
M1	0.62% (18)	0.34% (3)	0	
Unknown	5.03% (146)	4.01% (35)	0	

Table 2: *Postoperative outcomes of all hepatectomy patients (n = 3,844).*

	ODDS	95 % C.I.	P-Value
Biliary Stents Placed Preoperatively	2.799	0.342 -22.900	0.337
Liver Texture			
Cirrhotic	1.988	1.242-3.181	0.004
Congested	2.339	1.131-4.836	0.022
Fatty	1.25	0.812-1.923	0.311
Normal	0.927	0.647-1.328	0.679
Viral Hepatitis			
Hepatitis B	0.637	0.351-1.157	0.139
Hepatitis B and C	0.484	0.321-0.729	0.001
Hepatitis C	1.26	0.340-4.670	0.729
Hepatic Reconstruction	0.292	0.179-0.477	<0.0001
Pringle Maneuver	0.647	0.480-0.871	0.004
Concurrent Hepatic Ablation	1.209	0.758-1.930	0.425
Neoadjuvant Therapy	0.665	0.497-0.890	0.006
Major Hepatectomy	1.301	0.815-2.077	0.27
Bile Leak	5.084	3.666-7.049	<0.0001
Postoperative Drain Billirubin on or after POD #3 (mg/dl)	1.001	0.999-1.004	0.288

Number of Days of Drain Removal after Surgery	1	0.997-1.003	0.832
Peak Postoperative INR (on or after POD #5)	1.019	1.013-1.026	<0.0001
Peak Postoperative Billirubin (on or after POD #5)	1.021	1.015-1.027	<0.001
Open Hepatectomy	13.6	1.568-117.945	0.018
Laparoscopic Hepatectomy	2.5	0.608-10.277	0.204
Robotic Hepatectomy	0.676	0.153-2.987	0.606

***Table 3**: Predictors of post-hepatectomy liver failure.*

Discussion

Post-hepatic Liver Failure is a deadly postoperative complication. By analyzing the quantitative risk associations of perioperative factors, our institution hopes to add to the current research on PHLF in order to reduce the prevalence and mortality rate of this complication. 218 (5.7%) of patients, other studies have shown a prevalence as high as 8% among patients undergoing major hepatectomy [16]. The lower rate seen in the NSQIP data are due to the fact that there is a larger sample size of patients than previous studies. The study showing an 8% prevalence was of a mere 85 patients.

Procedure modality was the most prognostic factor in determining incidence rate of PHLF. Open hepatectomy was associated with a 13-fold risk of developing PHLF compared to minimally invasive hepatectomy ($p = 0.018$). The high increase risk of PHLF with open hepatectomy could be associated with the severity of the underlying liver pathology. More serious or urgent conditions tend to require open hepatectomy rather than minimally invasive hepatectomy, which would help explain the higher rate of PHLF in these patients. Minimally invasive hepatectomy is also associated with a better prognosis than open hepatectomy in general and is associated with a lower postoperative morbidity and better short term outcomes [17]. The choice of the most appropriate operative technique will have the greatest effect on the incidence of PHLF.

Postoperative bile leak is a common preventable complication of hepatectomies. It is associated with a 5-fold risk for developing PHLF ($p < 0.0001$). A bile leakage test has been shown to reduce the rate of postoperative bile leak and did not show any increase in the rate of any other complication. If a bile leak was found using a bile leakage test it could be sealed using biological glue thus reducing the risk of PHLF.

Liver cirrhosis and parenchymal congestion was associated with a 2-fold risk for develop PHLF ($p = 0.004$ and 0.02). Both of these risk factors are serious conditions suggestive of liver failure. Compromised liver function predisposes the patient to PHLF. Increased INR and bilirubin at postoperative day five were associated with a slightly increased risk in PHLF ($p < 0.0001$ and $p < 0.001$). Increased bilirubin can be diagnostic for impaired conjugative function while the increased INR shows impairment in the liver's ability to produce coagulation factors.

The Pringle maneuver and hepatobiliary reconstruction were shown to be protective against PHLF. Controlling blood flow with the Pringle maneuver helps prevent excess blood loss from the liver thus preventing the likelihood of PHLF. Hepatobiliary reconstruction can restore biliary flow thus preventing any biliary leak which would also decrease the incidence of PHLF. Maintaining the integrity of the tissue is important in reducing the risk factor for complications.

It is possible to minimize the risk of PHLF by monitoring patient's for perioperative risk factors that are associated with an increased risk for PHLF while also ensuring that necessary procedures such as the Pringle maneuver, bile leakage test, and hepatobiliary reconstruction are used when necessary to actively decrease the risk. Further studies are needed to focus on protective factors against PHLF as well as preoperative liver condition and its association with PHLF.

Conclusion

Overall, MIS hepatectomies performed for hepatobiliary malignancies were found to have lower complication rate in both major and minor hepatic resections. When possible, MIS surgery should be attempted in all hepatectomy patients. Focus in training of future surgeons should be given to minimally invasive techniques.

Bibliography

1. Jin S., *et al.* "Management of post-hepatectomy complications". *World Journal of Gastroenterology* 19.44 (2013): 7983-7991.
2. Tzeng CW., *et al.* "Predictors of morbidity and mortality after hepatectomy in elderly patients: analysis of 7621 NSQIP patients". *HPB* 16.5 (2014): 459-468.
3. Nanashima A., *et al.* "Reducing the incidence of post-hepatectomy hepatic complications by preoperatively applying parameters predictive of liver function". *Journal of Hepato-Biliary-Pancreatic Sciences* 17.6 (2010): 871-878.
4. Tomuș C., *et al.* "[Liver resection for benign hepatic lesion: mortality, morbidity and risk factors for postoperative complications]". *Chirurgia* 104.3 (2009): 275-280.
5. Aloia TA., *et al.* "Predicting poor outcome following hepatectomy: analysis of 2313 hepatectomies in the NSQIP database". *HPB* 11.6 (2009): 510-515.
6. Dan RG., *et al.* "Postoperative morbidity and mortality after liver resection. Retrospective study on 133 patients". *Chirurgia* 107.6 (2012): 737-741.
7. Vibert E., *et al.* "Actual incidence and long-term consequences of posthepatectomy liver failure after hepatectomy for colorectal liver metastases". *Surgery* 155.1 (2014): 94-105.
8. Rahbari NN., *et al.* "Posthepatectomy liver failure: a definition and grading by the International Study Group of Liver Surgery (ISGLS)". *Surgery* 149.5 (2011): 713-724.
9. Van den Broek MA., *et al.* "Liver failure after partial hepatic resection: definition, pathophysiology, risk factors and treatment". *Liver International* 28.6 (2008): 767-780.
10. Ribeiro HS., *et al.* "Extended preoperative chemotherapy, extent of liver resection and blood transfusion are predictive factors of liver failure following resection of colorectal liver metastasis". *European Journal of Surgical Oncology* 39.4 (2013): 380-385.
11. Hammond JS., *et al.* "Prediction, prevention and management of postresection liver failure". *British Journal of Surgery* 98.9 (2011): 1188-1200.
12. Wibmer A., *et al.* "Liver failure after major liver resection: risk assessment by using preoperative Gadoxetic acid-enhanced 3-T MR imaging". *Radiology* 269.3 (2013): 777-786.
13. Jin YJ., *et al.* "Prediction of postoperative liver failure using gadoxetic acid-enhanced magnetic resonance imaging in patients with hepatocellular carcinoma". *European Journal of Gastroenterology and Hepatology* 31.7 (2016): 1349-1356.
14. De Liguori Carino N., *et al.* "Perioperative use of the LiMON method of indocyanine green elimination measurement for the prediction and early detection of post-hepatectomy liver failure". *European Journal of Surgical Oncology* 35.9 (2009): 957-962.

15. Sugimoto H., *et al.* "Early detection of liver failure after hepatectomy by indocyanine green elimination rate measured by pulse dye-densitometry". *Japanese Society of Hepato-Biliary-Pancreatic Surgery* 13.6 (2006): 543-548.

16. Vibert E., *et al.* "Actual incidence and long-term consequences of posthepatectomy liver failure after hepatectomy for colorectal liver metastases". *Surgery* 155 (2014): 94-105.

17. Bagante Fabio*., et al.* "Minimally invasive vs. open hepatectomy: a comparative analysis of the national surgical quality improvement program database". *Journal of Gastrointestinal Surgery* 20.9 (2016): 1608-1617.

18. Wang, Hai-Qing., *et al*. "Bile leakage test in liver resection: a systematic review and meta-analysis". *World Journal of Gastroenterology: WJG* 19.45 (2013): 8420.

Volume 4 Issue 2 February 2021