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Defining the risk of liver failure after minor hepatectomy: a NSQIP analysis of 7029 patients

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Abstract

Background—Post-hepatectomy liver failure (PHLF) remains a significant complication after hepatic resection. This study aims to determine the rate of PHLF in patients undergoing resection of 3 or fewer segments and analyze the association of PHLF with perioperative characteristics and postoperative complications.

Methods—The ACS hepatectomy-targeted NSQIP database was queried for patients undergoing left hemi-hepatectomy or partial resection from 2014-2018. The primary outcome was PHLF, defined by ISGLS. Multivariable logistic regression models assessed the association between PHLF, preoperative and operative variables and postoperative complications.

Results—Among 7029 patients, 187 (2.7%) experienced PHLF, with clinically significant (grade B/C) PHLF in 1.4%. PHLF was associated with older age, male gender, higher ASA classification, ascites, and elevated SGOT. Preoperative ascites (OR 4.94, 95%CI:2.45-9.94, p<0.001) had the strongest association with PHLF. There was no association between PHLF and concurrent colorectal resection, neoadjuvant therapy, or concurrent ablation. Surgical site infection (OR 3.64, 95%CI:2.40-5.54, p<0.001), sepsis (OR 3.78, 95%CI:2.16-6.61, p<0.001), postoperative invasive procedure (OR 6.92, 95%CI:4.91-9.76, p<0.001), and bile leak (OR 4.65, 95%CI:3.04-7.12, p<0.001) were associated with PHLF.

Discussion—PHLF after minor hepatectomy is rare and associated with signs of preoperative liver dysfunction. The association with infectious complications suggests a multifactorial etiology and provides targets for quality improvement.

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Introduction

Partial hepatectomy (PH) is a potentially curative treatment option for primary and secondary hepatic malignancies. While perioperative morbidity and mortality associated with PH have significantly decreased due to improved patient selection and perioperative management[1-4], post-hepatectomy liver failure (PHLF) remains a significant cause of postoperative mortality after PH.[5,6] Reported incidence of PHLF is widely variable, ranging from 0.7 to 32%, likely attributable to patient selection, extent of hepatic resection, baseline liver function, and perioperative management.[7-9] Given the gravity of this complication, multiple risk-calculators and models have been developed to predict PHLF by incorporating clinical predictors, laboratory values, and imaging features.[5,7,10-14]

Continued efforts to adopt parenchymal-sparing techniques in liver surgery have reduced morbidity and altered the composition of postoperative complications. A recent multi-institutional series evaluating non-cirrhotic patients undergoing open PH observed lower 90-day mortality and severe morbidity for minor hepatectomy (MiH) compared to right hepatectomy (RH). In this series, PHLF was observed in 2.4% of MiH and 11.6% of RH.[15] Previously published data by Kingham et al. from Memorial Sloan Kettering Cancer Center further illustrated a decreased rate of PHLF over time, likely in part due to increased use of parenchymal-sparing resections, with a reported rate of 2%.[1] Notably, in this study, only 2 of the 31 mortalities after MiH were due to PHLF, a total of 0.1% of all MiH. Based on this single institution experience, the current study aims to test the hypothesis that national rates of PHLF after MiH are extremely low. Such a finding would support further adoption of parenchymal-sparing techniques, whenever possible.

The introduction of a hepatectomy-targeted dataset in 2014 from the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) offers the unique opportunity to both quantify the national rates of PHLF after MiH and to determine associated clinical variables with this complication. While the number of patients and hospitals included in the ACS-NSQIP vary per year, the hepatectomy-targeted dataset includes up to 133 hospitals per year from which data on between 3,854 and 4,773 patients are submitted annually.

Understanding the factors associated with PHLF in the perioperative period can help guide therapeutic decision-making and prognosticate for patients requiring PH. With increased adoption of parenchymal-sparing techniques, studies that focus specifically on outcomes after MiH are indicated, as these may differ from more extensive resections. The aims of this project were to 1) determine the rate of PHLF in patients undergoing MiH, defined as resection of 3 or fewer segments; 2) understand the high-risk patient and perioperative characteristics associated with PHLF in patients undergoing MiH and 3) characterize the association between PHLF and other postoperative complications that may serve as other targets for quality improvement.

Methods

National Surgical Quality Improvement Program

ACS NSQIP is a national prospective clinical data registry, which includes over 250 variables for a variety of surgical procedures. These variables include patient demographics, comorbidities, operative variables, and postoperative complications. Full details of the NSQIP database have been previously described elsewhere.[16] Since 2014, NSQIP has maintained a targeted database for patients who undergo hepatectomy. This dataset includes procedure-specific variables such as neoadjuvant therapy; viral hepatitis; liver texture; intraoperative Pringle maneuver and biliary reconstruction, as well as hepatectomy-specific complication data including PHLF and bile leakage. Data collected by NSQIP are de-identified and Health Insurance Portability and Accountability Act (HIPAA)-compliant. Institutional Review Board approval at Memorial Sloan Kettering Cancer Center was obtained for this study.

Patient and Variable Selection

The hepatectomy-targeted participant use file was queried for Current Procedural Terminology (CPT) codes 47125 (left hemi-hepatectomy) and 47120 (partial hepatectomy) to identify all patients undergoing resection of three or fewer liver segments from 2014 through 2018. Patients with concurrent partial resections were excluded to ensure that the study cohort was limited to those with three or fewer resected segments. Selected variables included demographic factors, such as age, race/ethnicity, gender, and body mass index (BMI); comorbidities including diabetes mellitus (DM), hepatitis, smoking, preoperative ascites, preoperative bleeding disorders and American Society of Anesthesiologists (ASA) physical status classification; preoperative laboratory variables including hematocrit, international normalized ratio (INR) and liver function tests; operative variables including surgical approach, wound class, liver texture, drain placement, Pringle maneuver and biliary reconstruction; and postoperative complications. Bleeding disorders are defined by NSQIP as any chronic or active condition that places a patient at an increased risk for excessive bleeding; these include vitamin K deficiency, hemophilia, thrombocytopenia, or chronic anticoagulation therapy that has not been discontinued prior to surgery and exclude chronic aspirin or NSAID use, remote history of heparin-induced thrombocytopenia, and use of prophylactic anticoagulants. Liver texture, defined as cirrhotic, fibrotic, congested, fatty, or normal, is also captured in the hepatectomy-targeted dataset. Cirrhotic, fibrotic, congested, and fatty liver textures were defined as abnormal for this study. Thirty-day mortality was also captured.

Outcomes

The primary outcome of the study was PHLF after MiH, defined by the International Study Group of Liver Surgery (ISGLS) as elevated INR and hyperbilirubinemia on or after postoperative day 5 (POD 5) or hyperbilirubinemia and the need for fresh frozen plasma (FFP) on or after POD 5. Patients with PHLF are further categorized in the NSQIP dataset based on ISGLS grade, which characterizes the severity of PHLF based on the required intervention. In this classification system, Grade A PHLF represents deterioration of liver function in the postoperative period requiring no change in clinical management;

Grade B PHLF is defined as a deterioration requiring deviation from regular postoperative care without the need for invasive intervention; and Grade C PHLF requires an invasive procedure. While clinically relevant PHLF may be limited to grade B and C in practice, all PHLF patients were included in this study to appropriately characterize the severity of this outcome after MiH.

Statistical Analysis

The association between PHLF and patient preoperative and operative variables was tested using Fischer's exact test for binary variables, Chi-square testing for non-binary categorical variables, t-tests for continuous parametric variables, and Wilcoxon rank-sum for continuous non-parametric variables. To estimate adjusted associations, a multivariable logistic regression model was constructed including all covariates with $p < 0.1$ on univariable analysis. A backward stepwise selection method was used to incrementally remove noncontributory predictors. Next, the relationship between PHLF and other postoperative complications including surgical site infection, sepsis, postoperative invasive intervention, unplanned reoperation, bile leak, pneumonia, failure to wean from ventilator > 48 hours, pulmonary embolism and myocardial infarction was evaluated using Fisher's exact test. Individual multivariable logistic regression models were estimated to evaluate the association between PHLF and each complication, including all covariates from the prior model. Estimation of variance in models was adjusted to account for clustering at the hospital level.[17] Tests of significance were two-sided with a threshold of $p < 0.05$. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Results

A total of 7029 patients were identified between 2014-2018. Of these, 187 (2.7%) patients experienced PHLF. Eighty-seven patients experienced Grade A PHLF (46.5% of PHLF, 1.2% of overall sample); 49 patients Grade B PHLF (26.2% of PHLF, 0.7% of overall sample); and 51 patients Grade C PHLF (27.3% of PHLF, 0.7% of overall sample). The most common indication for resection was secondary hepatic malignancy (2864/7029, 40.8%) and most patients underwent open resection (4928/7029, 70.1%). Receipt of neoadjuvant chemotherapy or concurrent ablation was heterogenous in this sample, with rates of 19.3% (1357/7029) and 9.5% (669/7029), respectively. Concurrent colorectal resection was performed in 5.9% of patients (415/7029) and hepatic arterial infusion pumps (HAIP) were concurrently placed in 62 patients (0.9%). Clinicopathologic characteristics associated with PHLF are listed in Table 1 and 2.

Multivariable analysis of variables predicting PHLF are shown in Table 3. The multivariable model was subsequently performed evaluating only patients with grade B or C PHLF. While preoperative ascites, elevated SGOT, primary hepatobiliary pathology, and abnormal liver texture remained associated with PHLF in this subgroup, the associations with patient age, gender, and ASA classification were no longer statistically significant ($p = 0.057$-0.739). (Table 4)

As patients who developed PHLF appeared to have evidence of preoperative liver dysfunction, a subgroup analysis was performed evaluating only patients without evidence

of liver dysfunction, by excluding patients with preoperative ascites, abnormal preoperative bilirubin, SGOT, or alkaline phosphatase, viral hepatitis, abnormal liver texture, or elevated INR. A total of 3353 patients met these criteria, of which 41 (1.2%) developed PHLF. The distribution of PHLF by grade in this cohort was as follows: 22 (0.7%) grade A; 12 (0.4%) grade B; and 7 (0.2%) grade C. In these patients, older age (mean 67.2 years, OR 1.59, 95%CI: 1.29-1.97, $p < 0.001$), longer operative time (mean 4.3 hours, OR 1.24, 95%CI: 1.07-1.44, $p = 0.005$), and open approach (1.7%, OR 6.22, 95%CI: 1.57-24.63, $p = 0.010$) were independently associated with PHLF, while female gender was protective (0.6%, OR 0.43, 95%CI: 0.23-0.81, $p = 0.009$).

An additional subgroup analysis assessed outcomes for patients with primary hepatobiliary malignancy including hepatocellular carcinoma (HCC) and cholangiocarcinoma (CC), as these patients are presumably at higher risk for PHLF, given potential associated underlying liver disease. We identified 1894 patients with HCC or CC, with a PHLF rate of 5.9% ($n = 111$). Older age (mean 67.1, OR 1.28, 95%CI: 1.05-1.55, $p = 0.014$), preoperative ascites (36.8%, OR 6.53, 95%CI: 2.55-16.71, $p < 0.001$) or bleeding disorders (13.7%, OR 2.46, 95%CI: 1.18-5.14, $p = 0.017$), SGOT > 40 (9.7%, OR 2.10, 95%CI: 1.30-3.38, $p = 0.003$), longer operative time (mean 4.3 hours, OR 1.20, 95%CI: 1.11-1.30, $p < 0.001$), open approach (7.0%, OR 2.31, 95%CI: 1.34-4.00, $p = 0.003$), and abnormal liver texture (7.6%, OR 1.85, 95%CI: 1.21-2.82, $p = 0.005$) were all independently associated with PHLF in patients with primary hepatobiliary malignancy.

Postoperative complications including surgical site infection, sepsis, postoperative invasive procedures, bile leak, and unplanned reoperation were associated with PHLF on univariable analysis. Notably, 16.6% of patients with PHLF experienced death within 30 days after surgery compared to 0.4% in the cohort without PHLF ($p < 0.001$). A multivariable model confirmed an independent association between surgical site infection, sepsis, unplanned return to the operating room, postoperative invasive procedures, bile leak, pneumonia, failure to wean from the ventilator > 48 hours, myocardial infarction and PHLF. Notably, pulmonary embolism was not associated with PHLF. (Table 5) Similarly, for the subgroup of patients without evidence of liver dysfunction and for the subgroup of patients with primary hepatobiliary malignancy, PHLF remained independently associated with all complications, except pulmonary embolism.

Discussion

PHLF is a significant, potentially fatal complication after PH. With increased utilization of parenchymal-sparing surgical techniques and better perioperative management, rates of PHLF have decreased.[18-20] While prior studies have focused on developing diagnostic criteria and predictive models for PHLF, few have attempted to characterize patients with PHLF after MiH and understand the relationship between PHLF and other complications. In this large, national database, a very low rate of PHLF was observed in patients who underwent resection of 3 or fewer segments, with clinically significant PHLF in only 1.4% of patients. High risk patients included those with preoperative ascites, primary hepatobiliary disease, bleeding disorders, elevated liver function tests, and abnormal liver texture. Notably, other complications, including infection, bile leak, and sepsis,

were associated with PHLF, signifying a potential multifactorial etiology of PHLF in these patients. These associated complications may serve as additional targets for quality improvement initiatives.

Rates of PHLF after PH are heterogenous in the literature.[5,8] MiH has traditionally been associated with lower rates of PHLF compared to major resection.[21] A recently published study by Vigano et al. evaluating MiH reported PHLF rates ranging from 1.4% in limited resections to 9.7% for right posterior sectionectomy.[15] In our series, the rate of PHLF after MiH was 2.7%. Notably, only 1.4% of these patients had clinically significant (grade B or C) liver dysfunction, suggesting that this complication is rare and likely mild for most affected patients. As NSQIP does not report prior PH, this rate of PHLF may overestimate PHLF for patients with no prior surgical history.

Predictive factors associated with PHLF have been previously described.[22-27] Patient-related risk factors include diabetes, obesity, malnutrition, renal insufficiency, lung disease, and advanced age. Similarly, patients with PHLF in our series were more likely to be older and have higher ASA classification, a proxy for patient fitness. Interestingly, other co-morbidities including diabetes, obesity, renal insufficiency and pulmonary disease were not found to be associated with PHLF for patients undergoing MiH. In this study, the primary risk of PHLF appeared to be related to preoperative evidence of liver dysfunction, given the association with preoperative ascites, abnormal liver texture and elevated liver function tests. These associations remained present when evaluating only patients with grade B and C PHLF, whereas other patient factors such as age and ASA classification were no longer statistically significant in this select cohort. When excluding patients with evidence of liver disease, rates of clinically significant PHLF were less than 1%. Taken together, these results, which are specific to MiH, are clinically informative and demonstrate that patients undergoing MiH may require a different risk stratification strategy than those undergoing major hepatectomy.

In addition to those with evidence of preoperative liver dysfunction, patients with primary hepatobiliary malignancies were also more likely to develop PHLF, with a rate of 5.9% in this subgroup. Risk factors for PHLF were similar, including older age, ascites, bleeding disorders, open surgery, longer operative time, and abnormal liver texture. Ascites remained the most significant risk factor for PHLF, suggesting that even MiH in patients with HCC or CC *and* ascites may carry substantial risk. Given the high risk of cirrhosis and potential chronic liver dysfunction in these patients, careful, upfront evaluation of liver function and portal hypertension is essential for appropriate patient selection prior to MiH for these indications.

Operative factors previously associated with PHLF include blood loss > 1200 milliliters, transfusion requirements, operative time, major hepatectomy, and postoperative complications.[23,26] In this series, operative approach and total operative time were associated with PHLF, whereas use of Pringle maneuver and drain placement were not. One anecdotal hypothesis for this finding is that patients with grossly diseased livers are less likely to be offered minimally invasive surgery, given the technical difficulty associated with this approach in these patients. As such, while not directly related to underlying

liver disease, operative approach may serve as a surrogate for liver dysfunction. Longer operative times may similarly be a proxy for worse underlying liver disease or increased case complexity.

In this study, preoperative chemotherapy and ablation were not associated with PHLF. For patients undergoing PH for malignancy, prior associations between chemotherapy use, steatohepatitis, and mortality have been demonstrated.[28,29] A recent ACS-NSQIP based risk calculator assessing all PH patients similarly found an association between PHLF and chemotherapy.[10] This discordant finding suggests that the effects of hepatic toxicity secondary to chemotherapy may not be as clinically significant with resection of less parenchyma. Such data may advocate for greater use of cytotoxic chemotherapy, HAIP, or concurrent use of ablation, as techniques to decrease tumor burden to minimize parenchymal resection. Further studies to confirm this association are indicated.

Several other postoperative complications, including surgical site infection, sepsis, pneumonia, myocardial infarction and bile leak were associated with PHLF in this study. Although the direction of causality is unknown, patients with cardiopulmonary or infectious complications postoperatively may be more likely to subsequently develop PHLF. An association between sepsis and PHLF has been previously described in a series of 19 patients with intraperitoneal sepsis after hepatectomy, where reported PHLF-related death occurred in 13 patients.[30] Endotoxin production has also been associated with PHLF, through a mechanism of impaired cytokine release and reduced availability of growth factors necessary for hepatic regeneration.[31,32] Based on these findings, it is possible that postoperative complications in patients with MiH contribute to a multifactorial process that drives the uncommon scenario of PHLF. Notably, this association is present in patients with and without evidence of preoperative liver dysfunction and regardless of indication for resection. While further study must be performed to establish this causal association in MiH patients, complications such as postoperative infection may serve as a reasonable target for hepatectomy-specific quality improvement initiatives.

This study has several limitations. First, data from ACS-NSQIP is retrospective, may not be fully generalizable, and does not allow exploration of specific process measures that may be targets for quality improvement. Future studies evaluating rates of PHLF based on hospital volume and practice patterns may help identify specific processes and areas for improvement. Second, thorough evaluation of preoperative risk factors such as duration and type of neoadjuvant therapy, etiology of preoperative ascites or indication for biliary stent placement is limited in the NSQIP dataset. Clear delineation of the clinical decision making to perform resection versus ablation is also not readily available. Third, as NSQIP diagnoses are categorized by CPT code, more granular evaluation of specific minor anatomic resections is not possible. Previous published data by Vigano et al. suggest that minor resections have wide variation in outcomes based on anatomy and complexity of resection.[15] Those findings cannot be reproduced by these data. Fourth, there is no variable in NSQIP to capture prior liver resection or liver volume prior to PH, limiting any conclusions about volumetrics and PHLF. The dataset also does not provide information regarding different modalities used clinically to risk-stratify patients with primary hepatic malignancy. Fifth, PHLF is characterized by NSQIP using the ISGLS classification; while

this classification scheme is widely accepted for PHLF, validation using other classification methods is not possible. Finally, morbidity and mortality data in NSQIP is limited to 30 days postoperatively.

In this large national hepatectomy-specific dataset, PHLF was found to be rare and mild in presentation after MiH. High-risk patients, such as those with evidence of preoperative liver dysfunction, remain at elevated risk of PHLF, despite utilization of parenchymal-sparing surgical techniques. These data suggest that PHLF, while devastating, may not be a predominant driver of morbidity for patients undergoing MiH. Efforts to increase adoption of hepatic parenchymal-sparing surgery and to focus attention on the prevention of associated complications, such as postoperative infections, after MiH should be pursued.

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Table 1.

Patient Characteristics associated with Post-Hepatectomy Liver Failure after Minor Hepatectomy

	Total, n (%)	PHLF, n (%)	No PHLF, n (%)	P value
Overall	**7029**	**187 (2.7)**	**6842 (97.3)**	
Age, mean (SD)	59.8 (14.0)	64.9 (11.2)	59.7 (14.0)	< 0.001
Sex				
Male	3399 (48.4)	132 (3.9)	3267 (96.1)	< 0.001
Female	3630 (51.6)	55 (1.5)	3575 (98.5)	
BMI, mean (SD)	28.6 (6.4)	28.3 (5.8)	28.6 (6.4)	0.650
Race/Ethnicity				0.349
Non-Hispanic white	4383 (62.4)	107 (2.4)	4276 (97.6)	
Non-Hispanic black	529 (7.5)	13 (2.5)	516 (97.5)	
Hispanic	332 (4.7)	9 (2.7)	323 (97.3)	
Other/Unknown	1785 (25.4)	58 (3.3)	1727 (96.8)	
ASA Class				< 0.001
I/II	1972 (28.1)	21 (1.1)	1951 (98.9)	
III/IV/V	5057 (71.9)	166 (3.3)	4891 (96.7)	
Diabetes				0.098
Yes	1247 (17.7)	42 (3.4)	1205 (96.6)	
No	5782 (82.3)	145 (2.5)	5637 (97.5)	
Smoking				0.303
Yes	1079 (15.4)	34 (3.1)	1045 (96.9)	
No	5950 (84.7)	153 (2.6)	5797 (97.4)	
Preoperative ascites, n (%)				< 0.001
Yes	48 (0.7)	9 (18.8)	39 (81.3)	
No	6981 (99.3)	178 (2.6)	6803 (97.5)	
Preoperative sepsis, n (%)				0.095
Yes	91 (1.3)	5 (5.5)	86 (94.5)	
No	6938 (98.7)	182 (2.6)	6756 (97.4)	
Bleeding disorder, n (%)				< 0.001
Yes	250 (3.6)	20 (8.0)	230 (92.0)	
No	6779 (96.4)	167 (2.5)	6612 (97.5)	
Preoperative transfusion, n (%)				0.095
Yes	41 (0.6)	3 (7.3)	38 (92.7)	
No	6988 (99.4)	184 (2.6)	6804 (97.4)	
Emergency surgery, n (%)				0.052
Yes	53 (0.8)	4 (7.6)	49 (92.5)	
No	6976 (99.3)	183 (2.6)	6793 (97.4)	
Bilirubin >1.2				< 0.001
Yes	421 (6.0)	26 (6.2)	395 (93.8)	
No	6608 (94.0)	161 (2.4)	6447 (97.6)	
SGOT > 40				< 0.001

	Total, n (%)	PHLF, n (%)	No PHLF, n (%)	P value
Yes	1216 (17.3)	82 (6.7)	1134 (93.3)	
No	5813 (82.7)	105 (1.8)	5708 (98.2)	
INR > 1.5				0.148
Yes	187 (2.7)	4 (5.2)	73 (94.8)	
No	6842 (97.3)	183 (2.6)	6769 (97.4)	
Preoperative alkaline phosphatase	106.1 (80.6)	134.1 (106.0)	105.3 (79.7)	< 0.001
Preoperative hematocrit	39.6 (4.9)	39.4 (5.9)	39.6 (4.9)	0.625
Neoadjuvant Therapy, n (%)				0.511
Yes	1357 (19.3)	32 (2.4)	1325 (97.6)	
No/Unknown	5672 (80.7)	155 (2.7)	5517 (97.3)	
Viral Hepatitis, n (%)				< 0.001
B and/or C	888 (12.6)	46 (5.2)	842 (94.8)	
None/Other/Unknown	6141 (87.4)	141 (2.3)	6000 (97.7)	
Biliary Stent				0.024
Yes	248 (3.5)	13 (5.2)	235 (94.8)	
No	6781 (96.5)	174 (2.6)	6607 (97.4)	

Abbreviations: SD, standard deviation; BMI, body mass index; ASA, American Society of Anesthesiologists Classification; SGOT, aspartate transaminase; INR, international normalized ratio

Table 2.

Treatment, Pathologic and Operative Characteristics associated with Post-Hepatectomy Liver Failure after Minor Hepatectomy

	Total, n (%)	PHLF, n (%)	No PHLF, n (%)	P value
Overall	**7029**	**187 (2.7)**	**6842 (97.3)**	
Wound Class				0.239
Clean, n (%)	1117 (15.9)	23 (2.1)	1094 (97.9)	
Clean-Contaminated, n (%)	5455 (77.6)	148 (2.7)	5307 (97.3)	
Contaminated/Dirty, n (%)	457 (6.5)	16 (3.5)	441 (96.5)	
Surgical Pathology				< 0.001
Benign, n (%)	1964 (27.9)	19 (1.0)	1945 (99.0)	
Primary Hepatobiliary, n (%)	2201 (31.3)	120 (5.5)	2081 (94.6)	
Secondary/Unknown, n (%)	2864 (40.8)	48 (1.7)	2816 (98.3)	
Liver Texture				< 0.001
Normal/Not documented, n (%)	5320 (75.7)	97 (1.8)	1619 (94.7)	
Cirrhotic/Congested/Fatty/Fibrotic, n (%)	1709 (24.3)	90 (5.3)	5223 (98.2)	
Number of tumors, median (IQR)	1 (1 - 2)	1 (1 - 1)	1 (1 - 2)	< 0.001
Operative Time (min), mean (SD)	207.1 (107.1)	262.5 (121.9)	205.6 (106.4)	< 0.001
Surgical Approach				< 0.001
Minimally Invasive, n (%)	2101 (29.9)	25 (1.2)	2076 (98.8)	
Open/Other, n (%)	4928 (70.1)	162 (3.3)	4766 (96.7)	
Procedure Type				0.111
Partial Lobectomy, n (%)	6047 (86.0)	149 (2.5)	5898 (97.5)	
Left hemi-hepatectomy, n (%)	982 (14.0)	38 (3.9)	944 (96.1)	
Concurrent colorectal resection				0.521
Yes, n (%)	415 (5.9)	9 (2.2)	406 (97.8)	
No, n (%)	6614 (94.1)	178 (2.7)	6436 (97.3)	
Concurrent ablation, n (%)				0.379
Yes	669 (9.5)	14 (2.1)	655 (97.9)	
No	6360 (90.5)	173 (2.7)	6187 (97.3)	
Pringle Maneuver, n (%)				< 0.001
Yes	1291 (18.4)	59 (4.6)	1232 (95.4)	
No	5738 (81.6)	128 (2.2)	5610 (97.8)	
Biliary Reconstruction, n (%)				< 0.001
Yes	274 (3.9)	21 (7.7)	253 (92.3)	
No	6755 (96.1)	166 (2.5)	6589 (97.5)	
Surgical Drain, n (%)				< 0.001
Yes	2866 (40.8)	113 (3.9)	2753 (96.1)	
No	4163 (59.2)	74 (1.8)	4089 (98.2)	

Abbreviations: SD, standard deviation; IQR, interquartile range

Table 3.

Multivariable Analysis for All Patients with PHLF

	PHLF n (%)	Adjusted Odds Ratio (95% CI)	P value
Age, mean (SD) *	64.9 (11.2)	1.21 (1.05 - 1.38)	0.008
Sex			
Male	132 (3.9)	1.00 (REF)	-
Female	55 (1.5)	0.62 (0.45 - 0.85)	0.003
ASA Class			
I/II	21 (1.1)	1.00 (REF)	-
III/IV/V	166 (3.3)	1.85 (1.10 - 3.11)	0.021
Ascites	9 (18.8)	4.94 (2.45 - 9.94)	< 0.001
Bleeding disorder	20 (8.0)	2.10 (1.18 - 3.44)	0.011
Elevated SGOT > 40	82 (6.7)	2.11 (1.53 - 2.92)	< 0.001
Surgical Pathology			
Benign	19 (1.0)	1.00 (REF)	-
Primary Hepatobiliary	120 (5.5)	2.14 (1.29 - 3.54)	0.003
Secondary/Unknown	48 (1.7)	1.09 (0.74 - 1.59)	0.677
Operative Time (hours), mean (SD) **	4.4 (2.0)	1.17 (1.09 - 1.26)	< 0.001
Surgical Approach			
Minimally Invasive	25 (1.2)	1.00 (REF)	-
Open/Other	162 (3.3)	1.98 (1.33 - 2.94)	< 0.001
Liver Texture			
Normal/Not documented	97 (1.8)	1.00 (REF)	-
Cirrhotic/Congested/Fatty/Fibrotic	90 (5.3)	1.92 (1.36 - 2.72)	< 0.001
Pringle Maneuver	59 (4.6)	1.60 (0.91 - 2.82)	0.100
Surgical Drain	113 (3.9)	1.57 (0.95 - 2.60)	0.078

* OR reported for each additional 10 years

** OR reported for each additional hour

Abbreviations: PHLF, post-hepatectomy liver failure; SD, standard deviation; ASA, American Society of Anesthesiologists Classification; SGOT, aspartate transaminase; MIS, minimally invasive surgery

Table 4.

Multivariable Analysis for Patients with Grade B/C PHLF

	Grade B/C PHLF n (%)	Adjusted Odds Ratio (95% CI)	P value
Age, mean (SD) *	65.0 (10.5)	1.19 (0.99 - 1.42)	0.069
Sex			
Male	65 (1.9)	1.00 (REF)	-
Female	35 (1.0)	0.93 (0.59 - 1.46)	0.739
ASA Class			
I/II	10 (0.5)	1.00 (REF)	-
III/IV/V	90 (1.8)	1.99 (0.98 - 4.05)	0.057
Ascites	6 (12.5)	4.63 (1.56 - 13.78)	0.006
Bleeding disorder	14 (5.6)	2.62 (1.09 - 6.32)	0.032
Elevated SGOT > 40	50 (4.1)	2.51 (1.72 - 3.64)	< 0.001
Surgical Pathology			
Benign	6 (0.3)	1.00 (REF)	-
Primary Hepatobiliary	70 (3.2)	4.03 (2.12 - 7.64)	< 0.001
Secondary/Unknown	24 (0.8)	1.79 (0.94 - 3.40)	0.074
Operative Time (hours), mean (SD) **	259.1 (130.8)	1.16 (1.06 - 1.27)	0.002
Surgical Approach			
Minimally Invasive	12 (0.6)	1.00 (REF)	-
Open/Other	88 (1.8)	2.42 (1.44 - 4.06)	< 0.001
Liver Texture			
Normal/Not documented	47 (0.9)	1.00 (REF)	-
Cirrhotic/Congested/Fatty/Fibrotic	53 (3.1)	2.18 (1.40 - 3.39)	< 0.001
Pringle Maneuver	29 (2.3)	1.35 (0.75 - 2.41)	0.315
Surgical Drain	56 (2.0)	1.21 (0.78 - 1.88)	0.401

* OR reported for each additional 10 years

** OR reported for each additional hour

Abbreviations: PHLF, post-hepatectomy liver failure; SD, standard deviation; ASA, American Society of Anesthesiologists Classification; SGOT, aspartate transaminase; MIS, minimally invasive surgery

Table 5.

Adjusted odds of PHLF among patients with and without other postoperative complications

	PHLF among patients with complication n (%)	PHLF among patients without complication n (%)	Adjusted Odds Ratio (95% CI)	P value
Surgical Site Infection	61/604 (10.1)	126/6425 (2.0)	3.64 (2.40 - 5.54)	< 0.001
Sepsis	24/190 (12.6)	163/6839 (2.4)	3.78 (2.16 - 6.61)	< 0.001
Unplanned return to OR	31/138 (22.5)	156/6891 (2.3)	7.35 (4.21 - 12.83)	< 0.001
Invasive Intervention Post-op	77/511 (15.1)	110/6518 (1.7)	6.92 (4.91 - 9.76)	< 0.001
Bile Leak	47/357 (13.2)	140/6672 (2.1)	4.65 (3.04 - 7.12)	< 0.001
Pneumonia	35/180 (19.4)	152/6849 (2.22)	6.92 (4.63-10.34)	< 0.001
Failure to wean from ventilator >48h	38/97 (39.2)	149/6932 (2.2)	15.83 (9.02-27.76)	< 0.001
Pulmonary embolism	6/71 (8.5)	181/6958 (2.6)	2.37 (0.73-7.76)	0.152
Myocardial infarction	9/54 (16.7)	178/6975 (2.6)	5.15 (2.32-11.43)	< 0.001