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Development and Validation of Prediction Models and Risk Calculators for Post-Hepatectomy Liver Failure and Postoperative Complications using a Diverse International Cohort of Major Hepatectomies

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Running head: Predict Post-Hepatectomy Complications

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MINI ABSTRACT

We developed and validated models predicting post-hepatectomy liver failure (ISGLS Grade B&C) and a Comprehensive Complication Index®>40 in a diverse, international cohort of major hepatectomy patients. The models demonstrated good discrimination and calibration, and highlight the importance of holistically assessing patients and their postoperative courses, as not all complications are related to liver function.

ABSTRACT

Objective: The study aim was to develop and validate models to predict clinically significant post-hepatectomy liver failure (PHLF) and serious complications (a Comprehensive Complication Index® [CCI®]>40) using preoperative and intraoperative variables.

Summary background data: PHLF is a serious complication after major hepatectomy but does not comprehensively capture a patient's postoperative course. Adding the CCI® as an additional metric can account for complications unrelated to liver function.

Methods: The cohort included adult patients who underwent major hepatectomies at twelve international centers (2010–2020). After splitting the data into training and validation sets (70:30), models for PHLF and a CCI®>40 were fit using logistic regression with a lasso penalty on the training cohort. The models were then evaluated on the validation dataset.

Results: Among 2,192 patients, 185 (8.4%) had clinically significant PHLF and 160 (7.3%) had a CCI®>40. The PHLF model had an area under the curve (AUC) of 0.80, calibration slope of 0.95, and calibration-in-the-large of -0.09, while the CCI® model had an AUC of 0.76, calibration slope of 0.88, and calibration-in-the-large of 0.02. When the models were provided only preoperative variables to predict PHLF and a CCI®>40, this resulted in similar AUCs of 0.78 and 0.71, respectively. Both models were used to build two risk calculators with the option

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to include or exclude intraoperative variables (PHLF Risk Calculator; CCI®>40 Risk Calculator).

Conclusions: Using an international cohort of major hepatectomy patients, we used preoperative and intraoperative variables to develop and internally validate multivariable models to predict clinically significant PHLF and a CCI®>40 with good discrimination and calibration.

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INTRODUCTION

Hepatic resection is an essential component in the treatment of both benign and malignant liver pathologies. Complications after hepatectomy are multifactorial and range from minor deviations from care to severe complications impacting hepatic function, such as post-hepatectomy liver failure (PHLF)[1]. In fact, the most important determinant of mortality following major liver resection is PHLF, with a reported incidence of 1.2 to 32%[1,2]. Understandably, significant effort has been devoted to identifying the presence and severity of PHLF and numerous definitions have been proposed[2,3,4]. The International Study Group of Liver Surgery (ISGLS) developed a consensus definition of PHLF based on the liver's impaired function as evidenced by an increased international normalized ratio (INR) and concomitant hyperbilirubinemia[2]. However, it is essential to recognize that PHLF represents only a portion of overall post-hepatectomy morbidity, which has been reported to be as high as 56%[5,6]. Many studies have identified risk factors associated with complications after hepatectomy, including nutrition status, baseline liver function, and extent of resection[7,8].

In an effort to measure surgical morbidity and standardize the reporting of surgical complications, Slankamenac et al. developed the Comprehensive Complication Index® (CCI®), which is calculated using the Clavien-Dindo grade of each complication to provide a cumulative sum of all complications weighted by severity[9]. The CCI® has been shown to provide an accurate and more holistic assessment of patient morbidity than the highest Clavien-Dindo complication grade[10,11,12].

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Importantly, no studies to date have attempted to predict both PHLF and the CCI® in patients undergoing major hepatectomy. This is important because the assessment of both provides a more global view of a patient's clinical course and accounts for serious complications unrelated to liver function. Furthermore, even our best definitions of PHLF are not perfect and do not identify all patients who develop liver failure. Thus, incorporating the CCI® could help identify these patients who may not have been captured with PHLF definitions alone.

Ultimately, the ability to better predict PHLF and the CCI® in patients undergoing liver resection would allow for improved risk stratification, perioperative decision-making, and patient optimization. Therefore, this study aims to develop and validate prognostic models and risk calculators to predict PHLF and the CCI® using preoperative and intraoperative factors.

METHODS

This study was structured using the TRIPOD checklist for prediction model development and was approved by the Institutional Review Board of the University of California, San Francisco (IRB No: 20-31911).

Study Population

Patients were derived from a multicenter, international cohort that includes four centers in Europe, six in Japan, one in the United Kingdom, and one in the United States. All twelve institutions are academic centers or have their own research centers, and the complete list of participating institutions is noted in Supplemental Table 1, Supplemental Digital Content 1, http://links.lww.com/SLA/E615. The median (IQR) annual case volume for major hepatectomy

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across all centers over the study period was 19.5 (13.25, 25.25). Each participating center had a prospectively maintained database from which variables of interest were obtained. Additional variables were manually extracted by the corresponding authors via chart review of the electronic medical record of their respective institutions.

Inclusion criteria were adults age 18 or over who underwent major hepatic resection (≥ 3 segments or ≥2 segments in the context of cirrhosis) at a participating center from 2010-2020. Data regarding complications from the index admission and 90-day mortality were collected. Both benign and malignant indications for surgery were included, and surgical approaches included pure laparoscopic, robotic, hand-assisted, hybrid, and open liver resection. Both anatomic and non-anatomic hepatectomies were included. Exclusion criteria were preoperative portal vein embolization and two-stage hepatectomies.

Post-Hepatectomy Liver Failure

The ISGLS defines PHLF as an elevation in INR and concurrent hyperbilirubinemia on or after postoperative day (POD) 5. Thus, patients with both total bilirubin >1.2 mg/dL and INR >1.2 on or after POD5 were classified as meeting the ISGLS PHLF criteria[2]. These patients were further stratified into grades A to C depending on the degree of deviation from the normal postoperative course, with grade A requiring no deviation from standard care, grade B requiring non-invasive intervention, and grade C requiring invasive intervention[2,13]. The outcome of clinically significant PHLF was defined as patients meeting criteria for ISGLS grade B or C PHLF, consistent with prior studies[14,15]. In addition, our group previously determined that ISGLS grade A was not associated with 90-day mortality or a high CCI®, thereby suggesting that those who

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fall in this category do not develop clinically significant PHLF[16]. Finally, we chose to utilize the ISGLS criteria for PHLF instead of other commonly used definitions such as the Balzan and Mullen criteria, as we recently found that of the three definitions, ISGLS best predicted 90-day mortality[16].

Comprehensive Complication Index

The CCI® assigns each patient a score from 0 to 100, and represents an aggregate measure of their postoperative morbidity. It is computed based on a weighted sum of the Clavien-Dindo grade of each complication experienced by a patient[9]. For this analysis, we used a CCI® score >40 based on its use in existing literature and the fact that it corresponds to experiencing at least one organ-failure level complication (Clavien-Dindo IV) or multiple complications with lower Clavien-Dindo grades[17,18].

Preoperative and Intraoperative Variables

Preoperative variables considered as potential predictors included patient age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) classification[19], Charlson Comorbidity Index[20], indication for surgery (healthy living donor, colorectal liver metastases, hepatocellular carcinoma, cholangiocarcinoma, benign indication, other malignancy), number of lesions, lesion size, pre-existing liver impairment (viral hepatitis, alcohol, chemotherapy, metabolic), clinical cirrhosis (Child A-C), portal hypertension, varices, previous abdominal surgery, and previous liver resection. Preoperative lab values considered included hemoglobin (g/dL), platelets ($\times 10^9$/L), INR, total bilirubin (mg/dL), and creatinine (mg/dL).

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Intraoperative variables considered as potential predictors included operative approach (open, laparoscopic, hand-assist), number of segments resected, Pringle maneuver, concurrent surgery, synchronous ablation, and vascular reconstruction.

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Statistical Analysis

Descriptive statistics were tabulated. Continuous variables were reported as medians with interquartile ranges (IQR), and categorical variables were expressed as counts and percentages. First, the data was randomly split 70:30 into training and validation sets. Next, we performed single imputation in the training dataset and multiple imputation in the validation dataset, using the fully conditional specification method for variables with missing data <45%; variables with missing data >45% were excluded from the analysis. Rates of missing data for included variables are noted in Supplemental Table 2, Supplemental Digital Content 1, http://links.lww.com/SLA/E615. Outcome variables were not included in the imputation procedure to avoid over-optimistic estimates of model performance.

The predictive model for PHLF was fit using logistic regression with a lasso penalty on the imputed training cohort; the lasso penalty was used to both improve model performance and encourage variable selection[21]. To account for center-specific effects, the model included center-specific intercepts, also subject to the lasso penalty. Hyperparameters were tuned using 5-fold cross validation. The model was then evaluated on the validation dataset. Model discrimination was assessed using the area under the receiver operating characteristic curve (AUC). Of note, an AUC between 0.9-1.0 is considered outstanding discrimination, 0.8-0.9 considered excellent, 0.7-0.8 considered acceptable, and 0.5-0.7 considered poor[22]. Model calibration was assessed

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using calibration slope and calibration-in-the-large. Calibration is a distinct property that measures how well a model predicts the probability of an outcome. The calibration slope has a target value of 1.0 and reflects the spread of the estimated risk. For example, a slope of <1 reflects estimated risks that are too extreme, while a slope of >1 reflects estimated risks that are too moderate. The calibration-in-the-large has a target value of 0.0, and is calculated by comparing the average predicted risk to the overall event rate. Positive values reflect underestimation and negative values reflect overestimation. Estimates and confidence intervals for model calibration and discrimination were combined across the 20 imputed validation datasets using Rubin's rules. This analysis was repeated to create a predictive model for a CCI®>40.

Sensitivity analyses were then performed, in which the trained models for PHLF and a CCI®>40 were given only preoperative factors, while the intraoperative variables were set to the mean values in the dataset. All analyses were conducted using STATA/IC 16.1 and R 4.1.1[23]. Statistical significance was set at $p<0.05$.

RESULTS

Characteristics of the Cohort

In the complete cohort of 2,192 patients, 185 (8.4%) of patients met the criteria for clinically significant PHLF (ISGLS B or C, **Table 1**). The median CCI® of the entire cohort was 0 (IQR 0, 22.6; Range 0, 100), consistent with the finding that 51.1% of patients in the cohort experienced no postoperative complications, and 7.3% of patients had a CCI®>40. Among the patients who did experience complications, the median CCI® was 22.6 (IQR 20.9, 22.5; Range 8.7, 100). The

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most common cause of liver impairment was viral hepatitis (20.2%), and the prevalence of clinical cirrhosis was 38.7%. The most commonly reported indication for resection was hepatocellular carcinoma (31.0%), followed by colorectal liver metastases (27.6%). The median (IQR) number of segments resected was 4 (3-5), and 21.1% of the cohort underwent concurrent surgery at the time of liver resection. The in-hospital and 90-day mortality rate of the entire cohort were 3.23% and 3.97%, respectively.

Predicting PHLF

The final multivariable model predicting clinically significant PHLF contained 20 variables (**Table 2**). Preoperative factors included patient age, sex, BMI, ASA, Charlson Comorbidity Index, liver impairment, previous abdominal surgery, previous liver resection, indication for surgery, number of liver lesions, lesion size, and preoperative varices. Laboratory parameters included preoperative values for platelets, hemoglobin, INR, and total bilirubin. Intraoperative factors included operative approach, number of segments resected, concurrent surgery, and vascular reconstruction. The mean AUC from 20 imputations in the validation dataset was 0.80 (95% CI: 0.72, 0.88), with a calibration slope of 0.95 (95% CI: 0.66, 1.24) and a calibration-in-the-large of -0.09 (95% CI: -0.71, 0.52). This indicates excellent discrimination and calibration of the predictive model (**Figure 1**).

Predicting the CCI®

The final multivariable model predicting a CCI®>40 contained 21 variables (**Table 2**). Preoperative factors included patient age, sex, BMI, ASA, Charlson Comorbidity Index, liver impairment, previous abdominal surgery, previous liver resection, indication for surgery, number

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of liver lesions, lesion size, and preoperative varices. Laboratory parameters included preoperative values for platelets, hemoglobin, INR, and total bilirubin. Intraoperative factors included operative approach, number of segments resected, concurrent surgery, Pringle maneuver, and vascular reconstruction. The mean AUC from 20 imputations of the validation datasets was 0.76 (95% CI: 0.69, 0.84), with a calibration slope of 0.88 (95% CI: 0.60, 1.16) and calibration-in-the-large of 0.02 (95% CI: -0.72, 0.67). This indicates acceptable discrimination and calibration of the predictive model (**Figure 2**).

Although the majority of variables included in the PHLF and the CCI® models overlapped, the weight of each variable in predicting the risk of its respective outcome differed. For example, the coefficient for preoperative varices was 1.288 for PHLF and 0.396 for the CCI®. This means that while the presence of preoperative varices was important for predicting both outcomes, it carried more weight in the prediction of PHLF. In contrast, variables such as age and ASA had higher coefficients for the CCI® than PHLF. These data are provided in **Table 2**.

Sensitivity Analysis

Sensitivity analyses were then performed, in which the trained models for PHLF and a CCI®>40 were given only preoperative factors, while the intraoperative variables were set to the mean values in the dataset. The model predicting PHLF had an AUC of 0.78 (95% CI: 0.70, 0.86) (**Figure 3**), while the model predicting a CCI®>40 had an AUC of 0.71 (95% CI: 0.63, 0.79) (**Figure 4**).

Web-based Calculator

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Two calculators were created on the Evidencio platform (PHLF: PHLF Risk Calculator; the CCI®: CCI®>40 Risk Calculator) using both developed models. To offer surgeons a tool that can be used in both the preoperative and postoperative setting, the option to include or exclude intraoperative variables was included.

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DISCUSSION

Using a large, international cohort of major hepatectomy patients, we developed and internally validated two multivariable models to predict clinically significant PHLF and postoperative morbidity (a CCI®>40) with evidence of good calibration and discrimination. Specifically, the final models for PHLF and a CCI®>40 using both preoperative and intraoperative variables had AUCs of 0.80 and 0.76, respectively.

PHLF is a potentially catastrophic outcome following major hepatectomy. Our group had previously evaluated the ISGLS consensus definition of PHLF and investigated its grading system using the CCI® as an end point. We found that ISGLS was the best predictor of 90-day mortality compared to the Balzan and Mullen criteria, and also found that patients with ISGLS grades B and C PHLF were at proportionally increased odds of morbidity and mortality[16]. Given these findings, the next logical step was to assess whether we could develop models to predict PHLF (defined by the ISGLS criteria) and the CCI®.

Risk factors for the development of PHLF have been investigated in existing literature, and prior studies have devised risk scores through statistical modeling to predict PHLF. For example, Dasari et al. constructed a model using extent of surgery and preoperative bilirubin, INR, and

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creatinine to predict PHLF with an AUC of 0.82[24]. However, only about 50% of the patients in this cohort underwent major hepatectomy, which is the patient population most at risk for developing PHLF. More recently, Chin et al. constructed a PHLF nomogram using preoperative prothrombin time, albumin-bilirubin index, bilirubin, and POD1 bilirubin with an AUC of 0.88[25]. However, their study was limited by its single center design as well as the inclusion of only patients with hepatocellular carcinoma and colorectal liver metastases. Additionally, their study utilized the 50/50 criteria to define PHLF, as opposed to the more sensitive ISGLS criteria. Finally, Liu et al. published a study in 2020 that created a calculator to predict PHLF for patients undergoing major hepatectomy[26]. While their risk calculator had an AUC of 0.83, four of the eleven variables included in the final model were intraoperative in nature, posing a potential barrier to preoperative use. Importantly, when given only preoperative variables, their model's performance significantly decreased (AUC of 0.74 from 0.83), whereas ours remained similar (AUC 0.78 from 0.80). Thus, although our PHLF model may be more cumbersome due to the greater number of included variables, its discriminatory ability in the preoperative setting is superior.

One of the novel aspects of our study was the use of the CCI® as a comprehensive measure of postoperative complications to identify patients at high risk for overall postoperative morbidity. Notably, 5.6% (n=112) of patients developed PHLF grade B or C without a CCI®>40, and 4.0% (n=81) developed a CCI®>40 without PHLF grade B or C (Table 1). Developing clinically significant PHLF without having a CCI®>40 may not be intuitive but would occur, for example, in a patient who develops PHLF grade B, which requires non-invasive intervention. Specifically, this would correspond to a Clavien-Dindo grade II complication and a CCI® score of 20.9. On the other hand, having a CCI®>40 without meeting criteria for PHLF is more intuitive, as

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patients may have serious complications unrelated to liver function. Ultimately, by assessing both the CCI® and PHLF, we achieve a more holistic assessment of patients and their postoperative course, as complications are not limited to PHLF.

The clinical relevance of our study is multi-fold. First, a quality risk model can serve as a resource to providers in the perioperative period to direct patient selection and optimization. Similarly, it can be used to facilitate preoperative counseling and provider-patient discussions. To create a comprehensive model that captured as many pertinent risk factors as possible, intraoperative variables were included, which cannot be addressed preoperatively. However, the majority of these factors can be anticipated in the preoperative period, including operative approach, concurrent surgery, vascular resection, and anticipated number of resected segments. In addition, when given only preoperative variables, our models had comparable AUC. Furthermore, we gave clinicians the option to use our risk calculators with only preoperative variables, which may be uniquely suited to guide preoperative optimization and alternative treatments. For example, if patients are identified in the preoperative setting as being high risk for developing PHLF, they may be considered for additional therapies such as preoperative portal vein embolization to mitigate this risk. Other options for high risk patients may include a two-stage hepatectomy or ablation of the lesions. Finally, this model can provide anticipatory guidance in the postoperative period, as patients at the highest risk of developing PHLF and a high CCI® can be monitored more closely, and providers can have a lower threshold to initiate organ-supportive measures. Importantly, this study emphasizes that complications related to major hepatectomies are often multifactorial, and surgeons must perform a comprehensive assessment of their patients. Finally, nearly half of the patients in the cohort experienced at least

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one complication following major hepatectomy, and yet the in-hospital mortality rate remained low at 3.23%. This suggests that patients at high risk for serious postoperative complications should be referred to experienced centers that likely have lower "failure to rescue" rates.

Risk calculators have become an increasingly important component of modern medical decision-making[27]. To translate our study findings to potential clinical use, we developed calculators with the option to include or exclude intraoperative variables so that clinicians can utilize the calculators in both the preoperative and postoperative setting. They also further highlight the importance of assessing both the CCI® and PHLF when risk-stratifying patients undergoing major hepatectomy. For example, if one inputs high risk values such as increased age, BMI, ASA, and Charlson Comorbidity Index, but inputs normal values for parameters reflecting hepatic function such as INR, platelets, and bilirubin, the calculated risk is low for PHLF but high for a CCI®>40; assessing PHLF alone would not have adequately captured the post-surgical risk. Importantly, although the risk calculators can be helpful as clinical adjuncts, we note that they do not necessarily reflect causal relationships between variables and outcomes and rather reflect learned associations only. Specifically, we were not able to adjust for all possible confounders in the analysis, as we were restricted to only those available in this dataset. Thus, the calculators should be used to additionally screen for patients at high risk for PHLF and/or a CCI®>40, but should not be used in isolation to dictate surgical planning or preclude patients from receiving surgery.

Some limitations of this study must be acknowledged. First, the retrospective nature of the study inherently leads to selection bias. Second, given the data were collected from multiple centers in

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various countries, there were likely differences in patient selection and perioperative management. For example, some centers routinely utilize the estimated indocyanine green clearance rate of the future liver remnant as a safety measure prior to resection, while others do not. However, the added benefit of a heterogeneous cohort was the generalizability of our findings. In addition, data on future liver remnant were not included due to a high number of missing variables (60.1%), although we used number of resected segments as a proxy. This was likely because not all centers routinely perform preoperative volumetry. Furthermore, because we excluded patients who underwent preoperative portal vein embolization, we did not have data on post-portal vein embolization future liver remnant size or liver growth rate, which are also important predictors of PHLF. Data regarding complications were also collected from the index admission only, as readmission data were not uniformly collected across centers; the median (IQR) length of stay across centers was 10 (7, 17) days. However, one study reported a readmission rate of approximately 9% for patients undergoing major hepatectomy, of whom the majority were readmitted with a complication that was Clavien-Dindo grade 3 or lower[28]. Thus, we believe that most complications, especially those that were severe, were captured during the index admission, and that the final CCI® would not have been significantly impacted for the majority of the patients who were readmitted. In addition, our data were not granular enough to differentiate between patients who had previous upper versus lower abdominal surgery. This is notable because patients with the former are more likely to have supracolic adhesions that may impact the subsequent liver resection. Finally, because all participating institutions in this study were considered experienced centers, the calculators may not be applicable to all centers. However, as reported in the literature and as mentioned above, high risk patients should ideally be referred to experienced centers for major hepatectomy.

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CONCLUSION

Our internally validated models and risk calculators can accurately predict PHLF and a CCI®>40 in patients undergoing major hepatectomy, allowing for a more comprehensive and holistic assessment of a patient's postoperative course. These tools can serve as adjuncts to guide patient selection and optimization, provide anticipatory guidance in the postoperative period, and allow physicians to have well-informed discussions about operative risks with patients during informed consent. Next steps will include external and prospective validation of our findings.

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Figure 1. ROC Curve and Calibration Plot for the Prediction of PHLF: Preoperative and Intraoperative Factors

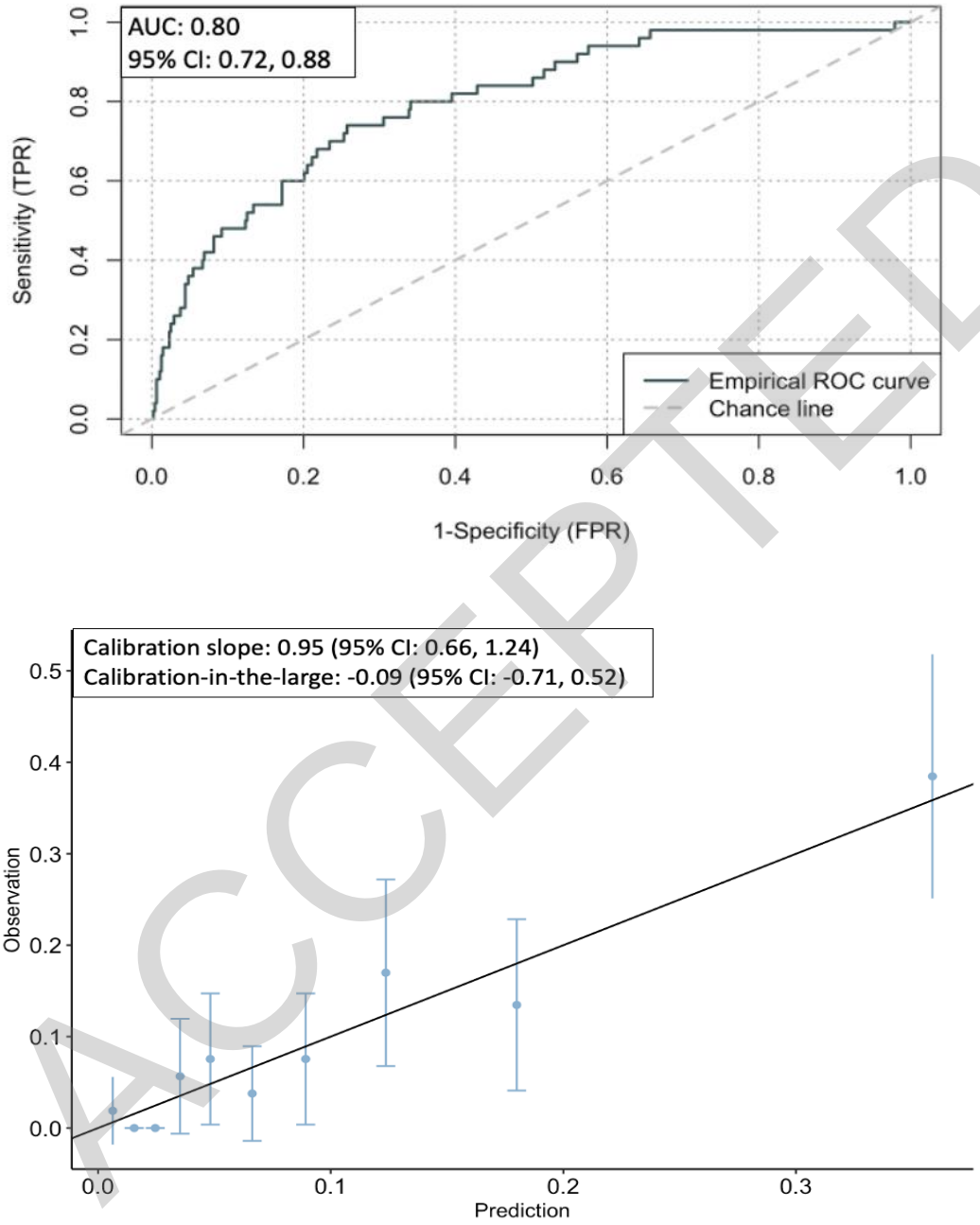

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Figure 2. ROC Curve and Calibration Plot for the Prediction of the CCI®: Preoperative and Intraoperative Factors

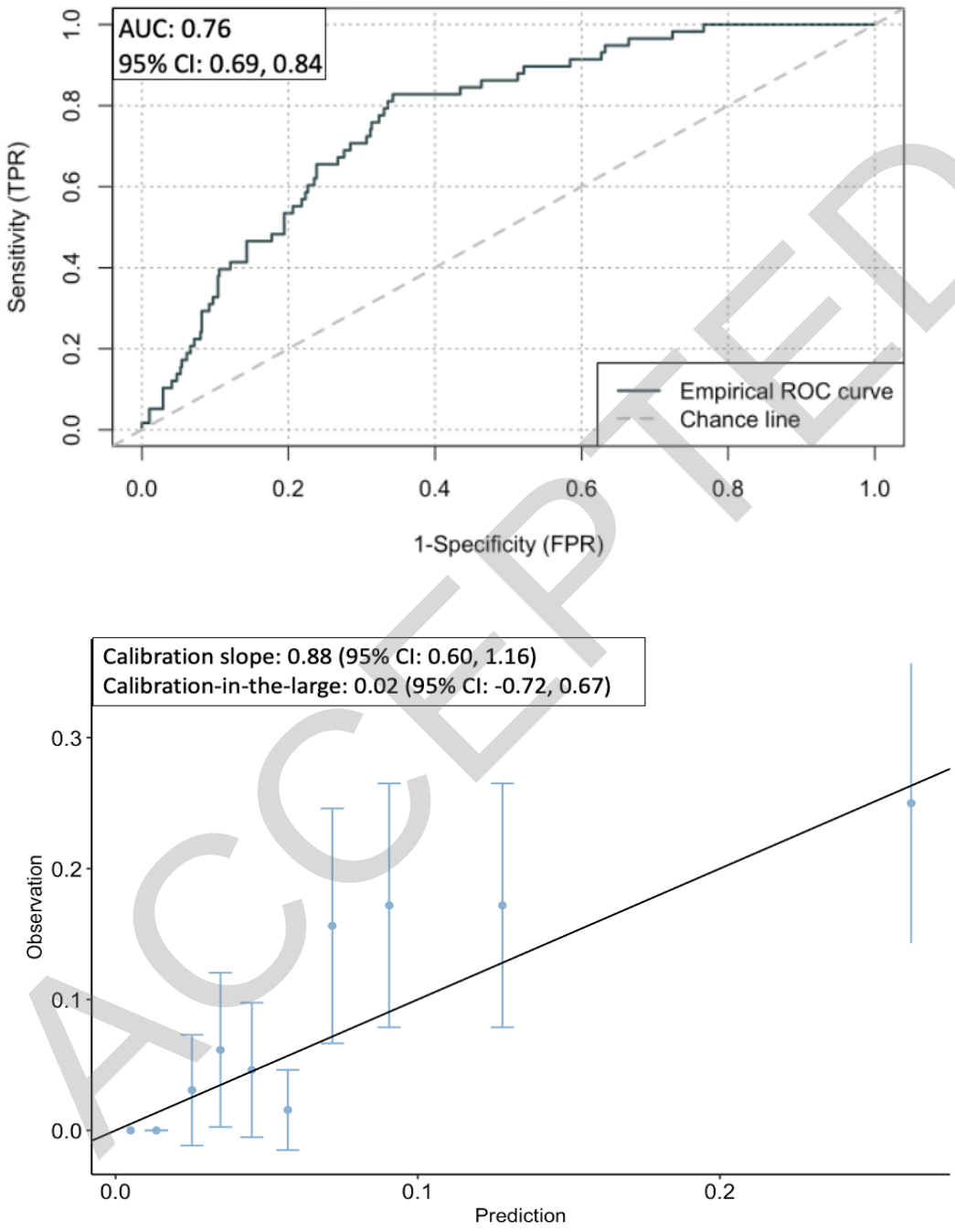

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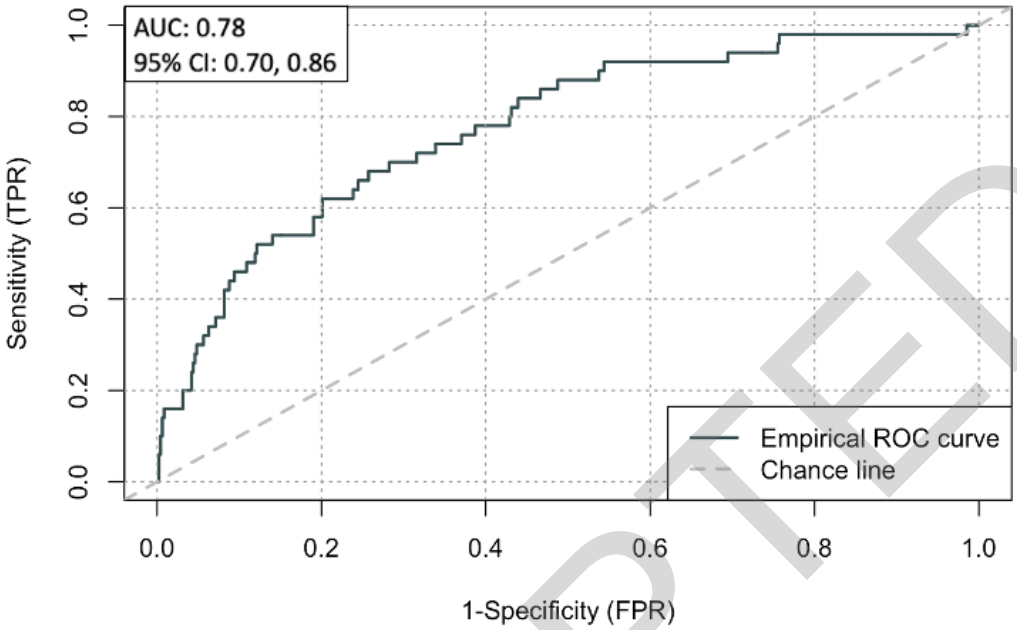
Figure 3. ROC Curve and Calibration Plot for the Prediction of PHLF: Preoperative Factors (note: intraoperative factors were set to their mean values)



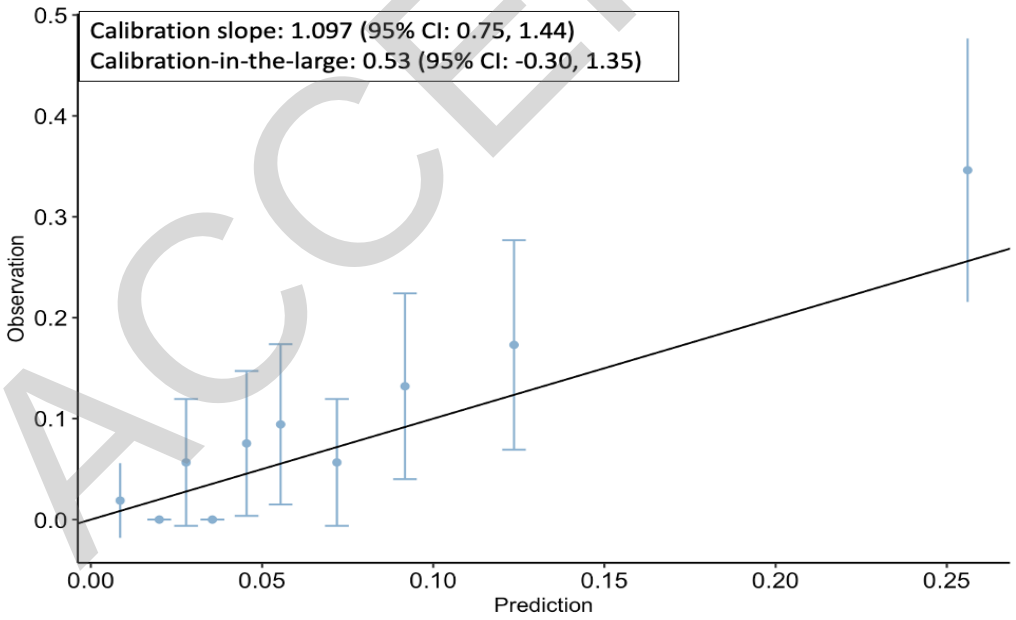


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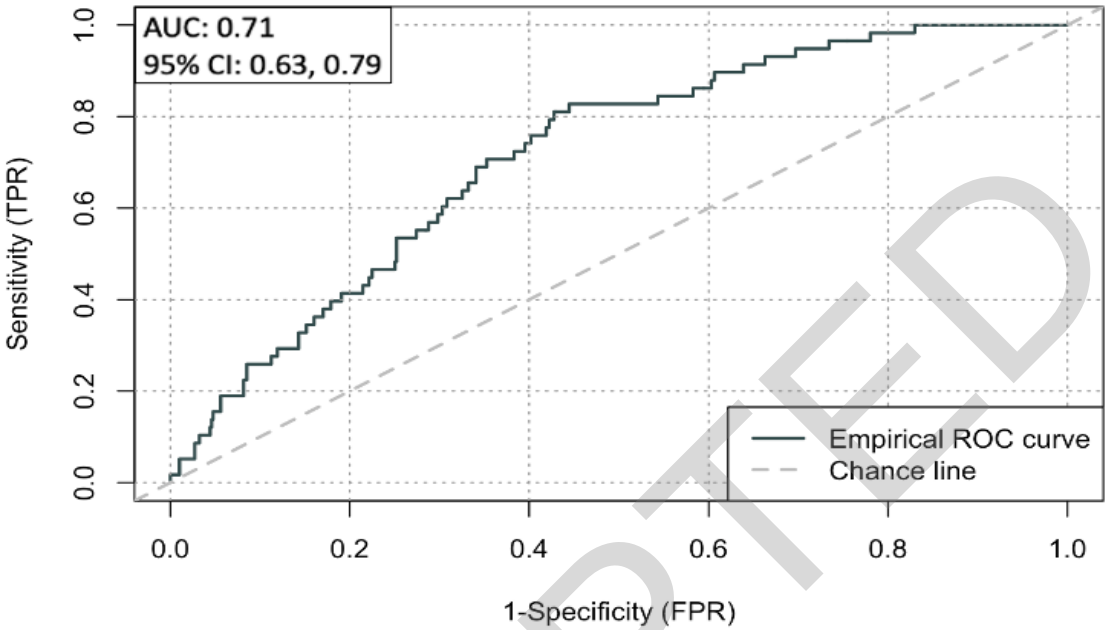
Figure 4. ROC Curve and Calibration Plot for the Prediction of the CCI®: Preoperative Factors (note: intraoperative factors were set to their mean values)



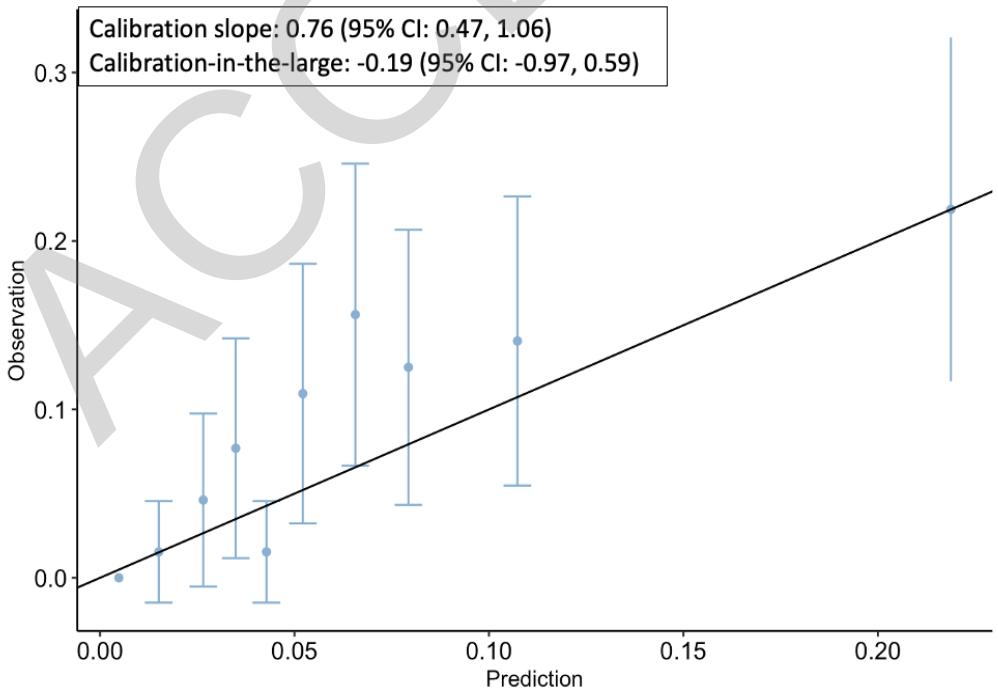


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Table 1. Characteristics of the Cohort (n=2,192)

Characteristic	Median (IQR), N (%)	Characteristic	Median (IQR), N (%)
CCI®	0.0 (0.0, 22.6)	**Indication for surgery**	
		Healthy living. donor	169 (7.7)
PHLF (grades B or C)	185 (8.4)	**CRLM**	604 (27.6)
		HCC	679 (31.0)
Age (years)	64.1 (55, 72)	**CCC**	322 (14.7)
		Benign	239 (10.9)
Sex (female:male)	808:1384 (36.9:63.1)	**NELM**	49 (2.2)
		nCRnNELM	103 (4.7)
BMI	24 (21.6, 26.7)	**Gallbladder cancer**	22 (1.0)
		Other	5 (0.2)
ASA	382 (17.8)	**Liver histology**	1015 (47.3)
1	1233 (57.5)	**Normal**	531 (24.7)
2	504 (23.5)	**Steatosis**	600 (28.0)
3	24 (1.1)	**Fibrosis/cirrhosis**	
4			1731 (79.0)
	4 (2, 7)	**Operative approach**	447 (20.4)
Charlson Comorbidity		**Open**	14 (0.6)
Index	160 (7.3)	**Laparoscopic**	
		Hand-assist	4 (3,5)
CCI®>40	112 (5.6)[a]		
		Number of segments	817 (37.5)
PHLF and no CCI®>40	81 (4.0)[a]	**resected**	1363 (62.5)
		Pringle maneuver	
CCI®>40 and no PHLF		**No**	
		Yes	

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Liver impairment	1020 (52.8)	**Concurrent surgery**	462 (21.1)
None	390 (20.2)		
Viral hepatitis (B or C)	105 (5.4)	**Synchronous ablation**	26 (1.2)
Alcohol	330 (17.1)		
Chemotherapy	86 (4.5)	**Vascular reconstruction**	80 (3.6)
NAFLD			
	1344 (61.3)	**Preoperative platelets**	217 (169, 275)
Cirrhosis	817 (37.3)	**(x10^9/L)**	
None	26 (1.2)		13.3 (12.1, 14.5)
Child A	4 (0.2)	**Preoperative hemoglobin**	
Child B		**(g/dL)**	1.0 (0.98, 1.1)
Child C	73 (3.3)		
		Preoperative INR	0.63 (0.5, 0.9)
Preoperative portal	66 (3.0)		
HTN		**Preoperative t-bili (mg/dL)**	640 (29.2)
	1 (1, 2)		
Preoperative varices		**Previous abdominal surgery**	277 (12.6)
	4 (2,7)		
Number of lesions		**Previous liver resection**	
Lesion size (cm)			

CCI®: comprehensive complication index; PHLF: post-hepatectomy liver failure; BMI: body mass index; ASA: American Society of Anesthesiology physical status classification; NAFLD: non-alcoholic fatty liver disease; HTN: hypertension; CRLM: colorectal liver metastasis; HCC: hepatocellular carcinoma; CCC: cholangiocarcinoma; NELM: neuroendocrine liver metastases; nCRnNELM: non-colorectal, non-neuroendocrine liver metastases; INR: international normalized ratio; t-bili: total bilirubin

[a]of the 2,004 patients for whom both variables were defined.

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Table 2. Logistic regression model for predicting PHLF B&C and the CCI®>40 using preoperative and intraoperative variables (fit using center-specific intercepts)

	PHLF B&C	CCI®>40
Predictor	**Coefficient**	**Coefficient**
Preoperative Variables		
Age	0.208	0.364
Sex (female)	0.249	-0.037
BMI	0.143	-0.047
ASA		
1	-	-
2	0.296	0.322
3	0.489	0.526
Charlson Comorbidity Index	0.059	0.129
Liver impairment		
None	-	-
Viral hepatitis (B or C)	0.018	-0.224
Alcohol	-0.585	-1.119
Chemotherapy	-0.340	0.034
NAFLD	0.478	-0.131
Number of lesions	0.130	0.072
Lesion size	0.024	0.102
Previous liver resection	-0.033	-0.232
Preoperative varices	1.288	0.396
Previous abdominal operation	-0.022	-0.356
Indication for surgery		
Healthy donor	-	-
CRLM	-	-0.778
HCC	0.226	0.449
CCC	0.630	0.251
Benign	-0.600	0.105
Other malignancy[a]	-0.316	0.161
Preoperative Laboratory Values		
Platelets	-0.124	0.031
Hemoglobin	-0.101	-0.198
INR	0.293	0.123
Total bilirubin	0.193	0.170
Intraoperative Variables		
Operative approach (laparoscopic)	-0.874	-0.736
Number of segments resected	0.250	0.055
Concurrent surgery	0.470	0.202
Pringle maneuver	-	-0.045

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Vascular reconstruction	-0.449	0.632

PHLF: post-hepatectomy liver failure; CCI®: comprehensive complication index; BMI: body mass index; ASA: American Society of Anesthesiology physical status classification; NAFLD: non-alcoholic fatty liver disease; CRLM: colorectal liver metastasis; HCC: hepatocellular carcinoma; CCC: cholangiocarcinoma; INR: international normalized ratio.

[a] other malignancy – NELM (neuroendocrine liver metastases), nCRnNELM (non-colorectal, non-neuroendocrine liver metastases), gallbladder cancer, other.

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