ORIGINAL ARTICLE

Developing and validating a pre-operative risk score to predict post-hepatectomy liver failure

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Abstract

Background: Post hepatectomy liver failure (PHLF) is a serious complication in patients undergoing liver resection. This study hypothesized that a new pre-operative risk score developed through statistical modeling to predict PHLF could be used to stratify patients at higher risk of PHLF.

Methods: Patients who underwent hepatectomy between 2008 and 2016 were included in the derivation and validation cohorts. A multivariable binary logistic regression model was performed to identify predictors of PHLF, and a prognostic score was derived.

Results: A total of 1269 patients were included in the derivation cohort. PHLF was encountered in 13.1% and was associated with significantly increased 90-day mortality and prolonged post-operative hospital stay (both $p < 0.001$). Multivariable analysis identified the extent of surgery ($p < 0.001$) and pre-operative bilirubin ($p = 0.015$), INR ($p < 0.001$), and creatinine ($p = 0.048$) to be independent predictors of PHLF. A risk score derived from these factors returned an area under the ROC curve (AUROC) of 0.816 ($p < 0.001$) for an internal validation cohort ($N = 453$), significantly outperforming the MELD score (AUROC: 0.643).

Conclusion: The PHLF risk score could be used to stratify the risk of PHLF among patients planned for hepatectomy.

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Introduction

Advances in perioperative management and operative techniques have improved the safety of liver resective surgery. This has led hepatobiliary surgeons to increasingly undertake more aggressive approaches, by offering extended liver resections after chemotherapy, major resections for patients with multiple co-morbidities, and also major resections with vascular reconstruction, with the aim to improve overall long-term survival. However, such strategies are bound to bring up new challenges in the management of postoperative complications, of which post hepatectomy liver failure (PHLF) is a significant concern. In the past decade, post-operative mortality after hepatectomy has reduced significantly and is reported to be less than 5%. Although the cause of death is multi-factorial, PHLF remains the predominant cause of hepatectomy-related mortality.[1–5] Pre-operative identification of patients who are at higher risk of PHLF would allow for the selection of patients needing detailed assessment of anatomical and functional liver volumes and the utilization of alternative strategies, including two-stage liver resection and parenchymal preserving surgery with or without further downstaging chemotherapy.

Definitions of PHLF such as 50–50[6] and peak bilirubin[7,8] are specific, but have low sensitivity, and are not accurate in predicting post hepatectomy outcomes.[9] The ISGLS proposed a definition of PHLF based on the serum bilirubin and INR.[10] The reported incidence of PHLF is between 1% and 30% and perioperative mortality rates among patients with PHLF grades A, B,

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and C were 0, 12, and 54%, respectively.[11] However, all these definitions are limited by the fact that PHLF is identified in the post-operative course once it is already established, with no effective treatment options other than supportive management. The clinical scoring systems of liver function, Child–Pugh and MELD (model for end-stage liver disease) scores, are of limited use prior to liver resection in Western populations, where the indication for resection is predominantly colorectal liver metastases with or without chemotherapy induced liver injury or hepatocellular cancer in pre-cirrhotic livers.

The aim of the current study was to use statistical modeling to derive and validate a pre-operative risk score, which could be used in the counseling and stratification of patients who are at risk of PHLF.

Materials and methods

A retrospective analysis was carried out using a prospectively maintained database of all liver resections performed at Queen Elizabeth Hospital, Birmingham in the United Kingdom, a large supra-regional referral center for the surgical management of the Hepatobiliary and Pancreatic disorders. The derivation cohort included 1269 consecutive patients who underwent liver resection between 2011 and 2016, inclusive. A second set of 480 consecutive patients undergoing liver resection between 2008 and 2010 was used as a validation cohort. The extent of resection was categorized as minor (<3 segments), major (right or left hepatectomy), and extra-major (extended resections, right or left hepatectomy with additional contralateral non-anatomical resections in patients with bilobar disease and major hepatectomy with vascular reconstruction). Anatomical remnant liver volumes were measured selectively in patients requiring extended hepatectomy, and functional volumes were not assessed during the study period. Low CVP anesthesia was used routinely during parenchymal division. The Pringle maneuver was performed at the discretion of the operating surgeon. Energy devices (Cavitron Ultrasonic Surgical Aspirator, Lotus, Thunderbeat) were used according to the surgeon's preference. It was departmental policy for patients who have had chemotherapy prior to liver surgery to wait at least six weeks between the completion of chemotherapy and liver resective surgery.

Definition of PHLF

The ISGLS definition[10] was used to identify patients with PHLF. Blood investigations are often not indicated on every post-operative day. Where bilirubin or INR measurements from post-operative day five were unavailable (N = 414, 32.6% of derivation cohort), the results from day seven or day four were used instead, which filled in 78.5% of the missing data (N = 325 of derivation cohort). Patients that were discharged less than five days post-operatively with normal bloods investigations were treated as not having PHLF (N = 164, 12.9% of derivation cohort).

Statistical analysis

Initially, the association between PHLF and patient outcomes, namely post-operative mortality and length of stay, were assessed using Fisher's exact test and a Mann–Whitney test, respectively. In addition, multivariable analyses were performed, to account for the confounding effects of pre- and intra-operative factors, using a forwards stepwise approach to variable selection. Post-operative mortality was assessed using a binary logistic regression model, whilst the length of stay values were log-transformed to reduce skew in the distribution, before being assessed using a linear regression model.

Associations between a range of pre-operative clinical factors and PHLF were then analyzed, using Mann–Whitney tests for continuous factors and Fisher's exact tests otherwise. Receiver operating characteristic (ROC) curves were used to quantify the predictive accuracy of pre-operative blood markers with respect to PHLF.

A multivariable binary logistic regression model was then produced, in order to identify significant independent predictors of PHLF. Prior to the analysis, the continuous variables were assessed using Hosmer–Lemeshow tests, with variables being log-transformed, or divided into categories where necessary, in order to ensure good model fit. A forward stepwise approach was then used to select variables for inclusion into a parsimonious model. Factors with large quantities of missing data (>20%) that were not found to be significantly associated with PHLF on univariable analysis were not considered for inclusion in the multivariable model, in order to maximize the included sample size.

The resulting model was then converted to a risk score by rounding the beta (log-odds) coefficients to the nearest integer, after multiplying by a constant to minimize the impact of rounding errors. Continuous variables were divided into categories, with the scores given within each range of values. This allowed the score to be calculated by the end user by adding together values from a lookup table, rather than having to perform multiplication or logarithmic transformations, which would have been required had the factors been treated as continuous. A ROC curve was then produced to assess the predictive accuracy of the score in the derivation cohort.

The risk score was then applied to a second cohort of patients for internal validation. The ROC curve analysis was repeated, and the area under the curved (AUROC) compared to that of the pre-operative MELD score. Predictive accuracy was also quantified using the Brier score, as well as using sensitivity, specificity and positive and negative predictive values, based on the cut off value with the highest value of Youden's J statistic.

All analyses were performed using IBM SPSS 22 (IBM Corp. Armonk, NY), and $p < 0.05$ was used to indicate statistical significance throughout. Cases with missing data were included where possible, only being excluded from any analyses that considered those factors where data were unavailable. The reporting of the results was in line with the TRIPOD statement.[12]

Table 1a Predictors of PHLF – patient factors

	PHLF		p-Value
	No	Yes	
Patient factors			
Age (Years)	65.1 (55.9–72.7)	65.4 (57.7–72.8)	0.531
BMI (kg/m^2)	27.7 (24.7–31.3)	27.4 (24.1–31.9)	0.649
Sex			**0.014**
Female	455 (89.7%)	52 (10.3%)	
Male	571 (84.8%)	102 (15.2%)	
Main diagnosis			0.168
Colorectal liver metastases	643 (87.2%)	94 (12.8%)	
Hepatocellular carcinoma	84 (84.0%)	16 (16.0%)	
Cholangio carcinoma	51 (79.7%)	13 (20.3%)	
Other malignant	131 (87.9%)	18 (12.1%)	
Benign	94 (87.9%)	13 (12.1%)	
Liver donor	23 (100.0%)	0 (0.0%)	
Comorbidities			
Diabetes mellitus			0.069
No	902 (87.7%)	127 (12.3%)	
Yes	124 (82.1%)	27 (17.9%)	
Alcoholic liver disease			0.318
No	1010 (87.1%)	150 (12.9%)	
Yes	16 (80.0%)	4 (20.0%)	
Hypercholesterolemia			**0.041**
No	998 (86.6%)	154 (13.4%)	
Yes	28 (100.0%)	0 (0.0%)	
Hypertension			**0.021**
No	783 (88.3%)	104 (11.7%)	
Yes	243 (82.9%)	50 (17.1%)	
Ischemic heart disease			0.757
No	940 (87.0%)	140 (13.0%)	
Yes	86 (86.0%)	14 (14.0%)	
Chronic kidney disease			0.098
No	1016 (87.1%)	150 (12.9%)	
Yes	10 (71.4%)	4 (28.6%)	
Cerebrovascular accident			0.112
No	994 (86.7%)	153 (13.3%)	
Yes	32 (97.0%)	1 (3.0%)	
Respiratory co-morbidities			0.694
No	898 (86.8%)	137 (13.2%)	
Yes	128 (88.3%)	17 (11.7%)	

Data reported as N (row %), with p-values from Fisher's exact tests, or as median (IQR), with p-values from Mann–Whitney tests, as applicable. Bold p-values are significant at $p < 0.05$.

Results

A total of 1269 patients undergoing liver resection between 2011 and 2016 were included in the derivation cohort, the demographics of whom are reported in Supplementary Table 1. Data were available for >99% of patients for all demographic factors considered, which the exception of BMI, which was only recorded in 87.8%. Data for PHLF was available for the majority of patients (N = 1180), and the overall PHLF rate was 13.1% (N = 154).

Outcomes in patients with PHLF

The median post-operative hospital stay was over three days longer in patients with PHLF (median: 9.8 vs. 6.5 days, $p < 0.001$). There was also a greater than five-fold increase in 90-day mortality (14.9% vs. 2.6%, $p < 0.001$), relative to those who did not develop PHLF. These differences remained significant on multivariable analysis, after accounting for other confounding factors, with PHLF being associated with a 38% (95% CI: 26%–52%, $p < 0.001$) increase in the length of stay, as well as a significant increase in 90-day mortality, with an odds ratio of 3.34 (95% CI: 1.45–7.70, $p = 0.005$).

Factors associated with PHLF

Univariable analyses (Table 1a–b) found that the most significant predictors of PHLF were those relating to extent of the surgery, with patients treated with major/extra major hepatectomy having significantly higher rates of PHLF ($p < 0.001$). In addition, male sex ($p = 0.014$) and systemic hypertension ($p = 0.021$) were associated with higher incidence of PHLF.

Table 1b Predictors of PHLF – treatment factors

	PHLF		p-Value
	No	No	
Pre-op chemotherapy			0.779
No	919 (87.0%)	137 (13.0%)	
Yes	107 (86.3%)	17 (13.7%)	
Extent of surgery			**<0.001**
Minor	540 (94.9%)	29 (5.1%)	
Major hepatectomy	311 (84.3%)	58 (15.7%)	
Extra major hepatectomy	171 (72.5%)	65 (27.5%)	
Uni/bilobar			**<0.001**
Unilobar	743 (90.8%)	75 (9.2%)	
Bilobar	276 (78.6%)	75 (21.4%)	
Number of segments resected			**<0.001**
1–3	550 (94.8%)	30 (5.2%)	
4+	476 (79.3%)	124 (20.7%)	

Data reported as N (row %), with p-values from Fisher's exact tests, or as median (IQR), with p-values from Mann–Whitney tests, as applicable. Bold p-values are significant at $p < 0.05$.

Associations between PHLF and range of pre-operative blood markers were then assessed (Table 2). The majority of these were recorded for at least 95% of the cohort, with the exceptions being CEA (60.1%), calcium (58.7%), total protein (58.6%), CA 19-9 (45.8%), CRP (31.4%), AFP (18.3%), magnesium (16.8%) and phosphate (10.4%). The strongest predictors of PHLF were bilirubin and INR, with areas under the ROC curve (AUROC) of 0.594 ($p < 0.001$) and 0.618 ($p < 0.001$), respectively. Other significant pre-operative predictors of PHLF were increased WCC ($p = 0.024$) or neutrophil counts ($p = 0.017$), as well as reduced levels of calcium ($p = 0.018$) or albumin ($p = 0.026$).

Multivariable analysis and risk score derivation

A multivariable analysis was then performed to identify patient and treatment factors (Supplementary Table 1) and pre-operative blood markers (Table 2) that were significant independent predictors of PHLF. The resulting model (Table 3) found that increasing extent of surgery and pre-operative INR were the strongest predictors of PHLF (both $p < 0.001$). Deranged pre-operative creatinine ($p = 0.048$) and bilirubin ($p = 0.015$) were also found to be independent predictors of PHLF. This model was then converted into a risk score, which is reported in Table 4. The coefficients for continuous variables (creatinine and bilirubin) were converted into ranges to make the score more easily calculable by end users. In order to generate the score for a patient, the values for each of the four factors for a patient are looked up in a table, and the sub-scores are added together to generate a final score. For example, a patient undergoing minor resection with a pre-operative creatinine of 50 μmol/L, bilirubin of 55 μmol/L, and INR of 1 would have a score of 0 + 1 + 3 + 1 = 5. The theoretical range of the score is 0–14, with the derivation cohort having a median score of 5 (interquartile range [IQR]: 3–7, Fig. 1). A ROC curve analysis of this risk score returned an area under the curve of 0.753 (SE = 0.020, $p < 0.001$).

Validation of the risk score

The risk score was then applied to a second cohort of 480 patients undergoing liver resection between 2008 and 2010 to

Table 2 Associations between pre-operative blood markers and PHLF

	PHLF				AUROC (SE)	p-Value
	No		Yes			
	N	Statistic	N	Statistic		
Hemoglobin (g/L)	999	134.1 ± 15.8	150	135.0 ± 18.2	0.521 (0.026)	0.407
Sodium (mmol/L)	1000	141.2 ± 2.8	151	141.1 ± 3.1	0.511 (0.027)	0.673
Potassium (mmol/L)	990	4.4 ± 0.4	148	4.4 ± 0.4	0.512 (0.026)	0.650
Phosphate (mmol/L)	103	1.0 ± 0.3	20	1.1 ± 0.3	0.528 (0.076)	0.691
Magnesium (mmol/L)	163	0.8 ± 0.1	35	0.8 ± 0.1	0.557 (0.055)	0.292
Calcium (mmol/L)	592	2.4 ± 0.2	101	2.3 ± 0.1	0.574 (0.031)	**0.018**
Albumin (g/L)	1001	44.5 ± 4.0	150	43.7 ± 4.4	0.556 (0.026)	**0.026**
Total protein (g/L)	591	70.4 ± 7.7	100	70.2 ± 7.6	0.518 (0.032)	0.562
Creatinine (μmol/L)	1001	76.0 (65.0–90.0)	151	79.0 (67.0–96.0)	0.548 (0.025)	0.055
CRP (mg/L)	303	6.0 (2.0–37.0)	67	9.0 (2.0–36.0)	0.546 (0.037)	0.243
WCC ($\times 10^9$/L)	998	6.9 (5.7–8.2)	150	7.2 (6.1–8.8)	0.557 (0.025)	**0.024**
Neutrophil ($\times 10^9$/L)	999	4.3 (3.3–5.4)	150	4.7 (3.6–6.0)	0.560 (0.025)	**0.017**
Lymphocyte ($\times 10^9$/L)	999	1.6 (1.2–2.1)	150	1.7 (1.2–2.0)	0.504 (0.025)	0.865
Neut/lymp ratio	999	2.6 (1.8–3.8)	150	2.9 (2.1–4.1)	0.547 (0.025)	0.061
Platelets ($\times 10^9$/L)	996	232.5 (189.5–285.5)	150	225.5 (184.0–276.0)	0.525 (0.026)	0.319
Bilirubin (μmol/L)	998	7.0 (5.0–10.0)	149	8.0 (6.0–12.0)	0.594 (0.025)	**<0.001**
CEA (μg/L)	621	4.3 (2.2–17.9)	88	5.7 (2.9–23.9)	0.564 (0.032)	0.051
AFP (ng/ml)	184	3.0 (2.0–7.0)	32	3.0 (2.0–8.0)	0.512 (0.055)	0.829
CA 19-9 (KU/L)	462	18.0 (9.0–44.0)	78	20.0 (9.0–79.0)	0.541 (0.038)	0.242
INR[a]	993		147		0.618 (0.025)	**<0.001**
<1		263 (92.9%)		20 (7.1%)		
1		497 (88.4%)		65 (11.6%)		
>1		233 (79.0%)		62 (21.0%)		

Data are reported as mean ± SD, or as median (IQR), as applicable.
p-Values are from ROC curves, with bold values significant at $p < 0.05$.
[a] INR is reported as the liver failure rate within categories, in order to make differences more clearly visible.

Table 3 Multivariable analysis of pre-operative predictors of PHLF

	Log-odds	Odds ratio (95% CI)	p-Value
Extent of surgery			**<0.001**
Minor	0	–	–
Major hepatectomy	1.407	4.08 (2.41–6.90)	**<0.001**
Extra major hepatectomy	1.863	6.44 (3.74–11.11)	**<0.001**
Pre-operative creatinine (μmol/L)	0.008	1.01 (1.00–1.02)	**0.048**
Log_2 pre-operative bilirubin (μmol/L)[a]	0.265	1.30 (1.05–1.61)	**0.015**
Pre-operative INR[b]			**<0.001**
<1	0	–	–
1	0.684	1.98 (1.06–3.72)	**0.033**
>1	1.406	4.08 (2.14–7.78)	**<0.001**

Results are from a binary logistic regression model, using a forwards stepwise procedure for variable selection. All factors from Supplementary Table 1 were considered for inclusion in the model, along with all pre-operative bloods from Table 2 where data were available for >80% of cases. The final model was based on N = 981 cases.
Bold p-values are significant at $p < 0.05$.
[a] Bilirubin was log_2-transformed, prior to analysis, in order to improve model fit. As a result, the quoted odds ratios relate to the increase in the odds of liver failure for a two-fold increase in bilirubin.
[b] INR was divided into categories, in order to improve model fit, due to poor fit when it was treated as continuous (Hosmer–Lemeshow test: $p < 0.001$).

internally validate the predictive accuracy (Supplementary Table 2). A total of 453 patients had sufficient data to apply the ISGLS definition and, of these, 68 (15.0%) were classified as having PHLF. This is a comparable rate to that observed in the derivation cohort (13.1%). For the 419 patients where the risk score was calculable, the AUROC for the prediction of PHLF was 0.816 (SE = 0.025, $p < 0.001$).

The risk score was then compared to the pre-operative MELD score, as both shared the same set of blood markers (creatinine, bilirubin and INR). For the 419 patients included in the validation analysis, the mean MELD score was found to be 13.9 ± 4.0. A moderate correlation was detected between the MELD and risk scores (Spearman's rho: 0.475, $p < 0.001$). On ROC curve analysis, the MELD score had an area under the curve of 0.643 (SE: 0.037, $p < 0.001$), which was significantly ($p < 0.001$) lower than that observed for the risk score (AUROC: 0.816).

Fig. 2 shows the relationship between the risk score and PHLF for both of the cohorts. In the validation cohort, the risk score returned a Brier score of 0.10, and Youden's J statistic identified >5.5 as being the optimal cut off value. Of the patients scoring 0–5.5, only 2.4% (5/208) developed PHLF, compared to 27.5% (58/211) of those scoring 6–14 points on the risk score. This yielded 92.1% sensitivity and 57.0% specificity, with positive and negative predictive values of 27.5% and 97.6%, respectively.

Discussion

In the current study, we were able to develop and internally validate a risk score to predict PHLF using variables that are routinely available at pre-operative assessment. PHLF is a recognized complication and its incidence is directly related to the extent of liver resection.[13–16] PHLF is multi-factorial by causation and its prediction is still an evolving science. The unique regenerative capacity of the liver has permitted the surgical removal of large or multiple liver tumors with curative intent. Nevertheless, when the functional liver remnant is too small, the altered blood-to-liver volume ratio causes elevated portal pressure, and sinusoidal endothelial injury. The activity of Kupffer cells in the liver remnant is inadequate to initiate or maintain the innate immune response that drives liver regeneration.

Patients with diabetes mellitus (DM) and renal insufficiency are reported to have poor post-hepatectomy outcomes.[17] In a meta-analysis comparing five studies, there was significant association between DM and PHLF (RR, 2.21; 95% CI, 1.3–3.76; $p = 0.028$).[18]

In our study, DM was a significant independent predictor of post-operative 90-day mortality but was not shown to have significant influence on the rate of PHLF. However, patients with raised pre-operative creatinine, indicating impaired renal function, had higher incidence of PHLF on multivariable analysis. It may be that the elevated pre-operative creatinine is an indicator of poor general health and of co-existing medical disorders, such as DM and chronic vascular disease and, hence, is associated with an increased risk of PHLF.

Anatomical volumes are calculated to help assess the adequate remnant volume. Minimum residual volumes of ≥25% in normal background residual liver and ≥40% in those with post-chemotherapy liver are estimated to prevent the development of PHLF.[19–21] It is increasingly acknowledged that the anatomical volumes do not necessarily represent the functional volumes of the liver.[22,23] Discrepancy in anatomical and functional residual volumes is commonly seen in patients undergoing liver resection with chemotherapy-induced liver injury,[24] obese individuals with fatty liver disease or those with established non-alcoholic steatohepatitis, established cirrhosis, siderosis, and jaundice secondary to hilar cholangiocarcinomas. This problem is also encountered in patients undergoing a major hepatectomy and requiring multiple non-anatomical resections in the remnant lobe, as these could result in parenchymal ischemia.

For these reasons, we have classified the extent of resection, in the proposed risk score, into three different categories: minor (less than or 3 segments), major (right or left hemihepatectomy), and extra-major resections that include extended resection, hemihepatectomy with non-anatomical resections on the contralateral side, or hepatectomy with vascular reconstruction. Such classification better represents the scenarios increasingly encountered in clinical practice than the more commonly used classification of uni/bilobar disease or 3 segments or more.

Table 4 Pre-operative risk score for PHLF

	Score
Type of surgery	
Minor	0
Major hepatectomy	3
Extra major hepatectomy	4
Pre-operative creatinine	
0–30	0
31–90	1
91–150	2
>150	3
Pre-operative bilirubin	
0–5	0
6–20	1
21–50	2.5
51–90	3
>90	4
Pre-operative INR	
<1	0
1	1
>1	3

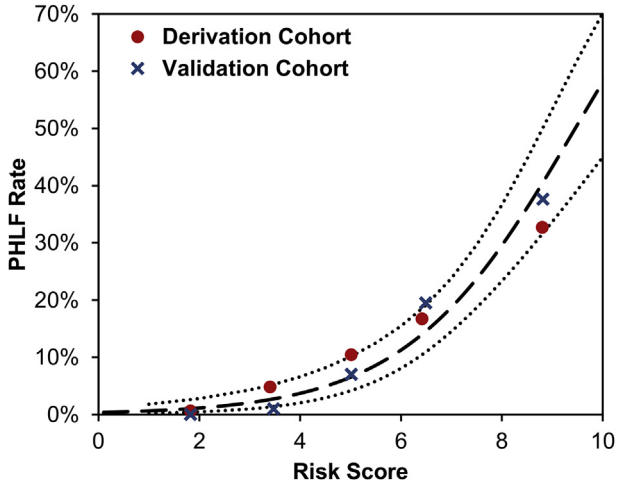

Figure 2 PHLF rate by risk score. Points are the observed rates at the quintiles of the data in the two cohorts. The broken line is from a binary logistic regression model on the validation cohort, with the risk score entered as a continuous covariate. The dotted lines represent the 95% prediction intervals of this model. The x-axis is truncated at a risk score of 10 as, although the highest potential score is 14, less than 2% of patients had scores greater than 10

Bilirubin and INR are components of the ISGLS definition, as well as the Child Pugh, MELD, and peak bilirubin definitions of PHLF.[8,10] Li *et al.* and colleagues reported pre-operative serum bilirubin level of ≥20.3 μmol/L to be a significant independent risk factor for PHLF.[25] The Schindl score[26] from Edinburgh is a post-operative PHLF score, also reporting ranges of PT (<4, 4–6, and >6 s) along with total serum bilirubin, serum lactate and grade of encephalopathy. INR and bilirubin are also significant factors in the proposed risk score from this study. In our cohort, the majority of patients do not have significant underlying liver disease and, hence, serum bilirubin and INR levels represented in the risk score are closer to normal range. This is similar to the reported ranges of PT in Schindl score.

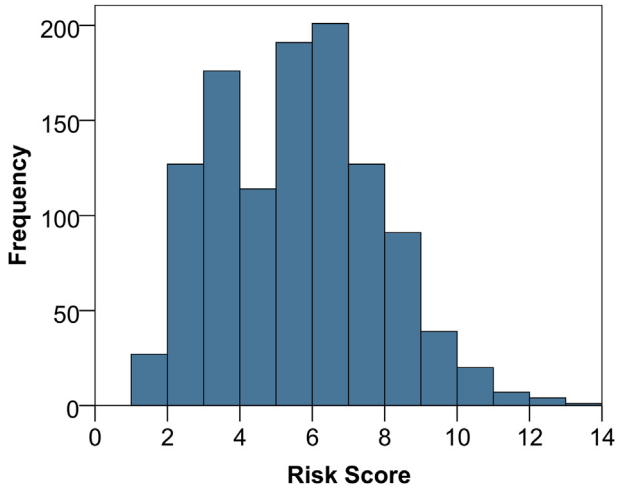

Figure 1 Distribution of the risk score in the derivation cohort

By decreasing the tumor size, pre-operative chemotherapy may lead to curative resection in 15–50% of patients initially presenting with unresectable disease. There is increased post-operative morbidity and mortality due to PHLF in patients with chemotherapy-associated changes in the liver; these include mainly fluorouracil-induced steatosis, especially in patients with a high body-mass index and irinotecan-induced steatohepatitis. The duration of chemotherapy and time interval between the cessation of chemotherapy and liver surgery were also identified as factors to predict PHLF.[27–29] This study did not demonstrate pre-operative chemotherapy to influence PHLF, probably because it is our policy to wait 6–8 weeks after chemotherapy before proceeding for surgery. The status of background liver is not routinely available in pre-operative settings; thus it is not included in the data analysis. Similarly, as the proposed risk score is intended to be used before surgery, intra-operative factors associated with PHLF, including hepatic inflow occlusion, duration of surgery, intra-operative blood loss, and postoperative sepsis, are not included in the current analysis. However, it should be the surgeon's prerogative to reduce such operative risks by taking the necessary technical precautions.

Of the proposed pre-operative investigations to assess liver function, indocyanine green (ICG) clearance is considered useful, but it only allows assessment of global function of the

liver and not the function of the selected remnant liver.[30,31] 99mTc-labeled galactosyl serum albumin (GSA) liver scintigraphy, 99mTc-mebrofenin hepatobiliary scintigraphy with single-photon emission computed tomography (SPECT), and gadolinium-enhanced MRI using gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (Gd-EOB-DTPA) are other imaging modalities considered useful to assess the function of the specific remnant volumes. Impaired enhancement of labeled contrast indicates decreased hepatic uptake and reflects compromised liver quality.[32–35] Performing functional studies in a resource-limited healthcare system could delay the time to surgery and it also has financial constraints. A pre-operative risk model is useful in selection of appropriate patients to go through a detailed pathway with additional functional assessments. In addition, such pre-operative models could allow pre-operative counseling, and risk stratification to compare post-operative outcomes. The current validated model, based on the extent of liver resection, pre-operative creatinine, serum bilirubin, and INR is a potentially useful tool in pre-operative settings.

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None.

Conflict on interest

None declared.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.hpb.2018.09.011.