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Development of a nomogram for predicting perioperative blood transfusions in major hepatobiliary and colorectal surgeries: a retrospective study

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Abstract

Background: Major hepatobiliary and colorectal surgeries are associated with a risk of blood transfusions. However, risk assessment tools for predicting blood transfusions have not been studied extensively among patients undergoing these types of surgeries. We aimed to evaluate the risk factors for perioperative blood transfusions in our patients who underwent major hepatobiliary and colorectal surgeries and subsequently to create a nomogram.

Methods: Medical records for patients who underwent elective major hepatobiliary and colorectal surgeries in a single tertiary university hospital in Malaysia from 2015 to 2020 were retrospectively reviewed. A nomogram to predict transfusions risk was developed, and its discriminatory ability was tested using the area under the receiver operating characteristic (ROC) curve.

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Results: Data from 293 patients (61.1% male) with an average age of 59.7 years old (± SD 14.51) were analysed. The prevalence of anaemia was 61.1%. A total of 127 patients (43.3%) received at least 1 unit of packed red cells transfusions. On multivariable analysis, gender (odds ratio [OR 1.646), preoperative haemoglobin of 8.0 g/dl or less (OR 0.777), Charlson Comorbidity Index score (OR 1.14) and procedure type (versus colonic surgery, major hepatectomy, OR 6.094; other pancreatomy, OR 1.487; Whipple's procedure, OR 9.667; and anterior resection, OR 3.569) were associated with a significantly higher risk of transfusions. All 4 of these factors were included in the nomogram. The nomogram's discrimination and calibration results showed good prediction abilities (AUROC curve 0.754).

Conclusion: The nomogram, which consists of gender, preoperative haemoglobin, Charlson Comorbidity Index, and procedure type effectively predicted the need for blood transfusions in major colorectal and hepatobiliary surgeries in our patients.

Keywords: blood transfusions, hepatobiliary and colorectal surgery, nomogram, risk prediction tool

Introduction

Colorectal and hepatopancreatic biliary surgeries are commonly performed for malignant and benign diseases and are associated with intraoperative and postoperative blood transfusions.[1] Blood transfusions are potentially lifesaving but also come with several adverse effects, such as immune suppression, increased infection rates, and increased mortality rates.[2-4] Identifying which patients are likely to need transfusions is a significant step towards better blood management. Scoring systems, regression models, nomograms, and artificial intelligence have been previously used to predict blood transfusions.[5-7]

A nomogram is a tool used to calculate charts graphically using scales that contain the values of 3 or more mathematical variables. Nomograms are primarily used in the fields of medicine, industry, engineering, and the physical and biological sciences to make predictions regarding the targeted aspect.[8] Several nomograms have been developed to predict blood transfusion in different types of surgery, such as total knee replacement, hip surgery, and pheochromocytoma surgeries.[5,6,9]

Kim *et al.* developed a nomogram to predict blood transfusions for hepatopancreatic biliary and colorectal surgeries.[10] Important predictive factors were age greater than 65 years, white and Asian race, preoperative haemoglobin levels, Charlson Comorbidity Index (CCI), preoperative international normalized ratio (INR), and type of surgery. The nomogram was created by assigning a weighted score to each independent prognostic factor; higher total score was associated with higher likelihood of blood transfusions. However, the nomogram developed by Kim and colleagues has not been validated in an external population. To our knowledge, the only local study in this field has been conducted by Yusof *et al.*, which found that preoperative platelet count was the most important factor associated with risk of blood transfusions in liver transplant surgeries.[11]

In this study, we aimed to evaluate the risk factors for perioperative blood transfusions in patients who underwent major hepatobiliary and colorectal surgeries in a single tertiary university hospital in Malaysia. Specifically, we aimed to create a nomogram from these risk factors that can be used to predict the need for blood transfusions in patients undergoing these types of surgeries.

Materials and methods

This retrospective observational study was approved by the Research Committee of the Department of Anaesthesiology and Intensive Care, Hospital Canselor Tuanku Muhriz, Universiti Kebangsaan Malaysia, and the institution's Medical Research and Ethics Committee (Project Approval Code: HTM-2021-028). All adult patients who underwent elective major hepatobiliary and colorectal surgeries from January 2015 to December 2020 were included in the study. Patients with missing data or medical records and those who underwent open and closed surgeries whereby the intended surgery did not proceed due to disease progression were excluded from the study.

The medical records of the included patients were retrieved, reviewed, and analysed retrospectively. Data were collected on demographic details (*i.e.*, age, gender, race, weight, height, body mass index [BMI], and American Society of Anaesthesiologists [ASA] fitness grade), underlying medical illness (*i.e.*, pulmonary disease, congestive heart failure, peripheral arterial disease, diabetes, renal conditions, and hypertension), along with anaemia, relevant preoperative haematological profile (*i.e.*, haemoglobin concentration, INR, platelet level, and CCI), operative profile type of surgery (*i.e.*, anterior resection, hemi-hepatectomy, pancreatectomy, duedenopancreactectomy, Whipple's procedure, open colectomy, or minor hepatectomy), estimated blood loss, surgery duration, and units of transfused packed red blood cells.

The sample size for this study was based on the work of Peduzzi *et al.*[12] The minimum number of samples to include was N = 10k/p, where k is the number of independent variables, and p is the proportion of cases. A proportion of 30% of blood transfusion cases was considered in the study population, with 7 independent variables included in the multiple logistic regression analysis and a total of 20% of dropout cases. The minimum sample size required was therefore 280 cases.

Data were cleaned, explored, and analysed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA) and STATA version 16.0 (STATACorp, College Station, TX, USA). The distribution of the continuous data was explored using skewness, kurtosis, and histograms. Continuous data were presented as mean and standard deviation if the data were normally distributed, otherwise median (25^{th} percentile, 75^{th} percentile) was used. Categorical variables were presented as frequency and percentage. Descriptive statistics were used to present the characteristics and perioperative details of the patients, and the differences in outcomes between those who did not receive and those who received perioperative blood transfusion were compared using the independent sample T test, Mann-Whitney U test, Pearson chi-squared test, and Fisher exact test, whichever was appropriate.

The factors affecting the requirement for blood transfusions after surgeries were analysed using logistic regression models that were employed in the nomogram's development. When conducting the univariable analysis using simple logistic regression to identify the factors associated with perioperative blood transfusions, variables with $p < 0.200$ were noted. The forward logistic regression approach was used to incorporate results from the univariable analysis into the multivariable model's variable selection procedure. Nomograms indicating the need for intraoperative blood transfusions were generated using regression coefficients from multivariable logistic regression models. Multicollinearity and interaction terms were checked, and model fit was assessed using the Hosmer-Lemeshow goodness of fit test and classification table.

Model discrimination (the capacity of a proposed model to identify patients with different outcomes) and calibration (the distance between forecasts and results) were also used to evaluate model performance. The area under the receiver operating characteristics (ROC) curve was used to determine the discriminatory ability of the nomogram (AUC). AUC values can range from 0.5, demonstrating poor discrimination, to 1.0, showing perfect discrimination. Model calibration was assessed using a calibration plot, in which the predicted probabilities were plotted against the observed outcome frequencies. Predictions from a properly calibrated model should lie along the 45° diagonal line. All tests were conducted as 2-tailed, and $p < 0.05$ was taken to denote statistical significance. Finally, a comparison was conducted between the AUC of the nomogram established by Kim *et al.* and our newly generated nomogram. This comparison aimed to assess the discriminatory power of both nomograms in predicting the need for blood transfusions.

Results

During the data collection process, a total of 305 patients were taken into consideration; however, 12 patients were excluded since they did not meet the inclusion criteria. The 293 individuals who were involved in the study were separated into 2 groups: those who required a transfusion (43.3%) and those who did not require a transfusion (56.7%) (Fig. 1).

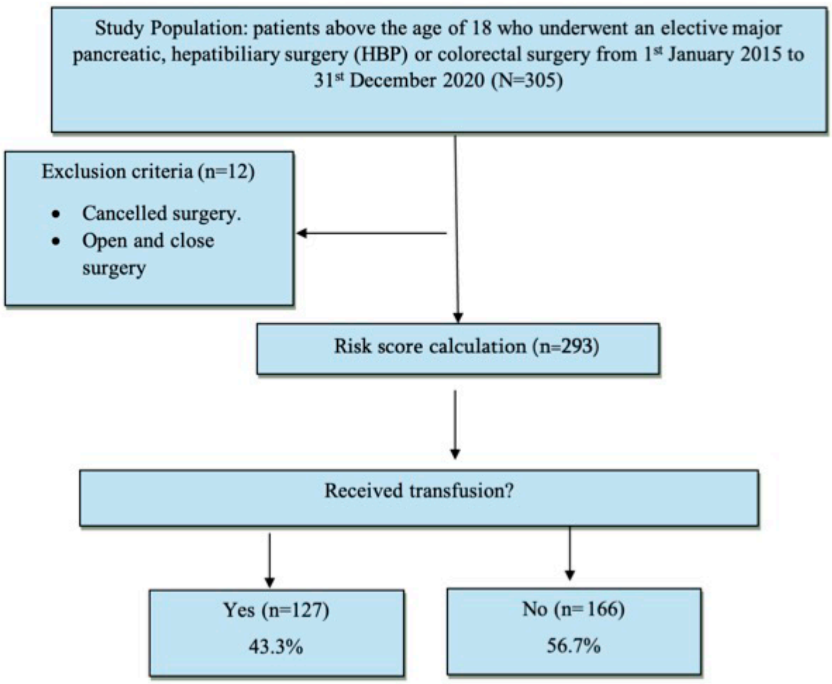

Fig. 1. Flow diagram of study.

Demographic and clinical data

The baseline characteristics of the included patients are shown in Table 1. The mean age was 59.69 years old (SD: 14.51). The majority were male (61.1%) and Malay (60.4%) with a median BMI of 23.31 kg/m^2 (IQR: 21.16, 26.39). Almost all patients were non-smokers (95.9%), with an ASA grade of I–II (93.2%). The reported mean perioperative haemoglobin was 11.84 g/dL (SD: 1.88), while the median perioperative INR and platelet were 1.01 (IQR: 0.98, 1.08) and 278.0 (IQR: 215.0, 364.0) x 10^9/L,

Table 1. Characteristics of the patients

Characteristics	Overall	Perioperative blood transfusion	
		No	Yes
Age in years, mean ± SD	59.69 ± 14.51	59.78 ± 14.79	59.56 ± 14.30
Gender, *n* (%)			
Female	114 (38.9)	73 (44.0)	41 (32.3)
Male	179 (61.1)	93 (56.0)	86 (67.7)
Race, *n* (%)			
Malay	177 (60.4)	97 (58.4)	80 (63.0)
Chinese	98 (33.4)	57 (34.3)	41 (32.3)
Indian	16 (5.5)	11 (6.6)	5 (3.9)
Others	2 (0.7)	1 (0.6)	1 (0.8)
BMI in kg/m^2, median (IQR)	23.31 (21.16, 26.39)	23.66 (21.43, 27.07)	22.97 (20.90, 26.12)
ASA grade, *n* (%)			
I–II	273 (93.2)	158 (95.2)	115 (90.6)
III–IV	20 (6.8)	8 (4.8)	12 (9.4)
Perioperative Hb, mean ± SD	11.84 ± 1.88	12.20 ± 1.79	11.35 ± 1.89
Perioperative INR, median (IQR)	1.01 (0.98, 1.08)	1.01 (0.99, 1.07)	1.02 (0.98, 1.10)
Perioperative platelet, median (IQR)	278.0 (215.0, 364.0)	276 (217.5, 434.8)	285.0 (211.0, 491.8)
Smoking status, *n* (%)			
Non-smoker	281 (95.9)	160 (96.4)	121 (95.3)
Smoker	12 (4.1)	6 (3.6)	6 (4.7)
Charlson Comorbidity Index, *n* (%)			
0–3	59 (20.1)	39 (23.5)	20 (20.1)
≥ 4	234 (79.9)	127 (76.5)	107 (84.3)
Coexisting medical condition, *n* (%)			
Diabetes	105 (35.8)	51 (30.7)	54 (42.5)
Hypertension	153 (52.2)	80 (48.2)	73 (57.5)
Ischaemic heart disease	14 (4.8)	7 (4.2)	7 (5.5)
Anaemia	9 (3.1)	3 (1.8)	6 (4.7)
Chronic kidney disease	10 (3.4)	4 (2.4)	6 (4.7)
Dyslipidaemia	33 (11.3)	20 (12.0)	13 (10.2)

respectively. The CCI of 4 or higher was reported among 234 (79.9%) of the patients. Reported coexisting medical conditions included diabetes (35.8%), hypertension (52.2%), ischaemic heart disease (4.8%), chronic kidney disease (3.4%), and dyslipidaemia (11.3%).

Factors associated with perioperative blood transfusions

The results of univariable and multivariable logistic regression analysis of factors associated with perioperative blood transfusion are shown in Table 2. On univariable analysis, factors that were significantly associated with perioperative blood loss were gender, perioperative haemoglobin, CCI, diabetes mellitus, and type of procedure.

The final multivariable model revealed that factors significantly associated with the perioperative blood transfusion included gender, perioperative haemoglobin, and type of procedure ($p < 0.05$). Males were observed to have 2.031 times higher odds for perioperative blood transfusion compared to females ($p = 0.012$). Every unit increase in perioperative haemoglobin will decrease the odds for blood transfusion by 25.5% ($p < 0.001$). A unit increase in CCI score was observed to increase the odds for perioperative blood transfusion by 9% ($p = 0.050$). The type of procedure also played an important role. Hemihepatectomy (or more), duodenopancreatectomy/Whipple's procedure, and anterior resection were observed to have 6.213 times ($p = 0.001$), 8.260 times ($p < 0.001$), and 3.550 times ($p = 0.011$) higher odds for perioperative blood transfusion compared to open colectomy, respectively.

Nomogram generation

Based on the results of multiple logistic regression, a nomogram was generated to predict perioperative blood transfusions (Fig. 2). The nomogram was created by assigning a weighted score to each of the independent prognostic factors. The total score was calculated from the sum of the assigned number of points for each risk factors in the nomogram. For example, a male (1.4 points) who underwent duodenopancreatectomy/Whipple's procedure (4.4 points) with a perioperative haemoglobin concentration of 9.95 g/dl (8.3 points) and CCI score of 0 (0.0 points) would score a total of 14.1 points, and therefore have a 94.9% predicted risk for blood transfusions.

The resulting model's ability to discriminate between patients requiring and not requiring perioperative blood transfusions was measured by its AUC (Fig. 3). The probability that a patient receiving a blood transfusion had a higher score than a patient who did not was 75.4%, indicating good discriminatory power of the prediction model.

Table 2. Univariable and multivariable logistic regression analysis of factors associated with perioperative blood transfusions

Factors	**Univariable**			**Multivariable**			**Points contributed**
	OR	**95% CI**	***P*-value**	**Adjusted OR**	**95% CI**	**‡*P*-value**	
Age	0.999	0.983, 1.015	0.896				
Gender							
Female	Ref			Ref			0
Male	1.646	1.017, 2.666	**0.043***	2.031	1.170, 3.526	**0.012***	1.4
Race							
Malay	Ref						
Chinese	0.872	0.530, 1.436	0.591				
Indian	0.551	0.184, 1.652	0.287				
Others	1.213	0.075, 19.693	0.892				
BMI in kg/m^2	0.982	0.933, 1.033	0.479				
ASA grade							
I–II	Ref						
III–IV	2.061	0.816, 5.204	0.126				
Perioperative haemoglobin	0.777	0.681, 0.887	**< 0.001***	0.745	0.640, 0.868	**< 0.001***	4.3–10.0
Perioperative INR	8.012	0.946, 67.838	0.056				
Perioperative platelets	1.001	0.999, 1.003	0.267				
Smoking status							
Non-smoker	Ref						
Smoker	1.322	0.416, 4.201	0.636				
Charlson Comorbidity Index	1.14	1.05, 1.22	**0.001***	1.090	1.000–1.188	**0.049***	0.0–3.3
Diabetes mellitus							
No	Ref						
Yes	1.668	1.030, 2.701	**0.038***				
Hypertension							
No	Ref						
Yes	1.453	0.913, 2.314	0.115				
Ischaemic heart disease							
No	Ref						
Yes	1.325	0.453, 3.879	0.608				
Anaemia							
No	Rf						
Yes	2.694	0.661, 10.988	0.167				
Chronic kidney disease							
No	Ref						
Yes	2.008	0.555, 7.273	0.288				
Dyslipidaemia							
No	Ref						
Yes	0.832	0.397, 1.745	0.627				
Type of procedure							
Open colectomy	Ref			Ref			0
Minor hepatectomy	1.074	0.266, 4.335	0.920	1.148	0.274, 4.820	0.849	0.3
Hemihepatectomy or more	6.094	2.164, 17.164	**0.001***	6.213	2.125, 18.166	**0.001***	3.8
Duodenopancreatectomy	9.667	3.398, 27.497	**< 0.001***	8.260	2.857, 23.879	**< 0.001***	4.4
Anterior resection	3.569	1.374, 9.274	**0.009***	3.550	1.333, 9.459	**0.011***	2.6
Other pancreatectomy	1.487	0.358, 6.179	0.585	2.015	0.445, 9.125	0.363	1.5

Ref: Reference value; OR: Odd ratio; CI; Confidence interval; BMI: body mass index; ASA: American Society of Anesthesiologists
*P value in univariable analysis, ‡P value in multivariable analysis
Multicollinearity and interaction terms were checked and not found; Negelkerke $R^2 = 0.242$
Hosmer Lemenshow goodness of fit test ($p = 0.276$); Classification table (overall correctly classified percentage: 70.3%); Area under ROC curve = 75.4%

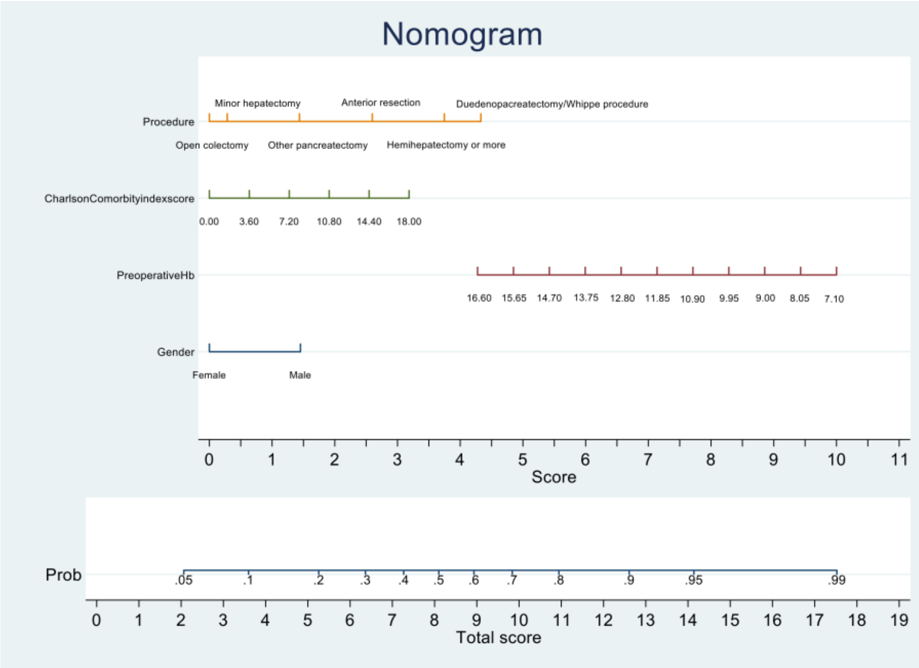

Fig. 2. Nomogram for predicting perioperative blood transfusion. Negative coefficient in variable perioperative haemoglobin was forced positive to facilitate the calculation so that the nomogram can be used by adding scores up only, instead of adding and subtracting scores.

The model fit was further assessed using a calibration plot (Fig. 4). The calibration plot revealed a satisfactory fit of the model predicting perioperative blood transfusion as the predictions fell along the 45° diagonal line.

The discriminative ability of the nomogram by Kim *et al.*[10] and our model were compared using AUC in Figure 5. It was observed that our model (AUC: 0.754) has better discriminative ability compared to the model by Kim *et al.* (AUC: 0.650). The sensitivity and specificity for the nomogram by Kim *et al.* was 43.41% and 76.83%, respectively; for ours, it was 62.02% and 76.83%, respectively. Our score has better sensitivity than the score by Kim *et al.*, with comparable specificity.

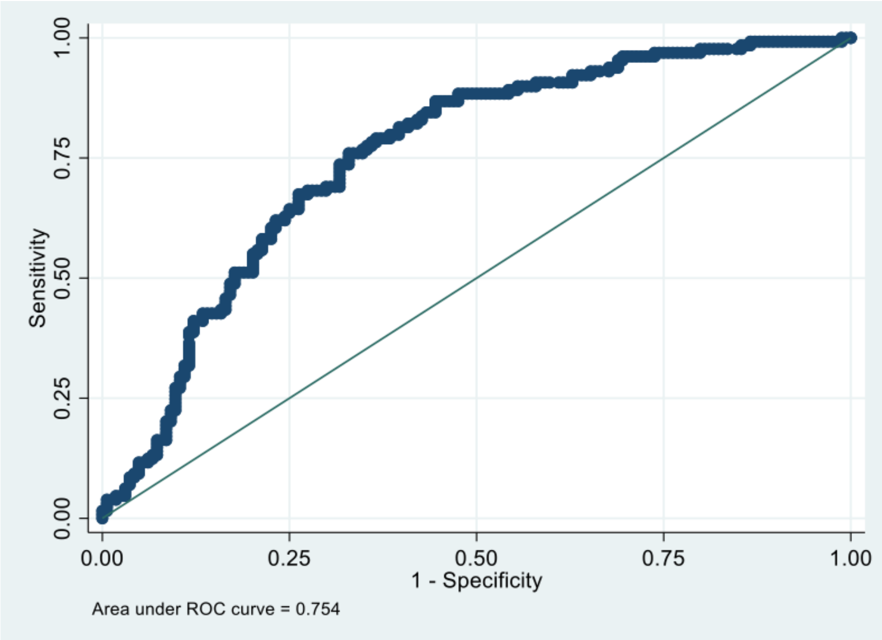

Fig. 3. Receiver operating characteristics (ROC) curve for the nomogram model.

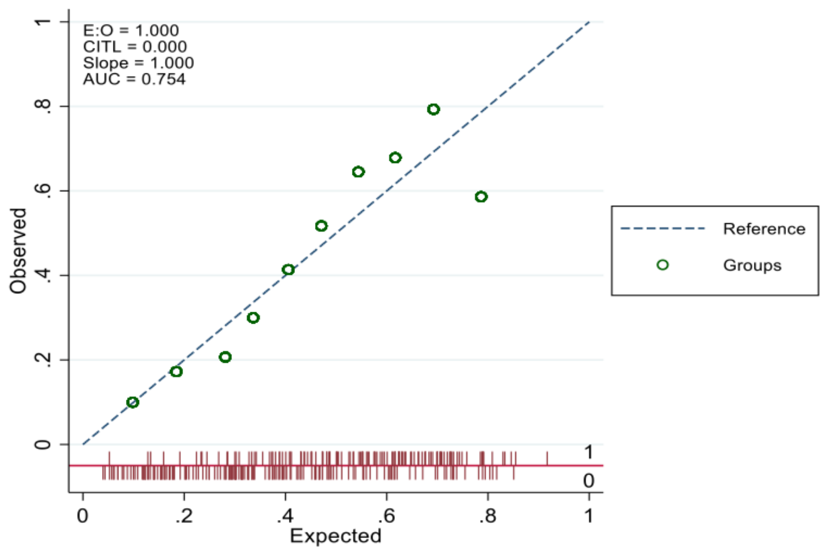

Fig. 4. Calibration plot for the nomogram model.

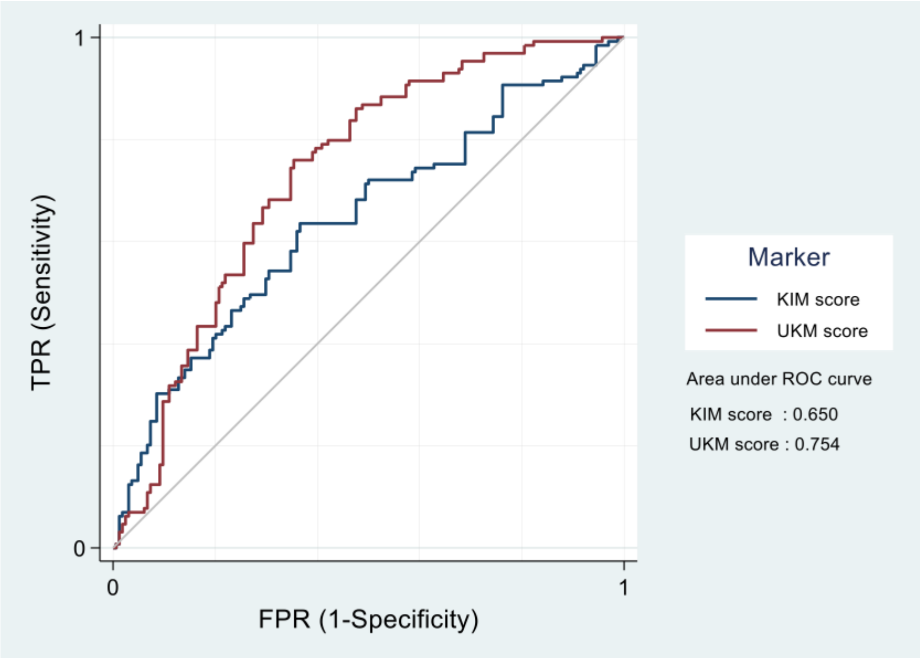

Fig. 5. Comparison of receiver operating characteristics (ROC) curves for the Kim *et al.* nomogram and our newly generated nomogram.

Discussion

Preoperative anaemia as an independent risk factor for adverse outcomes in major hepatobiliary and colorectal surgeries is well documented in the literature.[12,13] Even though transfusion of packed red blood cells can be vital in patients with severe anaemia, it also carries risk of complications and morbidity.[2] These include reduced immune function and transfusion-related events, such as infection and lung injury.[14] Therefore, to facilitate effective management of blood transfusions and reduce morbidity, early identification of patients who would require transfusions is useful.[15] The present study found no association between BMI, age, preoperative platelet count, and receipt of blood transfusions, as in the study by Pulitano *et al.*[16] Other sociodemographic variables were, however, predictive of increased odds of transfusions, such as gender, type of procedure, and CCI. Roubinian *et al.* found that preoperative variables such as age, comorbidities, type of surgery, and preoperative serum haemoglobin levels were enough to develop a model with high accuracy and performance in both medical and surgical cohorts of patients.[17]

Preoperative haemoglobin (OR 0.777, $p < 0.001$) emerged as the strongest factor in predicting whether a patient would require a transfusion in our study, as it carries the highest weightage in terms of points in the nomogram. As expected, similar results have been found by other groups.[18,19] A recent study found that serum haemoglobin greater than 13 g/dl reduces the risk of transfusions. Rather than just focusing solely on the level of haemoglobin, the inclusion of preoperative patient characteristics may help in deciding whether to transfuse or not and lead to much more effective blood management.[17]

CCI is another factor that is significant in this study (OR 1.14, $p = 0.049$). In 1987, Mary Charlson and coworkers devised the CCI, a numerical score that indicates how likely a patient is to die within a year of being hospitalised based on the presence of certain comorbid conditions.[20] The index covered a total of 19 medical issues. Every condition was assigned a score between 1 and 6 in order to calculate the hazard ratio for dying within a year using the Cox proportional hazards model. A total of these values was used to calculate the CCI score. Although CCI dates back more than 30 years, it still has a place in current practise. In 2017, Lakomkin *et al.* found that a higher CCI score was associated with an increased incidence of complications, transfusions events, and length of stay following revision hip arthroplasty.[21] Lee *et al.* showed that CCI score is one of the main predictors of mortality and blood transfusion among COVID-19 patients as recently as 2022.[7]

We noted that our patient cohort had a higher prevalence of anaemia (61.1 %) compared to the global prevalence dataset (23.2%) and among the dataset from Zwiep *et al.*, who studied the prevalence of anaemia in hepatopancreatic biliary patients (44.1%).[22,23] This variation in anaemia prevalence may have resulted in the limited utility of the Kim *et al.* nomogram outside the control cohort and may need to be recalibrated to retain generalizability.[24] The mean number of packed red blood cells transfused in this study was 2 (IQR 1–3), which is the same as the study by Kim *et al.*[10] In a large multicentre study, Kooby et al. reported that 43% of liver resection patients who needed a transfusion received only 1 to 2 units of packed red blood cells.[25]

To improve clinical utility and ease of use, a nomogram grading system was developed from commonly gathered preoperative data. The nomogram has good discrimination and calibration, and its performance has been internally verified. Most commonly, serum haemoglobin levels with wide variation in practice is used to decide on transfusion.[26] While many risk scoring tools have been developed to identify those at risk of requiring perioperative blood transfusions in other surgical fields, especially cardiothoracic surgery, this has not been the case in the hepatobiliary and colorectal field. Recently, Kim *et al.* developed a nomogram to predict the likelihood of blood transfusion in major hepatobiliary and colorectal surgery consisting of 7 factors with an area under ROC curve of 0.756 on internal validation. However, our validation of Kim's nomogram with dataset from our population resulted in an area under ROC curve of only 0.650. The lack of agreement between the predicted and observed probability of transfusion may be attributed to variations in perioperative haematological profiles, as well as differences in the demographic composition and racial diversity of the sample group.[27]

A particular strength of this study was that it advocates a patient profile adjusted to the Malaysian population. To provide safer therapy and better coordination of the blood management system, it is crucial to identify individuals at greater risk. Questions regarding the most effective way to care for a patient at increased risk arise as blood systems are increasingly focused on safe and responsible use of healthcare resources. As a result, this research provides a risk classification tool to guide decision making to boost cost-effectiveness and patient outcomes. Transfusion decisions are determined by the surgeon or anaesthesiologist in charge, who will take into account the patient's medical history and other circumstances unique to the case. However, each individual's clinical experience is bound by a unique set of constraints, making it challenging to standardise. Using the obtained retrospective data, we devised a simple and accurate scoring system to predict the risk of blood transfusion for patients having major colorectal and hepatobiliary surgery.

As a retrospective database analysis, our research is subject to the usual caveats, such as biases and erroneous data collection, as well as unaccounted-for confounders. This single-centre design meant that the sample size was limited, which could compromise the generalizability of results, as well as underpowered to detect other risks that could have significant impact on transfusions in major hepatobiliary and colorectal surgery. Potential unaccounted-for determinants of blood transfusion include surgeon expertise and other provider-level characteristics. Finally, further evaluation of this nomogram as a blood transfusion risk prediction tool, ideally using a prospective cohort study design with a larger sample size in a main hepatobiliary and colorectal centre is needed to ascertain its utility.

Conclusion

In summary, a nomogram using predictor variables of gender, type of surgery, preoperative haemoglobin level, and CCI score predicted the risk of perioperative blood transfusions with a good performance in our cohort of patients who underwent major hepatobiliary and colorectal surgeries. Further prospective studies are warranted to externally validate the performance of this nomogram and to evaluate whether this nomogram can provide better guidance for clinicians to intervene perioperatively.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and approved by the Medical Research and Ethics Committee of Universiti Kebangsaan Malaysia Medical Centre (HTM-2021-028). Informed consent was not required as the data employed were retrospective.

Competing interests

None to declare.

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None to declare.

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