Article

Using a Novel Machine-Learning Algorithm as an Auxiliary Approach to Predict the Transfusion Volume in Mitral Valve Surgery

Ruirui Sang^{1,†}, Qianyi Wu^{2,†}, Shun Liu³, Kai Wu⁴, Yining Nie⁴, Xingqiu Xia⁵, He Ren⁵, Mi Jiang^{1,4}, Guowei Tu⁶, Ruiming Rong^{1,7,8}, Lai Wei^{3,*}, Rong Zhou^{1,*}

¹Department of Transfusion, Zhongshan Hospital, Fudan University, 200032 Shanghai, China

⁴Department of Transfusion, Zhongshan Hospital (Shanghai Geriatric Medical Center), Fudan University, 200032 Shanghai, China

⁵Beijing HealSci Technology Co., Ltd., 100071 Beijing, China

⁶Cardiac Intensive Care Center, Zhongshan Hospital, Fudan University, 200032 Shanghai, China

⁸Shanghai Key Laboratory of Organ Transplantation, Zhongshan Hospital, Fudan University, 200032 Shanghai, China

*Correspondence: weilai_zshospital@163.com (Lai Wei); zhou.rong1@zs-hospital.sh.cn (Rong Zhou)

[†]These authors contributed equally.

Submitted: 15 April 2024 Revised: 24 May 2024 Accepted: 30 May 2024 Published: 19 June 2024

Abstract

Background: Blood transfusion is an indispensable supportive therapy. It plays a pivotal role in the perioperative management of cardiac surgery. The aim of this study was to develop a model for predicting the transfusion volume in isolated mitral valve surgery. Methods: We gathered data from 677 patients undergoing isolated mitral valve surgery with and without simultaneous tricuspid valve operation. The dataset was partitioned into a training dataset (70%) and a testing dataset (30%). We evaluated 18 machinelearning algorithms, incorporating inputs from 36 demographic and perioperative features. Additionally, the performance of multiple linear regressions was compared with machine-learning algorithms. CatBoost was selected for further analysis, and Shapley additive explanation (SHAP) values were employed to evaluate feature importance. Finally, we explored the impact of various features on the accuracy of CatBoost by analyzing the reasons for misjudgment. Results: CatBoost outperformed all 18 machine learning algorithms with an R-squared value of 0.420, mean absolute error of 0.702, mean squared error of 1.208, and root mean squared error of 1.090, surpassing multiple linear regression. The analysis of the testing group achieved 72.5% accuracy. SHAP identified 20 pertinent features influencing transfusion volume. No significant differences were observed between correctly and incorrectly predicted groups in tricuspid valve repair, American Society of Anesthesiologists classification, or platelet count. Conclusion: CatBoost effectively predicts the intraoperative transfusion volume in mitral valve surgery, aiding clinicians in transfusion decision-making and enhancing patient care.

Keywords

CatBoost; machine learning algorithms; perioperative management in cardiac surgery; transfusion volume

Introduction

Cardiac surgery is inherently associated with a high risk of intraoperative blood loss due to its invasive nature and the use of cardiopulmonary bypass. Evidence shows that perioperative anemia-induced tissue hypoxia in patients undergoing cardiac surgery increases the risk of mortality and postoperative complications [1,2]. Red blood cell (RBC) transfusion is generally considered to enhance oxygen delivery; thus, treating anemia is the main rationale for RBC transfusion in these patients [3]. Therefore, RBC transfusion is an indispensable supportive treatment for cardiac surgery, with intraoperative RBC transfusion rates varying from 9% to 100% across 16 countries [4]. However, studies confirm that RBC transfusion during cardiac surgery is associated with an increased risk of mortality and severe morbidity, such as renal failure, pneumonia, heart failure, prolonged mechanical ventilation, and extended stay in the intensive care unit [5-7]. Therefore, determining the optimal RBC transfusion strategy for patients undergoing cardiac surgery is crucial. This strategy involves the right indication, the appropriate quantity of RBC transfusion, and the correct timing. Although comprehensive RBC transfusion practice guidelines exist globally, in mitral valve surgery, surgeons often rely on their past experience to estimate a patient's anticipated blood consumption. Unfortunately, due to time constraints, doctors often base their predictions on a few indicators during surgery, which may result in unreliable estimates. Further-

²School of Computer Science, Fudan University, 200437 Shanghai, China

³Department of Cardiovascular Surgery, Zhongshan Hospital, Shanghai Cardiovascular Institution, Fudan University, 200032 Shanghai, China

⁷Department of Urology, Zhongshan Hospital, Fudan University, 200032 Shanghai, China

Publisher's Note: Forum Multimedia Publishing stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

more, some doctors tend to overestimate blood consumption to avoid liability, leading to unnecessary wastage. RBC transfusion remains one of the five most overused procedures in hospitals [8].

Cardiac surgery requires intraoperative extracorporeal circulation and often involves lengthy procedures, which increases the risk of intraoperative bleeding. It is characterized by an urgent onset, difficult operation, long operating times, large blood transfusion volumes, various complications, and high mortality [5,9,10]. The conventional methods for predicting intraoperative blood transfusions rely on formulas or personal experience. However, these approaches are limited due to the relatively few characteristic variables considered, their low prediction accuracy, the complexity of their operations, and their dependency on experience. Thus, these methods often fall short of clinical needs. Machine learning models have demonstrated the ability to predict individual outcomes by integrating diverse patient characteristics and have been successfully applied across various healthcare domains [11-13]. Although previous machine learning algorithms could reliably predict the need for transfusions, predicting the specific amount of RBC units to be transfused remains more challenging [14]. Given the substantial volume of blood involved and the numerous factors affecting blood transfusion in cardiac surgery, only a limited number of studies have employed models to address this issue effectively.

In our previous research, we utilized machine learning models to predict the need for RBC transfusion during mitral valve surgery [15], but we did not predict the number of RBC units required for transfusion. The primary goal of this study was to enhance the optimization of the model to precisely predict the required number of RBC units for individual patients during mitral valve surgery. A secondary goal was to provide surgeons with secure and personalized transfusion recommendations, thereby improving the clinical care of patients.

Methods

Study Population

We gathered clinical case information for a series of patients undergoing isolated mitral valve surgery, with and without simultaneous tricuspid valve operation, at the Department of Cardiology of Zhongshan Hospital of Fudan University from January to December 2019. The surgeries encompassed both conventional and minimally invasive approaches. Patients who underwent the maze operation, aortic valve surgery, and atrial septal repair, as well as those with a history of heart surgeries (except interventional therapy), were excluded.

The study adhered to the principles of the Declaration of Helsinki (revised in 2013). The approval for data uti-

Database

The data were gathered based on literature and physician expert reviews. This included patient demographics, preoperative laboratory results, intraoperative and postoperative transfusion data, intraoperative surgical and anesthetic management data, postoperative management data and laboratory results, the occurrence of prespecified intraoperative and postoperative complications, and the duration of both intensive care unit and hospital stay in calendar days. A sepsis-related postoperative complication was defined as the presence of positive pathogens in two blood cultures. Preoperative patients were classified based on anemia severity into mild (hemoglobin >90 g/L but lower than normal), moderate (hemoglobin = 60-89 g/L), severe (hemoglobin = 30-59 g/L), and extremely severe anemia (hemoglobin <30 g/L) [16]. Acute kidney injury was defined as an increase in serum creatinine level by ≥ 0.3 mg/dL ($\geq 26.5 \mu$ mol/L) within 48 h of surgery [17]. The continuous variable international normalized ratio (INR) was converted into a categorical variable $(\langle 2, \rangle 2)$ to facilitate better clinical interpretation and application. The severity of intraoperative valve stenosis or insufficiency was assessed using cardiac ultrasonography.

The data were obtained through extraction from the electronic medical record system and manual collection. After data extraction, preliminary processing of the data was carried out by statisticians and clinicians based on literature and reviews. This involved data cleaning, missing value interpolation, and data type conversion. Missing values were handled differently for measurement and count data. For measurement data, the missing values were replaced with the average value, whereas for count data, the missing values were substituted with the most frequently occurring values. After interpolating, body mass index (BMI) and other calculable variables were recalculated. However, the missing values for outcome variables were not subjected to interpolation.

Dependent and Independent Variables

The principal objective of this study was to predict the required number of RBCs for an individual during surgery. Intraoperative RBC transfusion refers to the number of allogeneic RBCs injected during surgery, excluding autologous and postoperative blood transfusions [18].

To construct a predictive model, we selected independent variables by considering the baseline characteristics of patients, encompassing both preoperative and intraoperative variables with the potential to be associated with blood transfusion (Table 1). The numbers of intraoperative RBCs transfused were designated as the dependent variable.

variable name		Mean \pm SD	variable name		$\frac{\text{Mean} \pm \text{SD}}{\text{Mean}}$		
Age (year)		55.95 ± 13.34	Aspartate transaminase (U/L)		21.23 ± 12.39		
Body weight (kg)		64.70 ± 12.69	Alanine transaminase (U/L)		21.43 ± 17.11		
Height (cm)		164.67 ± 8.95	RBC $(10^{12}/L)$		4.33 ± 0.65		
BMI (kg/m ²)		23.75 ± 3.50	Platelet $(10^9/L)$		192.10 ± 62.11		
INR		1.70 ± 6.01	Hematocrit (%)		39.36 ± 5.08		
Prothrombin time (s)		12.83 ± 7.50	hemoglobin (g/L)		131.16 ± 18.23		
Creatinine (µmol/L)		83.20 ± 51.13	EF (%)		63.72 ± 6.82		
Variable name		n (%)	Variable name		n (%)		
Candan	Male	351 (51.85)	Mitral males and a second	No	489 (72.23)		
Gender	Female	326 (48.15)	Mitral valve replacement	Yes	188 (27.77)		
TT / -	No	441 (65.14)		No	249 (36.78)		
Hypertension	Yes	236 (34.86)	Mitral valve repair	Yes	428 (63.22)		
D	No	625 (92.32)	m· · · · · ·	No	477 (70.46)		
Diabetes	Yes	52 (7.68)	Tricuspid valve repair	Yes	200 (29.54)		
	No	597 (88.18)		No	137 (20.24)		
Oral anticoagulants	Yes	80 (11.82)	Autologous blood transfusion	Yes	540 (79.76)		
	1	8 (1.18)		No	461 (68.09)		
NYHA	2	250 (36.93)		Mild	99 (14.62)		
	3	51 (7.53)	Tricuspid regurgitation	Moderate	86 (12.70)		
	4	368 (54.36)		Severe	31 (4.58)		
	No	289 (42.69)		No	589 (87.00)		
Pulmonary arterial hypertension	Yes	388 (57.31)	Preoperative anemia	Mild	78 (11.52)		
	No	546 (80.65)	1	Moderate	10 (1.48)		
Atrial fibrillation	Yes	131 (19.35)		1	1 (0.15)		
Infective endocarditis INR	No	636 (93.94)		2	26 (3.84)		
	Yes	41 (6.06)	ASA	3	601 (88.77)		
	<2	637 (94.09)		4	49 (7.24)		
	>2	40 (5.91)		No	653 (96.45)		
	Doc 1	78 (11.52)	Preoperative cerebral infarction	Yes	24 (3.55)		
Surgeon_id	Doc 2	38 (5.61)		No	517 (76.37)		
	Doc 3	34 (5.02)		Mild	28 (4.14)		
	Doc 4	56 (8.27)	Mitral stenosis	Moderate	70 (10.34)		
	Doc 5	44 (6.50)		Severe	62 (9.16)		
	Doc 6	44 (6 50)		No	51 (7 53)		
	Doc_0	26 (3.84)	Mitral regurgitation	Mild	47 (6 94)		
	Doc 8	64 (9.45)		Moderate	264 (39.00)		
	Doc_0	20 (2.95)		Severe	315 (46 53)		
	$Doc_{-}10$	98(1448)		Minimally invasive	216 (31 91)		
	Doc_{10}	32 (4 73)	Surgical method	Routine	461 (68 09)		
	Doc_{11}	21 (3.10)		No	651 (96 16)		
	Doc_{12}	38 (5.61)	Acute coronary syndrome	Yes	26 (3.84)		
	Doc_{13}	20 (2.95)		100	20 (0.04)		
	Doc_{14}	20(2.93) 31(4.58)					
	Doc_15	31(+.30)					
	100_10	33 (4.87)					

Table 1. Information on variables.

Abbreviations: EF, ejection fractions; INR, international normalized ratio; NYHA, New York Heart Association; ASA, American Society of Anesthesiologists; BMI, body mass index; RBC, red blood cell.

Model Selection and Training

The database was randomly split into a training dataset (70%) and a test dataset (30%), and 18 machine learning algorithms, including CatBoost, were employed for calculation. Tenfold cross-validation was implemented in the training dataset. These machine learning algorithms were

frequently employed to predict continuous variables. Each algorithm had unique characteristics and exhibited varying performance based on distinct prediction scenarios. This study chose the most effective algorithms for detailed analysis through a comparative evaluation of model performance. We calculated the mean absolute error (MAE), the mean squared error (MSE), the root MSE (RMSE), and

NO.	Model	MAE	MSE	RMSE	R^2	RMSLE
1	CatBoost Regressor	0.702	1.208	1.090	0.420	0.463
2	Random Forest	0.697	1.217	1.080	0.364	0.495
3	Extra Trees Regressor	0.685	1.244	1.095	0.344	0.482
4	Light Gradient Boosting Machine	0.718	1.206	1.087	0.338	0.487
5	Extra Trees Classifier	0.739	1.271	1.107	0.324	0.505
6	Extreme Gradient Boosting	0.725	1.269	1.109	0.317	0.494
7	Orthogonal Matching Pursuit	0.863	1.454	1.181	0.248	0.547
8	Lasso Regression	0.917	1.563	1.221	0.194	0.560
9	Elastic Net	0.922	1.551	1.218	0.191	0.566
10	Ridge Regression	0.875	1.538	1.213	0.179	0.562
11	Bayesian Ridge	0.922	1.571	1.227	0.176	0.569
12	Linear Regression	0.879	1.555	1.220	0.166	0.564
13	Adaboost Regressor	1.069	1.581	1.241	0.153	0.657
14	K Neighbors Regressor	0.763	1.749	1.271	0.152	0.542
15	Huber Regressor	0.871	1.755	1.280	0.141	0.533
16	Lasso Least Angle Regression	1.093	2.119	1.409	-0.033	0.629
17	Support Vector Machine	0.745	2.357	1.480	-0.130	0.588
18	Decision Tree	0.807	2.313	1.512	-0.297	0.643

Table 2-1. Performance results of each machine-learning models.

MAE, mean absolute error; MSE, mean squared error; RMSE, root MSE; RMSLE, root mean squared logarithmic error.

Table 2-2. Performance results of multiple linear regression

model.							
MLR	MAE	MSE	RMSE	R^2	RMSLE		
Backward elimination	0.886	1.179	1.086	0.318	0.240		
Forward selection	0.886	1.179	1.086	0.318	0.240		
Stepwise regression	0.877	1.167	1.080	0.332	0.239		

MLR, multiple linear regression.

the root mean squared logarithmic error (RMSLE) between the predicted and actual values of RBC transfusion units as the primary metrics of accuracy to compare the performance of these models. The MAE represents the average absolute difference between the actual and predicted values in the dataset, whereas the MSE represents the average squared difference between the original and predicted values in the dataset. The RMSE is the square root of MSE. RMLSE is computed by taking the logarithm of both the actual and predicted values, followed by determining the differences between them. RMSLE is robust against outliers, as it treats small and large errors with equal importance. Smaller values of MAE, MSE, RMSE, and RMSLE indicate better model performance. Additionally, we calculated the R-squared (R^2) metrics to further analyze the accuracy of these models. The closer the R^2 to 1, the better the performance of the model.

Besides, multiple linear regressions (MLRs) were executed on the database, employing three stepwise-type procedures: forward selection, backward elimination, and stepwise regression. The performance of MLR was then compared with that of the machine learning algorithms.

Feature Ranking

The optimal model, identified through comparison, was further analyzed using Shapley additive explanation (SHAP) values to evaluate feature importance (https://github.com/slundberg/shap) [19]. Following model training, a partial dependency graph (PDP or PD graph) was used to calculate the SHAP value for each feature. The SHAP value served as a metric to measure the contribution rate of each feature within the model, whether positively or negatively. By leveraging these calculations, a matrix of SHAP values was generated, providing a visualization of each feature's contribution to the model predictions. This analysis helped us explain the role of each feature in the model.

Statistical Analysis

IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA) and Python 3.6 (https://www.py thon.org/, Python Software Foundation, Wilmington, DE, USA) were used in this study, with the Python packages Scikit-learn, SHAP (feature analysis), and matplotlib (visualization). Continuous variables were summarized using the mean and standard deviation, whereas categorical variables were presented as proportions. A one-way analysis of variance was employed to compare the means across different groups. The chi-square test was used to identify any significant associations between variables and assess the distribution of each feature between the accurate prediction and misjudgment groups.



Fig. 1. Plot showing the relative importance of different variables for predicting how many units of RBC an individual patient will require during mitral valve surgery as derived from the CatBoost Regressor model. (A) The histogram shows the importance of different variables in predicting the amounts of intraoperative RBC transfusion units, sorted by importance from high to low. (B) Blue and green colors represent high and low levels of each predictor. The x-axis represents the SHAP value. A positive SHAP value implies likelihood of increase in use of intraoperative RBC transfusion units; a negative value means unlikelihood of increase in use of intraoperative RBC, red blood cell; SHAP, shapley additive explanation.

Results

RBC Transfusion

A total of 677 patients were included in the final dataset. Table 1 provides an overview of the demographic and perioperative data. The average age of the patients was 55.95 ± 13.34 years, and 48.15% of patients were female. The mean preoperative hematocrit was $39.36\% \pm 5.08\%$. Among these patients, 166 (24.52%) received intraoperative RBC transfusion, with transfusion amounts ranging from 2 and 10 units. Patients who did not receive blood transfusions were recorded as having 0 units. The average RBC transfusion was 0.71 ± 1.43 units.

The Best Model for Predicting the Intraoperative RBC Transfusion Units and Feature Importance

The training dataset was used to optimize the hyperparameters for each model. Table 2-1 and Table 2-2 present the performance results of each machine learning model and MLR. Among the models evaluated, the Cat-Boost model best predicted intraoperative transfusion requirements. Specifically, the CatBoost model achieved an

 R^2 value of 0.420, with MAE of 0.702, MSE of 1.208, RMSE of 1.090, and RMSLE of 0.463 in regression analysis.

The variables significantly influencing the amount of intraoperative RBC transfusion units included preoperative hematocrit, age, surgeon ID, body weight, height, BMI, surgical method, anemia, preoperative hemoglobin, and preoperative RBC counts, among others (Fig. 1). Further, the analysis also revealed the relative contribution of each variable in predicting the amount of intraoperative RBC transfusion units. Notably, preoperative hematocrit emerged as the most crucial feature for predicting the amounts of intraoperative RBCs transfused (Fig. 1). The impact of the main factors on the outcome variables is illustrated in Fig. 2A, whereas Fig. 2B illustrates the correlation between different surgeons and the quantities of intraoperative RBC transfusion.

Further analysis using the CatBoost model revealed that hematocrit (<37.88%), age (>64 years), body weight (<60.25 kg), BMI (<21.79 kg/m²), hemoglobin (<122.28 g/L), surgical method (median thoracotomy surgery), height (<161.28 cm), preoperative RBC counts (<3.87 × 10^{12} /L), and sex (female) were the main factors influencing the likelihood of increasing RBC transfusion units (Fig. 3).



Fig. 2. Main effects of each risk factor and outcome variable. (A) Effects of main risk factors on outcome variable. Surgical method includes Minimally Invasive (1) or Routine (2). Anemia includes No (0), Mild (1), or Moderate (2). Tricuspid regurgitation includes No (0), Mild (1), Moderate (2), or Severe (3). (B) SHAP value for the surgeon. When it was greater than 0, the surgeon was more likely to advise an increase in use of intraoperative RBC transfusion units.

Analysis of Reasons for Misjudgment

Of the 204 patients examined, 148 were accurately predicted (72.5%) and classified into the accurate prediction group. Ten were classified into the larger group, where the predicted value of RBC units exceeded the actual amount by more than 1 unit, whereas 46 patients were classified into the smaller group, where the predicted value of RBC units was more than 1 unit lower than what the patients actually received (Table 3).

The distribution of three features [tricuspid valve repair, American Society of Anesthesiologists (ASA) classification, and platelets] was not significantly different among groups. However, the distribution of other features, including demographics and laboratory results, exhibited significant differences among the three groups (Table 3).

Discussion

The CatBoost algorithm better predicted the intraoperative RBC transfusion units by incorporating 36 characteristics associated with patients undergoing cardiac surgery. Unlike traditional approaches where doctors rely on their experience to select a limited number of indicators for prediction, our algorithm incorporated 36 demographic and pe-



Fig. 3. The boundary values of main factors influencing the likelihood of increase in use of RBC transfusion units. Within the boundary values, the clinicians were more likely to advise an increase in use of intraoperative RBC transfusion units.

rioperative features. Our algorithm significantly enhanced the accuracy of predicting blood volume in cardiac surgery by analyzing the importance of various factors using SHAP values. The model provided safe and individualized datadriven recommendations for a patient's intraoperative RBC transfusion volume, achieving an accuracy rate of up to 72.5%.

Some studies have developed blood volume prediction formulas to enhance the accuracy of predicting blood volume [20]. These formulas typically employ multiple linear regression methods to predict surgical blood volume. However, as presented in Table 2-2, traditional machine learning algorithms such as decision trees, random forests, and the CatBoost outperformed linear regression algorithms in terms of evaluation indicators. This superiority could be attributed to the linear constraints of prediction formulas, limiting their ability to capture nonlinear relationships among features. In contrast, the machine learning algorithms can account for these nonlinear relationships, leading to higher prediction accuracy. As demonstrated in Table 2-1, decision trees and random forests achieve high accuracy in predicting surgical blood volume. However, although these machine learning algorithms excel in various domains, they may lack specialization in predicting surgical blood volume. Therefore, the scope still exists for further improvement in the prediction accuracy of learning algorithms within the specific domain of surgical blood volume prediction. The CatBoost algorithm employed in this study was optimized for predicting blood volume in cardiac surgery. CatBoost demonstrated superior performance compared with traditional machine learning algorithms by considering 36 characteristics specific to patients undergoing cardiac surgery. Its focus on the nuances of cardiac surgery enhanced its relevance and accuracy in predicting blood volume during these procedures.

CatBoost addressed the overfitting issue and enhanced the model's generalization capability and robustness, making it suitable for scenarios involving small sample sizes and unbalanced data. CatBoost reduced bias and improved the generalization ability of the model using order boosting instead of traditional gradient estimation methods. The Cat-Boost feature ranking indicated that variables such as hematocrit, age, surgeon ID, body weight, height, BMI, type of surgery, anemia, hemoglobin, and preoperative RBC counts were the primary factors affecting the amount of intraoperative RBC transfusion units, as illustrated in Fig. 1, which was consistent with previous findings [21]. Clinicians can use this feature ranking to adjust potentially modifiable fac-

Table 3. Analyzing the reasons for misjud	Igment through the distributio	n of main factors among groups
---	--------------------------------	--------------------------------

	Missing	Overall	Larger	Smaller	Accurate	n
	Wissing	n = 204	n = 10	n = 46	n = 148	P
Gender, <i>n</i> (%)	0					< 0.001*
Male		112 (54.9)	2 (20.0)	13 (28.3)	97 (65.5)	
Female		92 (45.1)	8 (80.0)	33 (71.7)	51 (34.5)	
Age, mean (SD)	0	54.9 (13.8)	59.2 (11.8)	63.5 (12.7)	51.9 (13.1)	< 0.001*
Weight, mean (SD)	0	64.9 (13.0)	56.7 (8.4)	54.9 (9.0)	68.6 (12.4)	< 0.001*
Height, mean (SD)	0	164.6 (9.1)	156.9 (6.5)	158.8 (7.4)	166.8 (8.7)	< 0.001*
BMI, mean (SD)	0	23.8 (3.5)	23.0 (2.6)	21.7 (3.1)	24.5 (3.4)	< 0.001*
Preoperative RBC, mean (SD)	0	4.4 (0.7)	3.7 (0.4)	4.0 (0.6)	4.5 (0.6)	< 0.001*
Preoperative Hematocrit, mean (SD)	0	39.9 (4.8)	34.3 (3.4)	36.3 (5.4)	41.4 (3.7)	< 0.001*
Preoperative Hemoglobin, mean (SD)	0	132.5 (17.8)	111.5 (12.9)	119.2 (20.1)	138.1 (13.6)	< 0.001*
Surgical method, n (%)	0					0.001
Minimally invasive		73 (35.8)	2 (20.0)	6 (13.0)	65 (43.9)	
Routine		131 (64.2)	8 (80.0)	40 (87.0)	83 (56.1)	
Heparin, mean (SD)	0	191.6 (44.9)	167.4 (23.8)	169.6 (43.8)	200.1 (43.5)	< 0.001*
Intraoperative blood transfusion, mean (SD)	0	0.7 (1.4)	0.0 (0.0)	3.0 (1.5)	0.0 (0.0)	< 0.001*
Intraoperative plasma transfusion, mean (SD)	0	108.8 (209.4)	40.0 (126.5)	473.9 (135.7)	0.0 (0.0)	< 0.001*
Postoperative hemoglobin, mean (SD)	0	110.9 (14.3)	96.8 (9.8)	104.0 (13.3)	114.0 (13.5)	< 0.001*
Postoperative RBC, mean (SD)	0	3.7 (0.5)	3.2 (0.3)	3.5 (0.4)	3.8 (0.5)	< 0.001*
Postoperative Hematocrit, mean (SD)	0	32.9 (4.9)	29.6 (3.1)	30.4 (5.3)	33.9 (4.6)	< 0.001*
Postoperative length of stay, mean (SD)	0	7.4 (4.1)	7.2 (1.2)	9.5 (7.2)	6.8 (2.4)	< 0.001*
Atrial fibrillation, n (%)	0					< 0.001*
No		170 (83.3)	8 (80.0)	29 (63.0)	133 (89.9)	
Yes		34 (16.7)	2 (20.0)	17 (37.0)	15 (10.1)	
ASA, n (%)	0					0.14
2		13 (6.4)	0	0	13 (8.8)	
3		172 (84.3)	10 (100.0)	37 (80.4)	125 (84.5)	
4		19 (9.3)	0	9 (19.6)	10 (6.8)	
Surgeon_id	0					0.002
Doc_1		12 (5.9)	0	2 (4.3)	10 (6.8)	
Doc_2		9 (4.4)	0	3 (6.5)	6 (4.1)	
Doc_3		18 (8.8)	1 (10.0)	2 (4.3)	15 (10.1)	
Doc_4		15 (7.4)	1 (10.0)	4 (8.7)	10 (6.8)	
Doc_5		18 (8.8)	0	5 (10.9)	13 (8.8)	
Doc_6		6 (2.9)	0	1 (2.2)	5 (3.4)	
Doc_7		22 (10.8)	0	1 (2.2)	21 (14.2)	
Doc_8		5 (2.5)	1 (10.0)	0	4 (2.7)	
Doc_9		29 (14.2)	3 (30)	17 (37)	9 (6.1)	
Doc_10		5 (2.5)	1 (10.0)	2 (4.3)	2 (1.4)	
Doc_11		9 (4.4)	0	2 (4.3)	7 (4.7)	
Doc_12		5 (2.5)	0	2 (4.3)	3 (2.0)	
Doc_13		7 (3.4)	0	0	7 (4.7)	
Doc_14		11 (5.4)	2 (20.0)	1 (2.2)	8 (5.4)	
Doc_15		9 (4.4)	0	0	9 (6.1)	
Tricuspid valve repair	0					0.002
No		153 (75.0)	4 (40.0)	29 (63.0)	120 (81.1)	
Yes		51 (25.0)	6 (60.0)	17 (37.0)	9 (6.1)	
Preoperative anemia, n (%)	0					< 0.001*
No		181 (88.7)	3 (30.0)	32 (69.6)	146 (98.6)	
Mild		22 (10.8)	7 (70.0)	13 (28.3)	2 (1.4)	
Moderate		1 (0.5)		1 (2.2)		

* *p* < 0.001.

tors when drawing conclusions from feature ranking, aiming to minimize unnecessary transfusions. In addition, the model offered precise boundary values for each factor to enhance the accuracy of predicting intraoperative RBC transfusion units (Fig. 3). Unlike traditional methods that rely on clinician experience to estimate RBC transfusion requirements, this new model could provide novel guidance in reducing unnecessary blood wastage during cardiac surgery.

We conducted an analysis to understand why misjudgments occurred, and found that certain factors exhibited statistically significant differences between the misjudgment and accurate prediction groups (Table 3). For example, patients without anemia were more likely to have their RBC transfusion values accurately predicted compared with those with mild or moderate anemia. Additionally, the misjudgment ratio was higher in female patients. This was potentially attributed to physical blood loss, as many women experience varying degrees of anemia [22]. Although factors such as tricuspid valve repair, ASA classification, and platelet count are known to influence the amount of intraoperative RBC transfusion units, our findings (Table 3 and Fig. 1) suggested that these factors did not significantly affect the misjudgment ratio of the model. This analysis provided valuable insights for further optimizing the model by comparing the distribution of each feature between the accurate prediction and misjudgment groups and analyzing the reasons for misjudgment. This model was based on retrospective registry data. The accuracy of future iterations of the model can be improved using higherfidelity data obtained through ongoing prospective data collection. Additionally, conducting a randomized controlled trial associated with this study can provide valuable validation. We strengthened the reliability of our results by incorporating multicenter data and performing robust crossvalidation. Moving forward, we plan to integrate prospective studies into our research to enhance the efficiency and accuracy of the algorithm.

The machine learning process for completing tasks operates like a black box, lacking interpretability and not being as intuitive and clear as traditional linear models. Previous studies showed that machine learning models were highly specialized and were only applicable in specific contexts. Therefore, this model applies to only patients undergoing isolated mitral valve surgery with or without concomitant tricuspid valve surgery. Developing a universal model without compromising prediction accuracy remains a key challenge for future research.

Conclusion

In conclusion, we employed a machine learning model to predict the required number of RBC units for individual patients undergoing mitral valve surgery. This model had the potential to provide clinicians with safe transfusion recommendations, aiding in the decision-making process to make preoperative orders for RBCs, enhancing patient care, and reducing unnecessary wastage of overordered RBCs. Our predictive calculator for blood product transfusion is novel. Our team is actively working on integrating this prototype calculator into future clinical workflows.

Availability of Data and Materials

Datasets are available through the corresponding authors upon reasonable request.

Author Contributions

RS and QW have contributed equally to this work and share first authorship. SL, KW, YN, MJ, GT and RR have substantially contributed to the study by collecting the data and instructing experiments. XX and HR have substantially contributed to the study by analyzing the data. All authors have contributed to the study including data curation and drafting the initial manuscript. LW and RZ contributed to the conception or design of the research. All authors contributed to editorial changes in the manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

The study adhered to the principles of the Declaration of Helsinki (revised in 2013). Approval for the utilization of data in research was granted by the Zhongshan Hospital Institutional Review Board (IRB) (NO.: B2020-218), with patient consent waived.

Acknowledgment

Not applicable.

Funding

This work was supported by the Science Fund for Management of Hospital affiliated to Fudan University (FDYGC20230501).

Conflict of Interest

The authors declares no conflict of interest. GT serves as editorial board member of this journal. GT declares that he was not involved in the processing of this article and has no access to information regarding its processing. XX and HR are the employee of Beijing HealSci Technology Corporation. The company had no role in the study design, data collection, data analysis, interpretation of data, writing of the manuscript, or the decision to submit the manuscript for publication.

References

- Cholette JM, Rubenstein JS, Alfieris GM, Powers KS, Eaton M, Lerner NB. Children with single-ventricle physiology do not benefit from higher hemoglobin levels post cavopulmonary connection: results of a prospective, randomized, controlled trial of a restrictive versus liberal red-cell transfusion strategy. Pediatric Critical Care Medicine. 2011; 12: 39–45.
- [2] Desmet L, Lacroix J. Transfusion in pediatrics. Critical Care Clinics. 2004; 20: 299–311.
- [3] Székely A, Cserép Z, Sápi E, Breuer T, Nagy CA, Vargha P, et al. Risks and predictors of blood transfusion in pediatric patients undergoing open heart operations. The Annals of Thoracic Surgery. 2009; 87: 187–197.
- [4] Snyder-Ramos SA, Möhnle P, Weng YS, Böttiger BW, Kulier A, Levin J, *et al.* The ongoing variability in blood transfusion practices in cardiac surgery. Transfusion. 2008; 48: 1284–1299.
- [5] Engoren MC, Habib RH, Zacharias A, Schwann TA, Riordan CJ, Durham SJ. Effect of blood transfusion on long-term survival after cardiac operation. The Annals of Thoracic Surgery. 2002; 74: 1180–1186.
- [6] Koch CG, Li L, Duncan AI, Mihaljevic T, Cosgrove DM, Loop FD, et al. Morbidity and mortality risk associated with red blood cell and blood-component transfusion in isolated coronary artery bypass grafting. Critical Care Medicine. 2006; 34: 1608–1616.
- [7] Paone G, Brewer R, Theurer PF, Bell GF, Cogan CM, Prager RL, et al. Preoperative predicted risk does not fully explain the association between red blood cell transfusion and mortality in coronary artery bypass grafting. The Journal of Thoracic and Cardiovascular Surgery. 2012; 143: 178–185.
- [8] Hofmann A, Spahn DR, Holtorf AP, PBM Implementation Group. Making patient blood management the new norm(al) as experienced by implementors in diverse countries. BMC Health Services Research. 2021; 21: 634.
- [9] Marik PE, Corwin HL. Efficacy of red blood cell transfusion in the critically ill: a systematic review of the literature. Critical Care Medicine. 2008; 36: 2667–2674.
- [10] Leal-Noval SR, Rincón-Ferrari MD, García-Curiel A, Herruzo-Avilés A, Camacho-Laraña P, Garnacho-Montero J, et al. Trans-

fusion of blood components and postoperative infection in patients undergoing cardiac surgery. Chest. 2001; 119: 1461– 1468.

- [11] Jalali A, Buckley EM, Lynch JM, Schwab PJ, Licht DJ, Nataraj C. Prediction of periventricular leukomalacia occurrence in neonates after heart surgery. IEEE Journal of Biomedical and Health Informatics. 2014; 18: 1453–1460.
- [12] Jalali A, Simpao AF, Gálvez JA, Licht DJ, Nataraj C. Prediction of Periventricular Leukomalacia in Neonates after Cardiac Surgery Using Machine Learning Algorithms. Journal of Medical Systems. 2018; 42: 177.
- [13] Lundberg SM, Nair B, Vavilala MS, Horibe M, Eisses MJ, Adams T, *et al.* Explainable machine-learning predictions for the prevention of hypoxaemia during surgery. Nature Biomedical Engineering. 2018; 2: 749–760.
- [14] Tschoellitsch T, Böck C, Mahečić TT, Hofmann A, Meier J. Machine learning-based prediction of massive perioperative allogeneic blood transfusion in cardiac surgery. European Journal of Anaesthesiology. 2022; 39: 766–773.
- [15] Liu S, Zhou R, Xia XQ, Ren H, Wang LY, Sang RR, et al. Machine learning models to predict red blood cell transfusion in patients undergoing mitral valve surgery. Annals of Translational Medicine. 2021; 9: 530.
- [16] McLean E, Cogswell M, Egli I, Wojdyla D, de Benoist B. Worldwide prevalence of anaemia, WHO Vitamin and Mineral Nutrition Information System, 1993-2005. Public Health Nutrition. 2009; 12: 444–454.
- [17] Levey AS, Eckardt KU, Dorman NM, Christiansen SL, Hoorn EJ, Ingelfinger JR, *et al.* Nomenclature for kidney function and disease: report of a Kidney Disease: Improving Global Outcomes (KDIGO) Consensus Conference. Kidney International. 2020; 97: 1117–1129.
- [18] Pieri M, Nardelli P, De Luca M, Landoni G, Frassoni S, Melissano G, et al. Predicting the Need for Intra-operative Large Volume Blood Transfusions During Thoraco-abdominal Aortic Aneurysm Repair. European Journal of Vascular and Endovascular Surgery. 2017; 53: 347–353.
- [19] Rube HT, Rastogi C, Kribelbauer JF, Bussemaker HJ. A unified approach for quantifying and interpreting DNA shape readout by transcription factors. Molecular Systems Biology. 2018; 14: e7902.
- [20] Jalali A, Lonsdale H, Zamora LV, Ahumada L, Nguyen ATH, Rehman M, et al. Machine Learning Applied to Registry Data: Development of a Patient-Specific Prediction Model for Blood Transfusion Requirements During Craniofacial Surgery Using the Pediatric Craniofacial Perioperative Registry Dataset. Anesthesia and Analgesia. 2021; 132: 160–171.
- [21] Clevenger B, Mallett SV, Klein AA, Richards T. Patient blood management to reduce surgical risk. The British Journal of Surgery. 2015; 102: 1325–1337; discussion 1324.
- [22] Mirza FG, Abdul-Kadir R, Breymann C, Fraser IS, Taher A. Impact and management of iron deficiency and iron deficiency anemia in women's health. Expert Review of Hematology. 2018; 11: 727–736.