Mathematical and Computational Applications

MDPI

Article

Predicting Red Blood Cell Transfusion in Elective Cardiac Surgery: A Machine Learning Approach

Beatriz Lau [1,*], Daniel Ramos [1], Vera Afreixo [1], Luís M. Silva [1], Ana Helena Tavares [1], Miguel Martins Felgueiras [1,2], Diana Castro Paupério [3,4] and João Firmino-Machado [3,4,5]

1 Centre for Research and Development in Mathematics and Applications, University of Aveiro, 3810-193 Aveiro, Portugal; danielsramos@ua.pt (D.R.); vera@ua.pt (V.A.); lmas@ua.pt (L.M.S.); ahtavares@ua.pt (A.H.T.); mfelg@ipleiria.pt (M.M.F.)
2 Polytechnic of Leiria and Centre for Statistics and Applications, University of Leiria, 2411-901 Leiria, Portugal
3 Local Health Unit of Vila Nova de Gaia Espinho, 4434-502 Vila Nova de Gaia, Portugal; diana.gomes@gmail.com (D.C.P.); firmino@ua.pt (J.F.-M.)
4 Egas Moniz Health Alliance Academic Clinical Centre, 3810-193 Aveiro, Portugal
5 Department of Medical Sciences, University of Aveiro, 3810-193 Aveiro, Portugal
* Correspondence: beatrizlau@ua.pt

Abstract: The benefits of Patient Blood Management can vary depending on a patient's risk profile for requiring a blood transfusion. The objective of this study is to develop and analyse machine learning models that can identify patients at risk of requiring red blood cell transfusion. This retrospective cohort study was conducted at a tertiary northern Portuguese hospital between 2018 and 2023. Two machine learning algorithms, extreme gradient boosting and neural networks, were employed due to their efficiency in handling complex feature interactions. Shapley additive explanations values were analysed to assess the contribution of each feature to the predictions generated by the models. The neural network achieved an accuracy of 0.735 and an area under the receiver operating characteristic curve of 0.798 (95% CI 0.747 to 0.849). The extreme gradient boosting model achieved an accuracy of 0.700 and an area under the receiver operating characteristic curve of 0.762 (95% CI 0.707 to 0.817). An analysis of Shapley additive explanations values revealed that the most important variable was preoperative haemoglobin levels, which can be optimised through the Patient Blood Management approach. These machine learning models demonstrate the potential to improve the accuracy of transfusion prediction at hospital admission, despite the absence of key variables such as surgeon identity and anaemia diagnosis.

Keywords: machine learning; cardiac surgery; blood transfusion

Academic Editor: Leonardo Trujillo

Received: 29 December 2024
Revised: 14 February 2025
Accepted: 20 February 2025
Published: 24 February 2025

Citation: Lau, B.; Ramos, D.; Afreixo, V.; Silva, L.M.; Tavares, A.H.; Felgueiras, M.M.; Castro Paupério, D.; Firmino-Machado, J. Predicting Red Blood Cell Transfusion in Elective Cardiac Surgery: A Machine Learning Approach. *Math. Comput. Appl.* **2025**, *30*, 22. https://doi.org/10.3390/mca30020022

1. Introduction

Cardiac surgery is well established as being associated with a considerable risk of perioperative blood loss and the need for allogeneic blood transfusions. This is due to the invasive nature of the procedures themselves, the necessity for high-dose anticoagulation, and exposure to cardiopulmonary bypass [1]. Despite its common practice, an increasing body of evidence suggests that the transfusion of one or more allogeneic blood components may be associated with an increased risk of prolonged hospital length-of-stay, morbidity, and mortality [2]. Moreover, the financial burden of transfusions is increasing, while the discrepancy between the supply and demand for this scarce resource is widening [3].

In response to this paradigm, there has been a shift in focus from the intervention itself to the patient's needs, which has led to the emergence of Patient Blood Management

(PBM) [4]. PBM is an approach that has been recognised by the World Health Organisation as representing the 'best clinical practice' [5]. It aims to preserve the patient's own blood [6] by adopting pre-operative, intra-operative, and post-operative measures, in accordance with the three pillars established by Goodnough and Shander: optimising erythropoiesis, minimising blood loss, and managing tolerance to anaemia [7]. In this way, PBM contributes to improving patient outcomes and to the reduction in healthcare costs [5]. While this approach confers benefits on all individuals undergoing cardiac surgery, the magnitude of these benefits may vary as the impact of a PBM intervention in a patient with an already low risk of blood transfusion will be less than in a patient with a high risk of blood transfusion [8]. As such, the identification of patients who are at an increased risk of requiring a blood transfusion throughout the perioperative and postoperative periods is crucial to prioritise PBM interventions.

Machine learning (ML) models, defined as algorithms capable of improving through experience and data [9,10], have shown promise in predictive tasks across different disciplines [11]. Among these, extreme gradient boosting (XGBoost) and neural networks have gained increasing attention in recent years due to their high computational efficiency and predictive accuracy [12,13]. In cardiac surgery, decision-making is a complex and important process, as it involves balancing multiple risk factors and individual patient characteristics. ML models can enhance outcomes by predicting high-risk patients, enabling healthcare providers to be more proactive and vigilant [14].

Several studies have explored the application of ML in predicting red blood cell (RBC) transfusion needs. For example, Mitterecker et al. [10] demonstrated that ML models, including gradient boosting and neural networks, achieved excellent predictive performance in predicting the need for at least one RBC transfusion across various types of surgeries, with an area under the receiver operating characteristics curve (AUROC) exceeding 0.9. Additionally, Tschoellitsch et al. [15] specifically focused on cardiac surgery and predicted massive perioperative transfusions ($\geq$10 red blood cells), with random forest and gradient boosting models achieving AUROCs of 0.810. However, despite the existence of many studies predicting red blood cell transfusion [16–24], none of these specifically focus on elective cardiac surgery, consider the context of the Portuguese National Healthcare Service, or incorporate a database that distinguishes between the presence and absence of PBM practices.

Therefore, the present study aims to develop and analyse machine learning models capable of identifying patients who underwent elective cardiac surgery and were at risk of requiring one or more red blood cell transfusions, thereby supporting healthcare professionals in assessing patients' risk levels of transfusion with and without PBM practices in a northern Portuguese healthcare setting.

2. Materials and Methods

2.1. Study Design

A prospective observational cohort study was conducted among patients who underwent elective cardiac surgery at a tertiary hospital—Vila Nova de Gaia-Espinho. Data collected from medical records were used to train and test machine learning models. This manuscript was prepared in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [25].

2.2. Settings and Participants

The study was conducted on individuals aged 18 years or older who underwent elective cardiac surgery between 2018 and 2022 at Vila Nova de Gaia-Espinho Hospital. Prior to 2019, the Patient Blood Management (PBM) approach was not applied to any

patient scheduled for elective cardiac surgery, with only anaemia screening being performed immediately before surgery.

Individuals with cognitive impairment, pregnant women, and those without data regarding allogeneic red blood cell transfusion were excluded. Reoperations were also excluded.

The data were obtained through extraction from the electronic medical records and through manual collection by an anesthesiologist.

Ethics Approval

The study was conducted in accordance with the Declaration of Helsinki, and approved by the ULSGE Ethical Health Committee, assigned with the number 196/2023. Patient consent was waived since this is an observational study (Law No. 21/2014 of April 16, amended by Law No. 73/2015 of July 27, Article 6, No. 2), and the data were fully anonymized.

2.3. Data Pre-Processing

2.3.1. Data Overview

An overview of the most important demographic and preoperative data included is presented in Table 1. The data preprocessing and cleaning were performed as follows:

1. From an initial sample of 1038 subjects, patients who had no information about the number of RBC transfused were removed, resulting in a sample of 1036 individuals;
2. Variables that contain information collected after admission were removed, as the objective was to develop a predictive model at admission time at the hospital. Moreover, variables with no information in the pre- and post-PBM datasets were also excluded. This procedure led to the final set of 14 features: age, sex, New York Heart Association classification (NYHA), Canadian Cardiovascular Society grading of angina pectoris (CCS), American Society of Anesthesiologists physical status classification (ASA), type of surgery, diagnosis of diabetes mellitus type II, hypertension and chronic kidney disease, glomerular filtration rate, creatinine, PBM approach implementation, preoperative haemoglobin level (g/L), and number of RBC transfusion;
3. NYHA, CCS, and ASA variables, were grouped into high level (III and IV), low level (I and II) and "not applicable", due to the low number of observations in levels I and IV. This led to more robust conclusions, impossible to achieve without a minimum number of observations in each category;
4. The number of RBC transfusions was recorded as a binary variable to specify the occurrence of transfusion (RBC > 0 coded as "with-transfusion") or not (RBC = 0 coded as "without-transfusion"). This transformation enabled the application of a classification model to predict the risk of an individual requiring RBC transfusion, which is the primary objective of this study;
5. All numerical variables (age, preoperative haemoglobin, glomerular filtration rate, and creatinine) were standardised using the Z-score approach, with the goal of adjusting the scales so that variables with high variance do not dominate the entire process;
6. All categorical variables were one-hot encoded, a technique that converts categorical data into binary vectors. Each vector uniquely represents a category, where a value of 1 signifies its presence, and 0 is its absence.

The models were firstly trained using the original data; however, due to the number of missing values and the imbalance between groups (with the group of patients who did not require transfusion being considerably larger), the models' performance was not acceptable, having AUROC close to 0.5. Hence, to obtain the best models, multiple imputation and data balancing techniques were applied.

Table 1. Sociodemographic and clinical data.

Characteristic	With Transfusion, N = 334 [1]	Without Transfusion, N = 702 [1]	*p*-Value [2]
Age—median [IQR]	73 [10]	69 [13]	**<0.001**
Sex—n (%)			**<0.001**
Female	204 (61%)	209 (30%)	
Male	130 (39%)	493 (70%)	
NYHA [3]—n (%)			0.183
High level (III and IV)	101 (30%)	187 (27%)	
Low level (I and II)	233 (70%)	515 (73%)	
CCS [4]—n (%)			0.200
High	68 (20%)	169 (24%)	
Low	266 (80%)	533 (76%)	
ASA [5]—n (%)			0.410
High	327 (98%)	681 (97%)	
Low	7 (2.1%)	21 (3.0%)	
High blood pressure—n (%)			0.270
No	57 (17%)	140 (20%)	
Yes	277 (83%)	562 (80%)	
Diabetes type II—n (%)			0.935
No	229 (69%)	479 (68%)	
Yes	105 (31%)	223 (32%)	
Chronic kidney disease—n (%)			**<0.001**
No	211 (63%)	556 (79%)	
Yes	123 (37%)	146 (21%)	
Dyslipidemia—n (%)			0.206
No	86 (26%)	152 (22%)	
Yes	248 (74%)	550 (78%)	
Creatinine—median [IQR]	0.90 [0.45]	0.89 [0.30]	0.104
Glomerular filtration rate—median [IQR]	65 [34]	79 [36]	**<0.001**
Pre-op haemoglobin—median [IQR]	13.00 [1.98]	14.30 [1.70]	**<0.001**
Patient blood management—n (%)			**<0.001**
Pre PBM	93 (28%)	109 (16%)	
Post PBM	241 (72%)	593 (84%)	
Surgery with extracorporeal circulation—n (%)			**<0.001**
Yes	308 (92%)	481 (69%)	
No	26 (7.8%)	221 (31%)	

[1] Median [IQR]; n (%); [2] Wilcoxon rank sum test; Pearson's Chi-squared test; [3] NYHA—New York Heart Association classification; [4] CCS—Canadian Cardiovascular Society grading of angina pectoris; [5] ASA—American Society of Anesthesiologists physical status classification.

2.3.2. Multiple Imputation

Data imputation is an important step for improving data quality and model performance [26]. For this purpose, multivariate imputation by chained equation (MICE) has emerged as one of the main methods in the statistical literature, as it is very flexible and can handle variables of different types and complexity [27]. In this study, MICE was applied separately for the pre- and post-PBM datasets to account for potential differences in the

relationships among variables. In the pre-PBM dataset, 2 out of 14 variables had more than 5% missing values, while in the post-PBM dataset, only 1 out of 14 variables had more than 5% missing values (see Figure A1 in the Appendix A). We use predictive mean matching for continuous variables, logistic regression for binary variables, and polytomous logistic regression for unordered categorical variables. Data were imputed using the **mice** package.

2.3.3. Data Balancing

The number of patients who required RBC transfusion and those who did not was imbalanced, with only 334 out of 1036 (32%) in the "with-transfusion" class. Imbalanced data can interfere with the development of effective classifiers because the lower representativeness of the minority class may lead to inadequate learning, resulting in poor predictive performance for that class [28]. In addition, it can make it difficult for evaluation metrics to accurately assess the model's performance [28].

The initial experiments with the original data showed a reduced discriminative capability of the machine learning models. To improve their predictive ability, we applied an oversampling technique called Synthetic Minority Oversampling Technique (SMOTE) to balance the classes. This technique generates synthetic samples for the minority class, increasing its size until it reaches a more balanced proportion with the majority class [29].

2.4. Models

We use the variables presented in Table 1 as inputs to develop our machine learning models. Training and test sets were created with an 80:20 ratio. A five-fold cross-validation scheme was used in the training phase to fine-tune the models, with the best hyperparameters being empirically selected in an iterative manner (see Table A1 in the Appendix A). The best model was selected according to the accuracy values obtained.

2.4.1. Extreme Gradient Boosting (XGBoost)

XGBoost belongs to the class of ensemble models and is an implementation of the more traditional gradient boosting machines focused on computational efficiency [30]. It is essentially an additive model of the form as shown below:

$$Y_B = \sum_{b=1}^{B} \alpha_b y_b$$

where each base model y_b is a decision tree. B is the number of trees in the model (usually in the order of hundreds or thousands) while the scalars α_b weigh the corresponding base model y_b in the sum according to its performance. The optimisation technique relies on a sequential application of the gradient descent method where at step m, α_m and the y_m parameters (splits and nodes of the tree) are optimised in order to correct the errors of the current model by minimising the following:

$$\sum_{n=1}^{N} E(t_n, Y_{m-1} + \alpha_m y_m)$$

over a training set of size N. $E(x, y)$ is an appropriate measure of the discrepancy between x and y and Y_{m-1} is fixed. XGBoost employs regularisation strategies (controlled by several hyperparameters) to mitigate overfitting, which is an excessive fitting of the model to the training data, leading to poor generalisation of unseen data [30,31]. The hyperparameters tuned were *max_depth*, *eta*, *gamma*, *subsample*, *min_child_weight* and *nrounds*. In the current study, the XGBoost model was developed using the **xgboost** package, while the hyper-

parameter tuning was using the **caret** package (for the final model, see Table A1 in the Appendix A).

2.4.2. Neural Network (NNs)

Neural networks are among the best-performing models for a large set of problems. Mathematically, a neural network is a composition of linear and non-linear functions that can be represented as a set of interconnected layers of simple processing units, called neurons. As Figure 1 illustrates, NNs have an input layer (whose non-processing units simply represent the input variables), one to many intermediate (hidden) layers and an output layer of neurons, constituting the architecture of the NN.

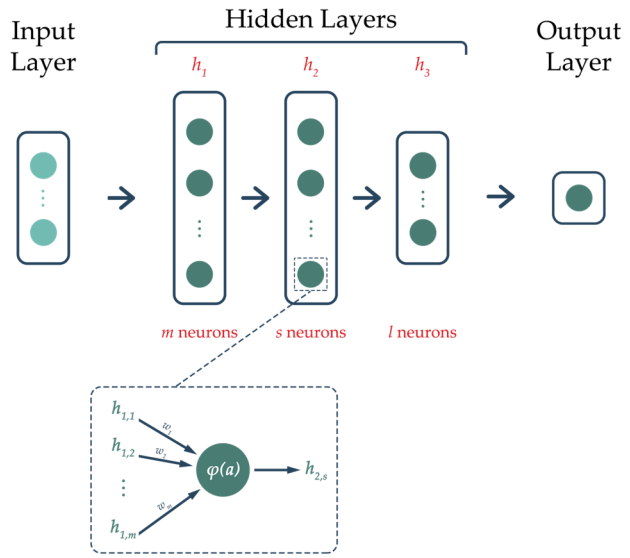


Figure 1. Schematic representation of a neural network with three hidden layers.

Each neuron computes a linear combination of its inputs (from the previous layer) followed by a non-linear function φ, the so-called activation function, enabling the algorithm to learn complex patterns and perform computationally intensive tasks [32]. For example, the output of the s^{th} neuron in the hidden layer h_2 is

$$h_{2,s} = \varphi(a) = \varphi(w_1 h_{1,1} + w_2 h_{1,2} + \cdots + w_m h_{1,m} + w_0)$$

which is then fed to the neurons of the following layer.

The optimisation of the model's weights (parameters) w_j is usually performed by gradient descent techniques, iteratively reducing the average error between the predicted and true outcome values as measured by a specific loss function. Regularisation techniques are also employed in NN training to prevent overfitting.

In this study, the NN has a single neuron at the output to cope with the 2-class nature of the problem, acting as a logistic regression layer. The NN model was developed using the **TensorFlow** and **Keras** packages. Hyperparameter tuning included adjusting the learning rate with the Adam optimizer, applying Lasso regularisation to prevent overfitting, and testing different activation functions (SoftPlus, ReLU, and ArcTan) (for the final model, see Table A1 in the Appendix A).

2.4.3. Interpretability

After training and testing the selected models, variable importance and interpretation were analysed using the Shapley additive explanations (SHAP) values. Derived from game theory, SHAP values provide an importance score for each feature, reflecting its contribution

to the model's prediction. Positive SHAP values indicate that a feature increases the value of the dependent variable, if it is numeric, or increases the probability of a particular event occurring if it is categorical. Conversely, negative SHAP values suggest that the feature has the opposite effect. The magnitude of the SHAP values represents the strength of each feature's effect on the outcome [33].

2.5. Statistical Analysis

To assess the normality of continuous variables, the Shapiro–Wilk test and QQ plot analysis were conducted. As the data did not meet the assumptions of normality, the Wilcoxon rank-sum test was used to compare median differences between groups (with- and without-transfusion). For categorical variables, the Pearson chi-squared test was applied.

Multiple imputation, data balancing, model training and testing were then carried out, with a seed of 1234 to guarantee reproducibility. The models were evaluated using different performance metrics such as accuracy, recall, specificity, area under the receiver operating characteristics curve (AUROC), F1 score and average precision (AP; the area under the precision–recall curve). To study the differences between the two AUROCs, the DeLong test was performed.

All analyses were performed using R version 4.4.1 with a significance value of 0.05.

3. Results

For the purpose of this work, we studied a cohort of patients eligible for elective cardiac surgery between 2018 and 2022 (n = 1036). Within this sample, 334 (32.2%) patients required the transfusion of at least one unit of red blood cells, while 702 patients did not. An overview of the demographic and clinical data is given in Table 1.

The median patient age was 73 for the with-transfusion group and 69 for the without-transfusion group (interquartile range of 10 and 13 years, respectively), and 39.9% of patients were women. As expected, preoperative haemoglobin was lower in the transfused group (13.00 [1.98] versus 14.30 [1.70], p-value < 0.001), as patients with lower haemoglobin levels tend to require more red blood cells transfusions.

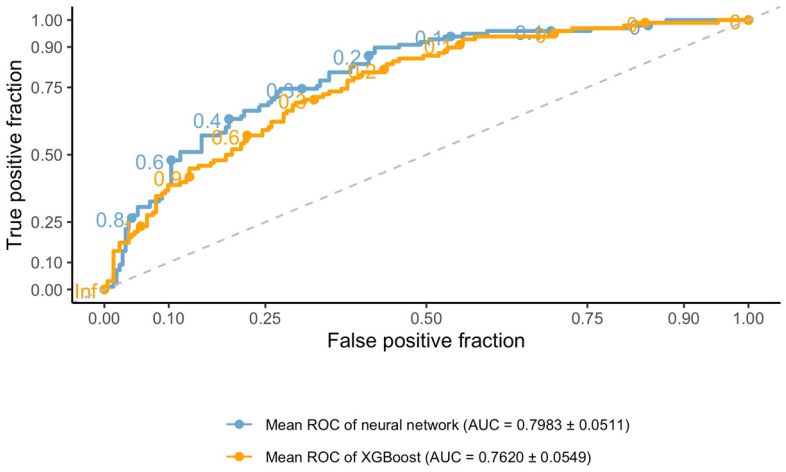
Our predictive models only partially predicted who needed transfusion of at least one unit of RBCs. Using XGBoost and NNs the AUROC was 0.762 and 0.798, respectively. Although they were different, the DeLong test showed no significant difference between those performances (p-value = 0.343). The F1 scores were 0.770 and 0.807 and the accuracies were 0.700 and 0.736, respectively (for details see Table 2 and Figure 2). Although the NN model had the best performance, its specificity is only fair (0.582), indicating that the model has more difficulty in correctly predicting the need for at least one transfusion. On the other hand, it performs well in identifying patients who did not require a transfusion (0.807).

Table 2. Evaluation of predictive models for transfusion of at least one RBC unit.

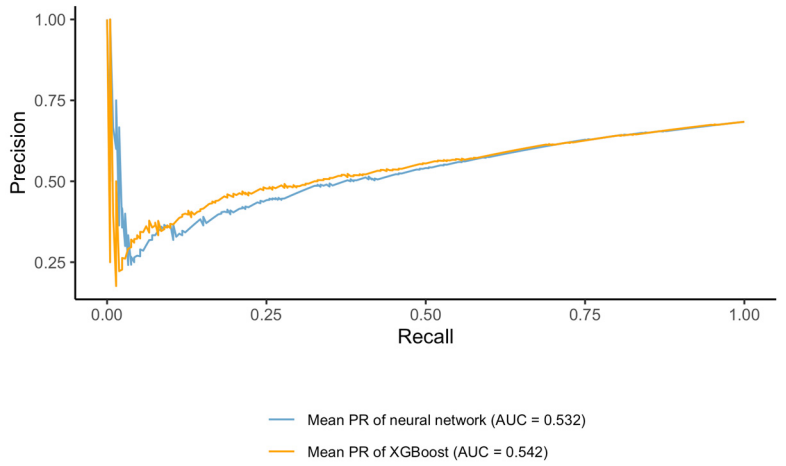
	Accuracy (Recall, Specificity)	AUROC (95% IC)	F1-Score
Neural Network	0.736 (0.807, 0.582)	0.798 (0.747–0.849)	0.807
XGBoost	0.700 (0.736, 0.622)	0.762 (0.707–0.817)	0.770

Although these two models perform similarly, the XGBoost model appears to predict with a higher probability the individuals who will require one or more RBC transfusions. This is clear in Figure 3, where a greater density of blue points is observed near the value 1 in the XGBoost model. In contrast, the neural network model exhibits a more dispersed distribution of blue points with no discernible region of higher density. However, the neural network model demonstrates a higher degree of certainty in predictions when the

probability is greater than 80%, as evidenced by a reduced number of false positives at this threshold.



(**a**)



(**b**)

Figure 2. Performance comparison of the models (**a**): ROC curves; (**b**): precision–recall curves.

The most important variables in predicting the need for transfusion of at least one unit of RBCs were preoperative haemoglobin and glomerular filtration rate (see Figure 4). Preoperative haemoglobin was negatively associated with transfusion requirement, with higher values decreasing the likelihood of transfusion requirement. This is illustrated in the graphic by the red bar extending towards the negative side. A decrease in glomerular filtration rate was associated with an increase in the likelihood of transfusion, as reflected by the negative SHAP value and a positive contribution indicated by the green bar pointing towards the positive side of the graphic.

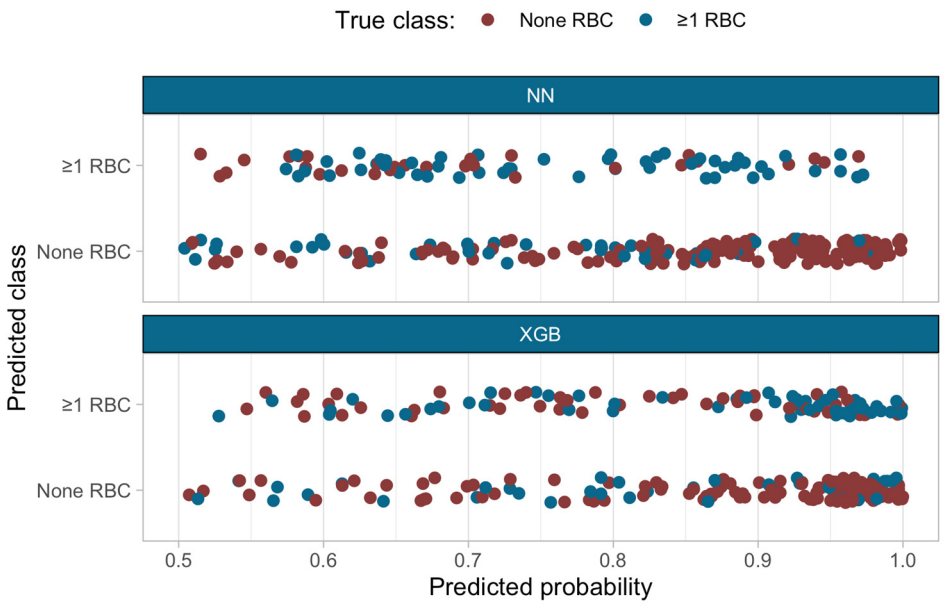
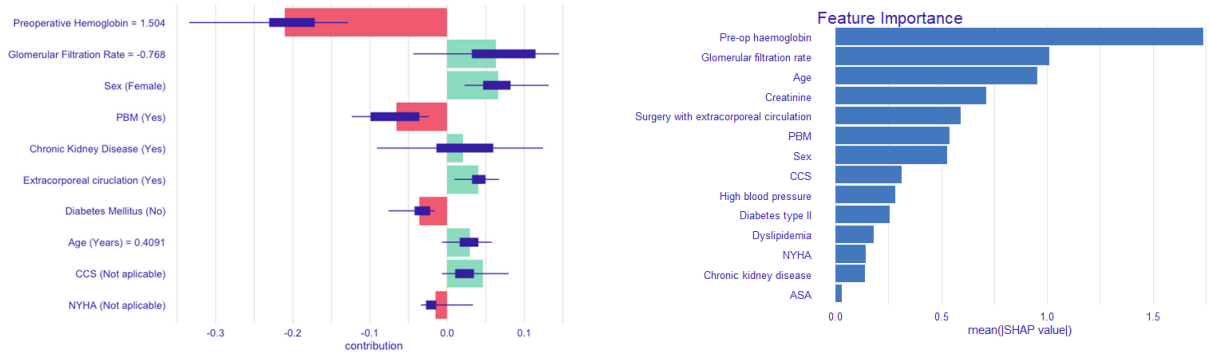


Figure 3. Prediction probabilities of the XGBoost and Neural Network models in the test set.



(**a**) (**b**)

Figure 4. Feature importance (using SHAP values) for transfusion of at least one RBC unit. (**a**): Neural Network model; (**b**): XGBoost model.

4. Discussion

Our models showed a moderate ability to effectively predict which patients would need a transfusion and which would not, with the most important variable being the haemoglobin level measured immediately before surgery.

Both of our models achieved an AUROC above 0.75, with the lower bound of the 95% confidence interval above 0.5, indicating a statistically significant ability to predict transfusion risk. In addition, our models showed similar performance to the Transfusion Risk Understanding Scoring Tool (TRUST) [34], a well-known risk score widely used in clinical practice, with the added benefit of incorporating information on the use of PBM interventions.

Nevertheless, the ability to predict at least one red blood cell transfusion could be improved. In our dataset, condition severity-related data were not explicitly available, which may have limited our models' performance. The only variable indirectly indicating it was the type of surgery. Extracorporeal circulation—known to stimulate a systemic inflammatory response following cardiac surgery, triggering complement activation, pro-inflammatory cytokine secretion, and leukocyte activation [35,36], resulting in cellular damage, bleeding disorders, anaemia, acute kidney injury, respiratory failure, haemodynamic instability, and neurological complications [37]—was performed in 92% of patients

requiring transfusion. This variable was among the top 10 most important in our models based on SHAP values, reflecting its positive association with transfusion requirements. However, it ranked below the top three features, suggesting its influence, while notable, may not be the primary determinant in our setting.

During data preprocessing, key variables such as platelet count, ferritin levels, transferrin saturation, and the International Normalised Ratio (INR)—a known predictor of transfusion requirements [38]—had to be excluded due to missing information on the pre-PBM dataset. Given the established associations of these variables with transfusion needs, their inclusion might have enhanced the models' predictive accuracy. Furthermore, collecting additional data, such as the surgical team responsible could also improve performance, as these are well-recognised factors influencing transfusion outcomes [38,39].

In both models, the most important feature identified was the haemoglobin level measured immediately before surgery, where a higher haemoglobin level was associated with a reduced need for transfusions. A principal distinction of the PBM approach in comparison to standard of care, is the preoperative anaemia assessment which identifies patients with or at risk for anaemia, enabling proactive intervention to correct haemoglobin levels before surgery. By increasing preoperative haemoglobin levels, the requirement for transfusion decreases, subsequently reducing the incidence of transfusion-associated risks, improving patient outcomes in the postoperative period [2,40]. This is a particularly relevant conclusion, as it highlights the efficacy of implementing the PBM approach within the Portuguese National Health Service.

Providing healthcare professionals with a tool able to predict the risk (probability) of requiring an allogeneic RBC transfusion, in the post-operative period, at the time of hospital admission, allows them to support the decision of prioritising high-risk individuals to receive PBM intervention. This targeted approach not only ensures personalised and patient-centred care but also helps to reduce the workload of healthcare professionals and improve overall hospital resource management through more efficient use of blood and PBM resources [41].

Strengths and Limitations

To the best of our knowledge, this is the first study to focus on predicting the need for at least one RBC transfusion in patients undergoing elective cardiac surgery using machine learning algorithms. In addition, the inclusion of individuals who underwent cardiac surgery before, during, and after the implementation of the PBM process allowed us to capture real-world clinical practice, increasing the generalisability of the results to other hospitals in the country currently adopting this approach. It is also the first study of its kind to use data from the Portuguese National Health Service. Nevertheless, certain limitations in our methodology must be acknowledged.

The limited automation in data collection resulted in a considerable number of variables with a high proportion of missing data, which prevented quality imputation, and consequently, restricted the model's predictive capacity.

Additionally, the smaller sample size, compared to other similar studies, may have further limited the model's performance.

The absence of variables that are well-established as being associated with the need for blood transfusion limited the predictive power of both models tested.

Finally, the lack of computational power prevented a more comprehensive and appropriate tuning of the hyperparameters, which had to be conducted through an iterative, empirical trial-and-error process. We believe that the employment of a more extensive grid of values for hyperparameter tuning would have resulted in an enhanced predictive capacity for both models, as well.

5. Conclusions

The application of contemporary machine learning algorithms has the potential to enhance the accuracy of transfusion prediction at the time of hospital admission. Both the XGBoost and neural network models demonstrated an AUC exceeding 0.75, despite the absence of critical core variables such as the surgical team and the diagnosis of anaemia. Despite the limited predictive capacity of the model, the interpretation of variable importance through SHAP values revealed that the implementation of the PBM approach has a significant impact on reducing transfusion needs. This, in turn, contributes to improved postoperative outcomes and more effective management of blood resources, which ultimately reduces the financial costs associated with blood transfusions. Future studies should focus on incorporating additional variables that are strongly associated with transfusion needs and using greater computational power, thereby allowing the development of a more effective tool to assist clinicians in making informed decisions regarding PBM implementation.

Author Contributions: Conceptualization, B.L. and D.R.; data collection, D.C.P. and J.F.-M.; methodology, B.L. and D.R.; formal analysis, B.L. and D.R.; writing—original draft preparation, B.L. and D.R.; writing—review and editing, V.A., L.M.S., A.H.T., M.M.F., J.F.-M., and D.C.P.; supervision, V.A., L.M.S., A.H.T., and M.M.F. All authors have read and agreed to the published version of the manuscript.

Funding: This research was partially supported by Portuguese funds through CIDMA, The Center for Research and Development in Mathematics and Applications of the University of Aveiro, and the Portuguese Foundation for Science and Technology (FCT—Fundação para a Ciência e a Tecnologia), within projects UIDB/04106/2020 (https://doi.org/10.54499/UIDB/04106/2020) and UIDP/04106/2020 (https://doi.org/10.54499/UIDP/04106/2020). B. Duarte and D. Ramos were supported by a Research Grant of the Thematic Line Biomathematics of CIDMA.

Data Availability Statement: The data used in this study were obtained from medical records collected by the author, Dr. Diana Castro Paupério, an anesthesiologist at Vila Nova de Gaia-Espinho Hospital, and are subject to ethical and privacy restrictions. To request access to the data, please contact the corresponding author.

Conflicts of Interest: The authors declare no conflicts of interest.

Appendix A

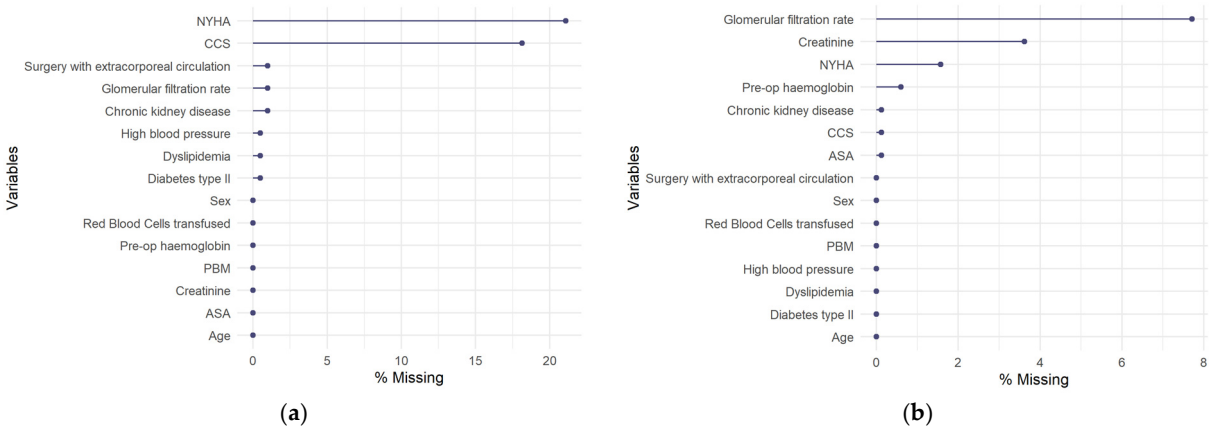


Figure A1. Missing data. (**a**): Pre-PBM dataset. (**b**): Post-PBM dataset.

Table A1. Final model.

Models	Hyperparameters	Values
Neural Network	Layers	3
	Neurons of the first layer	16
	Activation function of the first layer	ReLu
	Neurons of the second layer	16
	Activation function of the second layer	ArcTan
	Neurons of the third layer	10
	Activation function of the third layer	ReLu
	Lasso regularisation	5×10^{-5}
	Learning rate	0.004
	Epoch	500
XGBoost	max_depth	10
	eta	0.1
	gamma	0.1
	subsample	0.8
	min_child_weight	0.1
	nrounds	1000

References

1. Boer, C.; Meesters, M.I.; Milojevic, M.; Benedetto, U.; Bolliger, D.; von Heymann, C.; Jeppsson, A.; Koster, A.; Osnabrugge, R.L.; Ranucci, M.; et al. 2017 EACTS/EACTA Guidelines on Patient Blood Management for Adult Cardiac Surgery. *J. Cardiothorac. Vasc. Anesth.* **2018**, *32*, 88–120. [CrossRef] [PubMed]
2. Paone, G.; Likosky, D.S.; Brewer, R.; Theurer, P.F.; Bell, G.F.; Cogan, C.M.; Prager, R.L. Transfusion of 1 and 2 Units of Red Blood Cells Is Associated With Increased Morbidity and Mortality. *Ann. Thorac. Surg.* **2014**, *97*, 87–94. [CrossRef] [PubMed]
3. Kilic, A.; Whitman, G.J.R. Blood Transfusions in Cardiac Surgery: Indications, Risks, and Conservation Strategies. *Ann. Thorac. Surg.* **2014**, *97*, 726–734. [CrossRef]
4. Desai, N.; Schofield, N.; Richards, T. Perioperative Patient Blood Management to Improve Outcomes. *Anesth. Analg.* **2018**, *127*, 1211–1220. [CrossRef] [PubMed]
5. World Health Organization. *The Urgent Need to Implement Patient Blood Management: Policy Brief*; World Health Organization: Geneva, Switzerland, 2021.
6. Shander, A.; Hardy, J.-F.; Ozawa, S.; Farmer, S.L.; Hofmann, A.; Frank, S.M.; Kor, D.J.; Faraoni, D.; Freedman, J. A Global Definition of Patient Blood Management. *Anesth. Analg.* **2022**, *135*, 476–488. [CrossRef]
7. Goodnough, L.T.; Shander, A.; Riou, B. Patient Blood Management. *Anesthesiology* **2012**, *116*, 1367–1376. [CrossRef]
8. Klein, A.A.; Collier, T.; Yeates, J.; Miles, L.F.; Fletcher, S.N.; Evans, C.; Richards, T. The ACTA PORT-Score for Predicting Perioperative Risk of Blood Transfusion for Adult Cardiac Surgery. *Br. J. Anaesth.* **2017**, *119*, 394–401. [CrossRef]
9. Helm, J.M.; Swiergosz, A.M.; Haeberle, H.S.; Karnuta, J.M.; Schaffer, J.L.; Krebs, V.E.; Spitzer, A.I.; Ramkumar, P.N. Machine Learning and Artificial Intelligence: Definitions, Applications, and Future Directions. *Curr. Rev. Musculoskelet. Med.* **2020**, *13*, 69–76. [CrossRef]
10. Mitterecker, A.; Hofmann, A.; Trentino, K.M.; Lloyd, A.; Leahy, M.F.; Schwarzbauer, K.; Tschoellitsch, T.; Böck, C.; Hochreiter, S.; Meier, J. Machine Learning–Based Prediction of Transfusion. *Transfusion* **2020**, *60*, 1977–1986. [CrossRef] [PubMed]
11. Meier, J.M.; Tschoellitsch, T. Artificial Intelligence and Machine Learning in Patient Blood Management: A Scoping Review. *Anesth. Analg.* **2022**, *135*, 524–531. [CrossRef] [PubMed]
12. Mavrogiorgou, A.; Kiourtis, A.; Kleftakis, S.; Mavrogiorgos, K.; Zafeiropoulos, N.; Kyriazis, D. A Catalogue of Machine Learning Algorithms for Healthcare Risk Predictions. *Sensors* **2022**, *22*, 8615. [CrossRef] [PubMed]
13. Mateo, J.; Rius-Peris, J.M.; Maraña-Pérez, A.I.; Valiente-Armero, A.; Torres, A.M. Extreme Gradient Boosting Machine Learning Method for Predicting Medical Treatment in Patients with Acute Bronchiolitis. *Biocybern. Biomed. Eng.* **2021**, *41*, 792–801. [CrossRef]
14. Goodnough, L.T.; Maggio, P.; Hadhazy, E.; Shieh, L.; Hernandez-Boussard, T.; Khari, P.; Shah, N. Restrictive Blood Transfusion Practices Are Associated with Improved Patient Outcomes. *Transfusion* **2014**, *54*, 2753–2759. [CrossRef] [PubMed]
15. Tschoellitsch, T.; Böck, C.; Maletić, T.T.; Hofmann, A.; Meier, J. Machine Learning-Based Prediction of Massive Perioperative Allogeneic Blood Transfusion in Cardiac Surgery. *Eur. J. Anaesthesiol.* **2022**, *39*, 766–773. [CrossRef]

16. Levi, R.; Carli, F.; Arévalo, A.R.; Altinel, Y.; Stein, D.J.; Naldini, M.M.; Grassi, F.; Zanoni, A.; Finkelstein, S.; Vieira, S.M.; et al. Artificial Intelligence-Based Prediction of Transfusion in the Intensive Care Unit in Patients with Gastrointestinal Bleeding. *BMJ Health Care Inform.* **2021**, *28*, e100245. [CrossRef] [PubMed]
17. Pieri, M.; Nardelli, P.; De Luca, M.; Landoni, G.; Frassoni, S.; Melissano, G.; Zangrillo, A.; Chiesa, R.; Monaco, F. Predicting the Need for Intra-Operative Large Volume Blood Transfusions During Thoraco-Abdominal Aortic Aneurysm Repair. *Eur. J. Vasc. Endovasc. Surg.* **2017**, *53*, 347–353. [CrossRef] [PubMed]
18. Attali, E.; Many, A.; Kern, G.; Reicher, L.; Kahana, A.; Shemer, A.; Kagan, G.; Gamzu, R.; Yogev, Y.; Zakar, L. Predicting the Need for Blood Transfusion Requirement in Postpartum Hemorrhage. *J. Matern.-Fetal Neonatal Med.* **2024**, *35*, 7911–7916. [CrossRef] [PubMed]
19. Kadar, A.; Chechik, O.; Steinberg, E.; Reider, E.; Sternheim, A. Predicting the Need for Blood Transfusion in Patients with Hip Fractures. *Int. Orthop.* **2013**, *37*, 693–700. [CrossRef]
20. Li, Q.; Lv, H.; Chen, Y.; Shen, J.; Shi, J.; Zhou, C.; Yan, F. Development and Validation of a Machine Learning Prediction Model for Perioperative Red Blood Cell Transfusions in Cardiac Surgery. *Int. J. Med. Inform.* **2024**, *184*, 105343. [CrossRef] [PubMed]
21. Wang, Z.; Zhe, S.; Zimmerman, J.; Morrisey, C.; Tonna, J.E.; Sharma, V.; Metcalf, R.A. Development and Validation of a Machine Learning Method to Predict Intraoperative Red Blood Cell Transfusions in Cardiothoracic Surgery. *Sci. Rep.* **2022**, *12*, 1355. [CrossRef] [PubMed]
22. Liu, S.; Zhou, R.; Xia, X.-Q.; Ren, H.; Wang, L.-Y.; Sang, R.-R.; Jiang, M.; Yang, C.-C.; Liu, H.; Wei, L.; et al. Machine Learning Models to Predict Red Blood Cell Transfusion in Patients Undergoing Mitral Valve Surgery. *Ann. Transl. Med.* **2021**, *9*, 530. [CrossRef]
23. Chen, D.X.; Wang, Y.S.; Yan, M.; Du, L.; Li, Q. A Model Based on Electronic Health Records to Predict Transfusion Events in On-Pump Cardiac Surgery. *iScience* **2023**, *26*, 107798. [CrossRef] [PubMed]
24. Ranucci, M.; Castelvecchio, S.; Frigiola, A.; Scolletta, S.; Giomarelli, P.; Biagioli, B. Predicting Transfusions in Cardiac Surgery: The Easier, the Better: The Transfusion Risk and Clinical Knowledge Score. *Vox Sang.* **2009**, *96*, 324–332. [CrossRef] [PubMed]
25. Cuschieri, S. The STROBE Guidelines. *Saudi J. Anaesth.* **2019**, *13*, 31. [CrossRef] [PubMed]
26. Hasan, M.K.; Alam, M.A.; Roy, S.; Dutta, A.; Jawad, M.T.; Das, S. Missing Value Imputation Affects the Performance of Machine Learning: A Review and Analysis of the Literature (2010–2021). *Inform. Med. Unlocked* **2021**, *27*, 100799. [CrossRef]
27. Azur, M.J.; Stuart, E.A.; Frangakis, C.; Leaf, P.J. Multiple Imputation by Chained Equations: What Is It and How Does It Work? *Int. J. Methods Psychiatr. Res.* **2011**, *20*, 40–49. [CrossRef] [PubMed]
28. Japkowicz, N.; Stephen, S. The Class Imbalance Problem: A Systematic Study. *Intell. Data Anal.* **2002**, *6*, 429–449. [CrossRef]
29. Chawla, N.V.; Bowyer, K.W.; Hall, L.O.; Kegelmeyer, W.P. SMOTE: Synthetic Minority Over-Sampling Technique. *J. Artif. Intell. Res.* **2002**, *16*, 321–357. [CrossRef]
30. Chen, T.; Guestrin, C. XGBoost. In *Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining*; ACM: New York, NY, USA, 2016; pp. 785–794.
31. Tarwidi, D.; Pudjaprasetya, S.R.; Adytia, D.; Apri, M. An Optimized XGBoost-Based Machine Learning Method for Predicting Wave Run-up on a Sloping Beach. *MethodsX* **2023**, *10*, 102119. [CrossRef] [PubMed]
32. Akanbi, L.A.; Oyedele, A.O.; Oyedele, L.O.; Salami, R.O. Deep Learning Model for Demolition Waste Prediction in a Circular Economy. *J. Clean. Prod.* **2020**, *274*, 122843. [CrossRef]
33. Rodríguez-Pérez, R.; Bajorath, J. Interpretation of Machine Learning Models Using Shapley Values: Application to Compound Potency and Multi-Target Activity Predictions. *J. Comput. Aided Mol. Des.* **2020**, *34*, 1013–1026. [CrossRef] [PubMed]
34. Alghamdi, A.A.; Davis, A.; Brister, S.; Corey, P.; Logan, A. Development and Validation of Transfusion Risk Understanding Scoring Tool (TRUST) to Stratify Cardiac Surgery Patients According to Their Blood Transfusion Needs. *Transfusion* **2006**, *46*, 1120–1129. [CrossRef] [PubMed]
35. Fromes, Y. Reduction of the Inflammatory Response Following Coronary Bypass Grafting with Total Minimal Extracorporeal Circulation. *Eur. J. Cardio-Thorac. Surg.* **2002**, *22*, 527–533. [CrossRef] [PubMed]
36. Kraft, F.; Schmidt, C.; Van Aken, H.; Zarbock, A. Inflammatory Response and Extracorporeal Circulation. *Best. Pract. Res. Clin. Anaesthesiol.* **2015**, *29*, 113–123. [CrossRef] [PubMed]
37. Bical, O.M.; Fromes, Y.; Gaillard, D.; Fischer, M.; Ponzio, O.; Deleuze, P.; Gerhardt, M.-F.; Trivin, F. Comparison of the Inflammatory Response between Miniaturized and Standard CPB Circuits in Aortic Valve Surgery. *Eur. J. Cardio-Thorac. Surg.* **2006**, *29*, 699–702. [CrossRef] [PubMed]
38. Karkouti, K.; O'Farrell, R.; Yau, T.M.; Beattie, W.S. Prediction of Massive Blood Transfusion in Cardiac Surgery. *Can. J. Anesth./J. Can. D'anesthésie* **2006**, *53*, 781–794. [CrossRef] [PubMed]
39. Ferraris, V.A.; Ferraris, S.P.; Saha, S.P.; Hessel, E.A.; Haan, C.K.; Royston, B.D.; Bridges, C.R.; Higgins, R.S.D.; Despotis, G.; Brown, J.R.; et al. Perioperative Blood Transfusion and Blood Conservation in Cardiac Surgery: The Society of Thoracic Surgeons and The Society of Cardiovascular Anesthesiologists Clinical Practice Guideline. *Ann. Thorac. Surg.* **2007**, *83*, S27–S86. [CrossRef]

40. Karkouti, K.; Wijeysundera, D.N.; Yau, T.M.; Beattie, W.S.; Abdelnaem, E.; McCluskey, S.A.; Ghannam, M.; Yeo, E.; Djaiani, G.; Karski, J. The Independent Association of Massive Blood Loss with Mortality in Cardiac Surgery. *Transfusion* **2004**, *44*, 1453–1462. [CrossRef] [PubMed]
41. Munting, K.E.; Klein, A.A. Optimisation of Pre-Operative Anaemia in Patients before Elective Major Surgery—Why, Who, When and How? *Anaesthesia* **2019**, *74*, 49–57. [CrossRef]