

# Prediction Of Postoperative Pulmonary Complications Using Clinical Data And Machine Learning

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# Abstract

In this study, we aimed to predict postoperative pulmonary complications (PPC) with the help of machine learning (ML) in cardiac operations.

We prospectively gathered the preoperative and intraoperative data of 918 patients (random split:  $n=745$  and  $n=173$ ), who were candidates for elective cardiac surgeries. Patients were observed for any pulmonary complications 24, 48, and 72 hours after the surgery. Feature selection, univariate, and multivariate analysis were performed using an ML algorithm. We obtained the p-value and AUC with 95% CI for each feature and then all features together. We also utilized a Bayesian Network (BN) classifier.

Among the 16 selected features, 12 features showed a significant effect on PPC prediction in the testing dataset ( $p<0.05$ ). Peak expiratory flow rate was the most predictive feature (AUC = 0.75) in the testing dataset. Multivariate analysis showed that our features are highly robust in training ( $p\text{-value}<0.001$ , AUC=0.73) and testing ( $p\text{-value}=0.002$ , AUC=0.70) datasets. BN classifier showed that type of surgery, opium usage, renal dysfunction, and history of chronic obstructive pulmonary diseases have the highest conditional probability with the occurrence of PPC.

In conclusion, a combination of preoperative and postoperative features in patients can be used to predict PPCs in patients undergoing cardiac surgeries.

## Introduction

Cardiac surgeries usually coexist with postoperative complications, including postoperative pulmonary complications (PPCs), which lead to a greater amount of mortality and morbidity, and length of stay following cardiovascular operations [1]. Preoperative, intraoperative, and postoperative factors can all be responsible for the incidence of PPCs which can be categorized into pleural effusion, pneumonia, atelectasis, pulmonary edema/ARDS, and phrenic nerve injuries (e.g., diaphragm paralysis) [2].

Different risk assessment methods have shown qualification for predicting PPCs. For example, we can refer to the studies conducted by Canet et al. and Mazo et al., which applied a regression model to a dataset of 2464 and 5859 patients respectively, and reached C-statistics of 0.8–0.9 for the prediction of PPC incidence [3, 4]. Besides regression models, there has been a growing interest among researchers in using other machine learning (ML) algorithms. For example, Bolourani et al. could predict respiratory failure following pulmonary lobectomy with the help of ML approaches [5]. In addition, some researchers conducted a study of ML algorithms to see if they can differentiate types of PPCs after hematopoietic cell transplant operations, reaching an accuracy of 86% [6].

To name a few studies concerning cardiac surgeries and ML usage, Alshakhs et al. showed that ML can effectively predict the length of stay in patients undergoing CABG [7]. Two other studies by Tseng et al. and Lee et al. utilized AI-based models to predict acute kidney injury (AKI) following cardiac surgeries [8,

9]. Lastly, it has been shown that ML can improve the prediction of mortality risk in the performed cardiovascular surgeries [10, 11].

However, to date, few ML studies have been published on pulmonary or respiratory complications following cardiothoracic surgeries. For example, Hofer et al. conducted a study to investigate the prediction power of neural networks in patients who develop a need for reintubation or ventilator after different types of surgeries such as cardiac ones [12]. Mendes et al. also predicted reintubation and prolonged mechanical ventilation for post-CABG patients and compared neural networks with a logistic regression model [13]. Semenova et al. assessed CABG safety in patients who are on-pump using neural networks and considered respiratory disorders as complications [14].

As mentioned above, there is a growing body of evidence that shows that ML algorithms are capable of helping surgeons in terms of diagnosis, prognosis and risk stratification, prediction of surgery complications, and postoperative management. However, according to our literature review, few studies were conducted to predict PPCs using ML algorithms. In this light, we aimed to predict the risk of PPCs in patients undergoing cardiac surgeries using ML methods, which has the potential to be a significant contribution to the clinical setting.

## Results

With the help of MARS on the overall dataset, 16 features containing 12 preoperative and 4 intraoperative ones were selected and all of them were ordered based on their importance values (Table 2). Age, BUN, and adult congenital cardiac surgery (4th type of surgery) were the most important features related to our outcome i.e. pulmonary complications.

Table 1

preoperative and intraoperative features, types, and the distribution of them in the whole dataset

Preoperative features					
Feature	Type	Cases <sup>a</sup>	Feature	Type	cases
Age (years)	Cat	$\leq 45$ : 178 $46-55$ : 194 $56-65$ : 305 $\geq 66$ : 241	Gender	B	Female: 344 (37.5) Male: 574 (62.5)
BMI (kg/m <sup>2</sup> )	Con	26.62 $\pm$ 4.61	Smoking	B	290 (31.6)
Neck circumference (cm)	Con	37.02 $\pm$ 3.44	Opium usage	B	164 (17.9)
Diastolic Dysfunction	B	159 (17.3)	Renal Dysfunction history	B	102 (11.1)
Hypertension	B	328 (35.7)	Diabetes Mellitus	B	247 (26.9)
EF (%)	Con	42.34 $\pm$ 10.13	FBS (mg/dl)	Con	115.21 $\pm$ 52.54
Uric acid (mg/dl)	Con	6.49 $\pm$ 1.84	BUN (mg/dl)	Con	19.88 $\pm$ 8.82
GFR	Con	77.48 $\pm$ 30.99	Creatinine	Con	1.11 $\pm$ 0.55
Hb	Con	13.19 $\pm$ 1.61	PEFR	Con	6.64 $\pm$ 2.24
SPAP (cmH <sub>2</sub> O)	Cat	$\leq 25$ : 693 (75.5) $26-35$ : 153 (16.7) $36-45$ : 51 (5.6) $\geq 46$ : 21 (2.3)	ESS	Cat	0: 517 (56.3) 1-5: 305 (33.2) $\geq 6$ : 96 (10.5)
FEV1 (%)	Con	94.66 $\pm$ 17.24	FVC (%)	Con	92.94 $\pm$ 16.96

<sup>a</sup>Reported in the form of mean  $\pm$  SD (for continuous features), number of cases with the history of the mentioned features along with the percentage (for binary features), and the number of each category along with the percentage (for categorical features).

Abbreviations: B: binary variable, BMI: Body Mass Index, BUN: blood urea nitrogen, Cat: categorical variable, Con: continuous variable, EF: ejection fraction of the left ventricle, ESS: Epworth Sleepiness Scale, FEV1: forced expiratory volume in the first second, FVC: forced vital capacity, FBS: fasting blood sugar, GFR: Glomerular filtration rate, Hb: hemoglobin, MMEF: maximum expiratory flow rate, PEFR: peak expiratory flow rate, SPAP: systolic pulmonary artery pressure (as measured by echocardiography), Type of surgeries are defined as 1,2,3 and 4 which stand for CABG (Coronary Artery Bypass Graft), valve replacement surgery, large vessel surgery, and adult congenital heart surgery, respectively.

Preoperative features					
FEV1/FVC (%)	Con	106.63 ± 12.11	MMEF (%)	Con	85.37 ± 27.56
Intraoperative features					
Feature	Type	cases	Feature	Type	cases
Type of surgery: 1	B	626 (68.2)	Type of surgery: 2	B	246 (26.8)
Type of surgery: 3	B	18 (2.0)	Type of surgery: 4	B	28 (3.1)
Skin to skin time (min)	Con	246.22 ± 73.70	Pump time (min)	Con	91.97 ± 40.90
Clamp time (min)	Con	54.28 ± 27.68	Blood transfusion	B	605 (65.9)
<sup>a</sup> Reported in the form of mean ± SD (for continuous features), number of cases with the history of the mentioned features along with the percentage (for binary features), and the number of each category along with the percentage (for categorical features).					
Abbreviations: B: binary variable, BMI: Body Mass Index, BUN: blood urea nitrogen, Cat: categorical variable, Con: continuous variable, EF: ejection fraction of the left ventricle, ESS: Epworth Sleepiness Scale, FEV1: forced expiratory volume in the first second, FVC: forced vital capacity, FBS: fasting blood sugar, GFR: Glomerular filtration rate, Hb: hemoglobin, MMEF: maximum expiratory flow rate, PEFR: peak expiratory flow rate, SPAP: systolic pulmonary artery pressure (as measured by echocardiography), Type of surgeries are defined as 1,2,3 and 4 which stand for CABG (Coronary Artery Bypass Graft), valve replacement surgery, large vessel surgery, and adult congenital heart surgery, respectively.					

Table 2  
Feature selection by Multivariate Adaptive Regression Splines (MARS) algorithm based on the training dataset.

Selected Variables	Importance Value
Age	41%
BUN	40%
Type of surgery: 4	39%
Skin to skin time	34%
Pump Time	33%
Clamp Time	32%
Creatinine	30%
Hb	26%
MMEF	23%
PEFR	22%
O <sub>2</sub> Saturation	18%
Renal dysfunction	16%
PaO <sub>2</sub>	15%
History of COPD	8%
Opium usage	5%
Smoking	3%
<i>Abbreviations: BUN: blood urea nitrogen, COPD: chronic obstructive pulmonary disease. Hb: hemoglobin, MMEF: maximum expiratory flow rate, PaO<sub>2</sub>: partial pressure of oxygen, PEFR: peak expiratory flow rate, Type of surgery 4: adult congenital heart surgery.</i>	

The selected features were assessed by their prognostic performance in testing datasets as shown in Table 3. Except for Hb, MMEF, and Creatinine, and history of COPD, all of the features showed a significant effect on PPC prediction ( $p < 0.05$ ). PEFR was the most predictive feature with an AUC of 0.75 (95% CI: 0.66–0.83) in the testing dataset. The results of each univariate analysis was also reported in the training set as well the testing set in our Supplementary File Table. As it is shown, the univariate analysis of our features showed a little-to-no difference between the AUCs of the training dataset and those of the testing dataset.

Table 3  
Univariate and multivariate results of the selected features for the classification.

Selected features Dataset		P-value	AUC (95% CI)	OR (95% CI)
Age	Testing Set	<b>0.011</b>	0.69 (0.61–0.88)	1.16 (0.28–4.35)
Clamp Time	Testing Set	<b>0.017</b>	0.63 (0.57–0.69)	1.05 (0.95–1.10)
Pump Time	Testing Set	<b>0.030</b>	0.65 (0.58–0.74)	1.02 (1.01–1.04)
Skin to skin time	Testing Set	<b>0.026</b>	0.58 (0.54–0.79)	1.01 (1.001–1.022)
Creatinine	Testing Set	0.185	0.52 (0.49–0.61)	1.79 (0.52–3.19)
Smoking	Testing Set	<b>0.037</b>	0.54 (0.50–0.61)	1.81 (1.15–3.19)
MMEF	Testing Set	0.286	0.52 (0.48–0.56)	1.07 (0.88–1.67)
Opium	Testing Set	<b>0.048</b>	0.53 (0.50–0.56)	1.47 (0.55–2.13)
Type of surgery 4	Testing Set	<b>0.037</b>	0.58 (0.53–0.67)	4.99 (1.92–18.33)
Renal dysfunction	Testing Set	<b>0.042</b>	0.53 (0.51–0.57)	1.55 (1.02–2.78)
Hb	Testing Set	0.633	0.51 (0.48–0.63)	0.96 (0.73–1.27)
BUN	Testing Set	<b>0.009</b>	0.71 (0.60–0.89)	0.96 (0.90–0.99)
History of COPD	Testing Set	0.051	0.52 (0.50–0.61)	2.13 (1.56–7.65)
PEFR	Testing Set	<b>&lt; 0.001</b>	0.75 (0.66–0.83)	1.41 (1.07–1.66)
O <sub>2</sub> Saturation	Testing Set	<b>0.031</b>	0.58 (0.51–0.67)	0.88 (0.74–0.97)
PaO <sub>2</sub>	Testing Set	<b>0.044</b>	0.53 (0.51–0.69)	1.01 (0.95–1.06)
All of the selected features	Training Set	<b>&lt; 0.001</b>	0.73 (0.59–0.86)	NA
	Testing Set	<b>0.002</b>	0.70 (0.58–0.81)	NA
<i>P-value was calculated by ROC curve analysis. Bold p-values indicate significant values.</i>				
<i>Abbreviations: 95% CI: 95% confidence interval, AUC: area under ROC curve, BUN: blood urea nitrogen, COPD: chronic obstructive pulmonary disease, Hb: hemoglobin, MMEF: maximum expiratory flow rate, NA: not applicable, OR: odds ratio, PaO<sub>2</sub>: partial pressure of oxygen, PEFR: peak expiratory flow rate, Type of surgery 4: adult congenital heart surgery.</i>				

At last, our multivariable analysis (last row of Table 3) shows that our selected features are highly robust in the prediction of PPC in both the training (p-value < 0.001, AUC = 0.73) and the testing (p-value = 0.002, AUC = 0.70) datasets. In addition, Fig. 1 shows the non-significant difference of the selected features in their AUC between the datasets (p-value = 0.449).



As illustrated in Fig. 2 and Fig. 3, the BN classifier could also generate the same results for the training and testing datasets, respectively. These results showed that type of surgery, opium usage, renal dysfunction, SPAP, and history of COPD related highest with PPC based on the conditional probabilities (Fig. 2). In addition to the aforementioned features, smoking, diabetes, and hypertension were the most related features with PPC based on the conditional probabilities (Fig. 2). The same applies to our testing dataset (Fig. 3).

## Discussion

Our study consisted of applying machine learning algorithms to preoperative and intraoperative features of patients who underwent cardiac operations to predict postoperative pulmonary complications. Understanding the possible complications and predicting them can affect and play an important role in management, treatment, length of stay and will probably reduce morbidity and mortality in patients admitted to the hospital.

First, we used the multivariate adaptive regression splines, which is a potent method for feature selection and analysis of the data. This method can be applied to the dataset easier than many other algorithms and accepts multiple types of variables e.g. categorical, nominal, or numerical ones. Feature selection was conducted successfully, showing the 16 most important features in our data. The univariate analysis results could show that our features performed well in both training and testing datasets as shown in Table 3. Almost all of our selected features gained a P-value of less than 0.05, Except for hemoglobin, maximum expiratory flow rate, and creatinine.

In our multivariable analysis, we could also obtain a difference of AUC of less than 0.03 between training and testing datasets which showed the robustness of our selected features ( $p < 0.001$ ,  $p = 0.002$ , respectively). Following the MARS algorithm, we performed the BN classifier which is a probabilistic graphical model that represents a set of variables and their conditional probabilities. Based on the results of the BN method, most related features consisted of opium usage, 4th type of surgery, renal dysfunction, SPAP, history of COPD, smoking, diabetes, and hypertension. Although the most related features with PPCs in the BN method were similar to the selected features by the MARS method, the size of their associations between selected features and PPC were different in the two algorithms.

These findings are more or less compatible with the studies that used conventional statistical methods. In a study by Silva et al. [15], advanced age, excess weight (BMI), smoking, high pulmonary artery pressure, diabetes mellitus, abnormal results of pulmonary function tests, COPD, and emergency surgery were identified as risk factors for PPCs after cardiac surgeries. The most frequently identified respiratory risk factor for PPCs has been COPD, with a rate of postoperative complications that varies from 26 to 78 percent in several studies [16] but that was not appreciated in MARS analysis as high as in conventional statistical methods. There has been an association between PPCs with the obstructive pattern of spirometry in our study but it was not statistically significant and not validated by MARS.

There exist many studies conducted to evaluate ML methods' prediction power in the clinical and especially cardiac settings. For example, a recent study by Fernandes et al. [11] identified that extreme gradient boosting can play a key role in the prediction of mortality after cardiopulmonary bypass in 5015 patients with an AUC of 0.88 (95% CI: 0.83–0.94). Another study by Lapp et al. [17] found out that ML methods are able to predict severe postoperative complications after cardiovascular surgeries. They built models using RF, SVM, and NB machine learning methods and applied them to the data of 3700 patients. Among their models, RF gained the best performance (AUC = 0.71) and the best specificity (77.2%).

Several studies on the predictive power of ML results for the development of PPCs have shown similar findings to ours. Sharifi et al [6] recently showed that K-means clustering analysis and support vector machine can help predict and distinguish between pulmonary complications following hematopoietic cell transplantation. The latter method could reach an AUC of 0.85, along with a specificity of 88% and a sensitivity of 83%. Canet et al. employed a regression model for the data of 2464 patients from 59 hospitals in order to predict PPC occurrence and could identify a “predictive index” that excelled in their analysis, reaching an AUC of 0.90 for the development set and 0.88 for the validation set. They could identify some independent factors such as low SaO<sub>2</sub>, history of respiratory infections, and age which contributed to the PPC prediction in their model. In another study conducted recently, researchers established a model out of the data of 4062 patients undergoing pulmonary lobectomy. They identified and analyzed separate preoperative and postoperative factors contributing to the pulmonary complications prediction. At last, they reached two machine learning models, the first one suitable for performance evaluation (with high specificity and accuracy), and the second one best for decision making (with high sensitivity).

Some limitations need to be noted in our study. First, our findings remain to be further evaluated by an external validation dataset. Additionally, the bigger the sample size, the more accurate the results will be. Thus, we recommend future studies examine these models with bigger sample sizes and also with the help of more ML algorithms.

In conclusion, a selection of preoperative and postoperative features in patients undergoing cardiac operations and designing the consequent model can be an appropriate way to predict postoperative pulmonary complications.

## **Materials And Methods**

### ***1. Ethical Statement***

In this study, the Helsinki protocol was followed. The study was approved by our local ethical committee in Iran University of Medical Sciences (RHC.AC.IR.REC.1396.28) and patients' written informed consent was waived by the ethical committee at the Iran University of Medical Sciences.

### ***2. Patient and Study design***

In this prospective cohort, we gathered the data of patients from their health records in a hospital center for cardiovascular diseases (Rajaei Cardiovascular Medical and Research Center). In this study, we included patients who were admitted to the hospital from September 2016 to September 2017 and were candidates for elective CABG, congenital heart disease, large vessel or valve replacement surgeries. Those who underwent emergency surgeries were excluded and a total of 918 patients were included in our study.

Before the operations, the demographic data of the patients and the history of underlying diseases such as diabetes mellitus, hypertension, renal dysfunction, and pulmonary diseases (e.g. COPD) were obtained through the medical records. History of smoking, home bakery, opium usage was directly asked from the patients who then underwent the measurements of BMI and neck circumference. Laboratory tests for the analysis of the collected blood samples were performed for blood urea nitrogen (BUN), creatinine, uric acid, fasting blood sugar (FBS), and hemoglobin (Hb). Glomerular filtration rate (GFR) was calculated using plasma creatinine with the Cockcroft-Gault formula. Oxygen Saturation and  $\text{PaO}_2$  (partial pressure of oxygen) were added to the patient data 15 minutes prior to the operation. Besides, all of the patients were sent to undergo pulmonary function tests (PFT) to obtain data such as FEV1, FVC, FEV1 to FVC ratio, MMEF, and PEFR. Echocardiography was performed routinely and measurements of pulmonary artery pressure (SPAP), ejection fraction (EF), and diastolic dysfunction were assessed. Epworth Sleepiness Scale (ESS) sheets were filled up by an educated nurse on the day of admission. All of the patients were on the pump during the surgery and were performed median sternotomy regardless of the type of the operation. During the operation, the intraoperative feature set was completed by adding the type of the surgery, the time in which the patients were on the pump, the skin to skin time, and the clamp time. In the end, we included a positive blood transfusion if the patient received any of the blood products during the operation. The endpoint of this study was the development of pulmonary complications between 24 and 72 hours after the surgery. This can be specified as the diagnosis of one of the following: atelectasis; pleural effusion; pulmonary edema; pneumonia; and diaphragm paralysis, made by an expert pulmonologist by reviewing and commenting on chest X-rays and CT images.

### ***3. Feature Selection***

Feature selection is one of the core concepts in ML that hugely impacts the performance of the model. The features used to train ML models have a huge influence on the performance that can be achieved. Irrelevant or partially relevant features can negatively impact model performance. Details of the preoperative and intraoperative features are provided in Table 1.

We used two machine learning algorithms novel in the field of image processing, namely Multivariate Adaptive Regression Splines (MARS) for both the selection and prediction analysis, and Bayesian network classifier to assess the effects of selected features on the risk of PPC. The MARS method builds a model as described in equation (1) [18]:

$$\hat{f}(x) = \sum_{i=1}^k c_i B_i(x). \quad (1)$$

As the equation above shows, the model sums the basis functions , each weighted by a (constant coefficient). The basis function can be either a constant 1, a hinge function, or a product of two or more of the latter. This will help us gain a more flexible and easier-to-understand model compared with other ML algorithms such as random forest or neural networks. MARS automatically selects the most important features, ranks them in order of their “importance value”, and builds the model on them. Therefore, it does not need any previous preparation of data and also suits large datasets and complex data structures. Finally, the most important advantage of MARS is that it can handle features of any type such as numerical, categorical, and nominal ones, either binary or not. We employed this easily accessible algorithm in the “earth” package of the software R version 4.0.2.

Bayesian Network (BN) method is annotated directed graphs that represent a set of variables (selected features) as nodes in a network, connected by edges representing the conditional probabilistic relations between them [19,20]. BN is based on the Bayes theorem [21] and it consists of two steps: 1) structural learning to find the global optimum global structure 2) parametric learning to estimate the conditional probability. The structure of the BN model was built with Bootstrap by repeating 100 times and the Tabu search algorithm merging data information and prior knowledge. In addition, parameters of the model are learned with Maximum Likelihood Estimate (MLE) and 10-fold cross-validation was used. BN method is used to select the most important features [20]. A Bayesian network with uniform (non-informative) prior distributions was used in this study. A constraint-based algorithm (PC algorithm) was used to determine the BN structure using conditional independence tests. Then, we performed the Expectation–maximization (EM) algorithm as an iterative approach for parameter estimation in our model.

#### ***4. Model performance and evaluation***

After splitting the dataset into training and test, the MARS algorithm was employed to achieve the performance of the features in each of the training and testing datasets, assessed by the area under the receiver operating characteristic curve (AUC) along with its 95% confidence interval (CI). ROC curve analysis was performed by the “earth” R package. Additionally, the odds ratio (OR) with its 95% CI was achieved by utilizing the logistic regression (glm R function). Finally, statistical comparison of area under ROC curve was done by “pROC” R package [22]. Therefore, we could discover the possible significant prognostic performances of the features. The significance level of the P-value was considered <0.05.

## **Declarations**

### **Acknowledgments**

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epidemiologists, and nurses who helped us in this study.

### Author contributions

A.H.A., M.P., and I.S. were involved with the conception and design of the work; H.S., M.S.F., S.S., and M.Mirdamadi were involved with the acquisition and validation of the data; S.M. and F.C. were involved with the analysis and interpretation of the data; A.H.A. and M.P. drafted the manuscript; I.S., M.O, A.H.A., and M.P. have substantially revised the work; M.Maleki was involved in the funding acquisition; all authors have contributed substantially to the study content and approved the final revision of the manuscript.

### Data Availability

The datasets generated during and analyzed during the current study are not publicly available due to patient privacy, but are available from the corresponding author on reasonable request.

### Additional Information

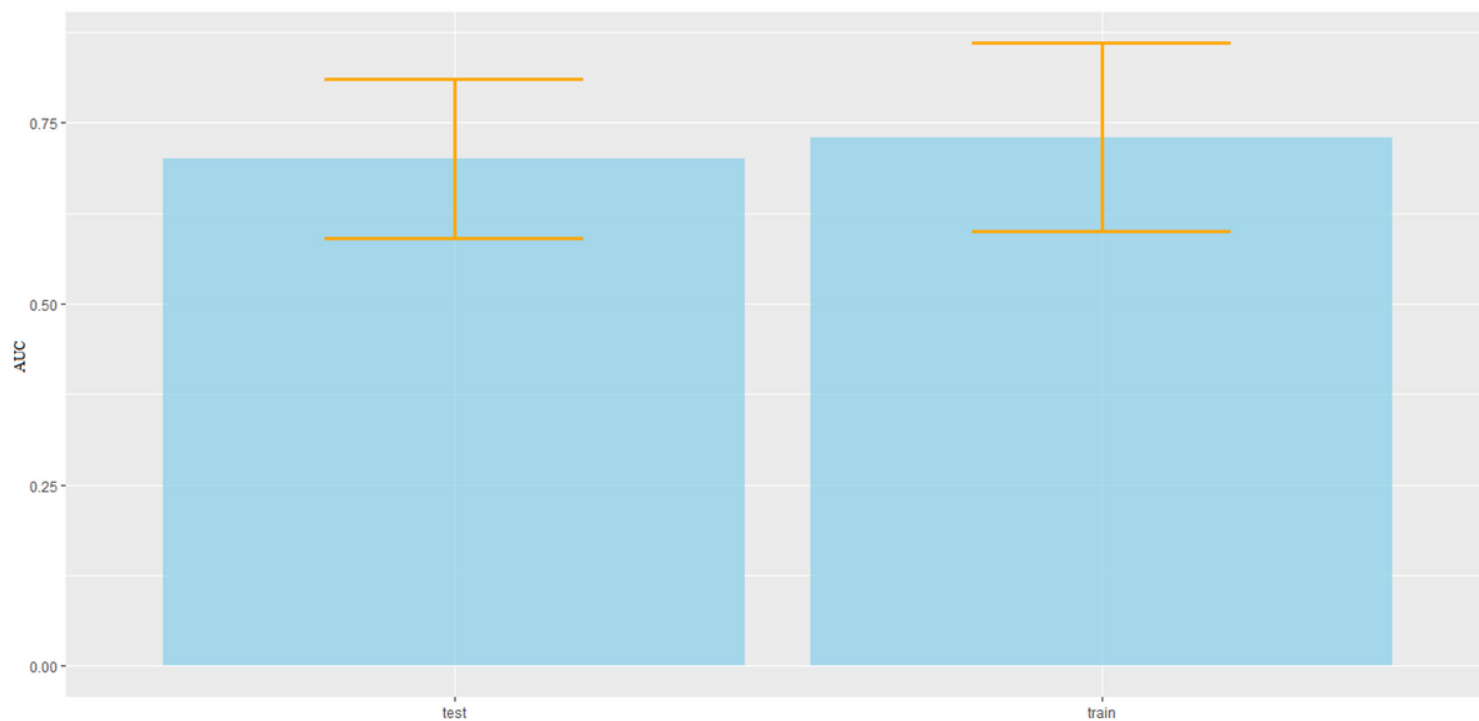
The authors declare no competing interests.

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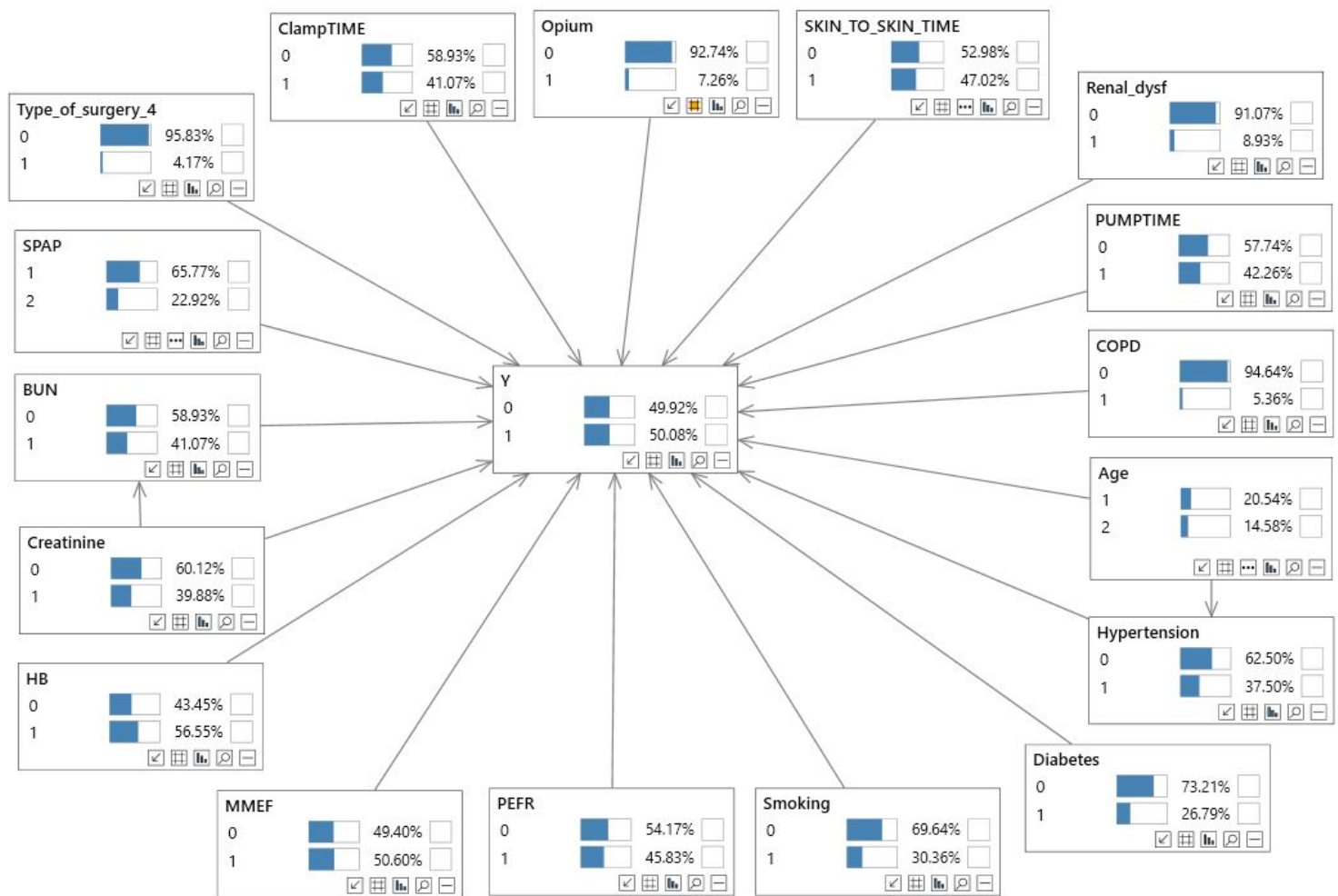
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## Figures



**Figure 1**

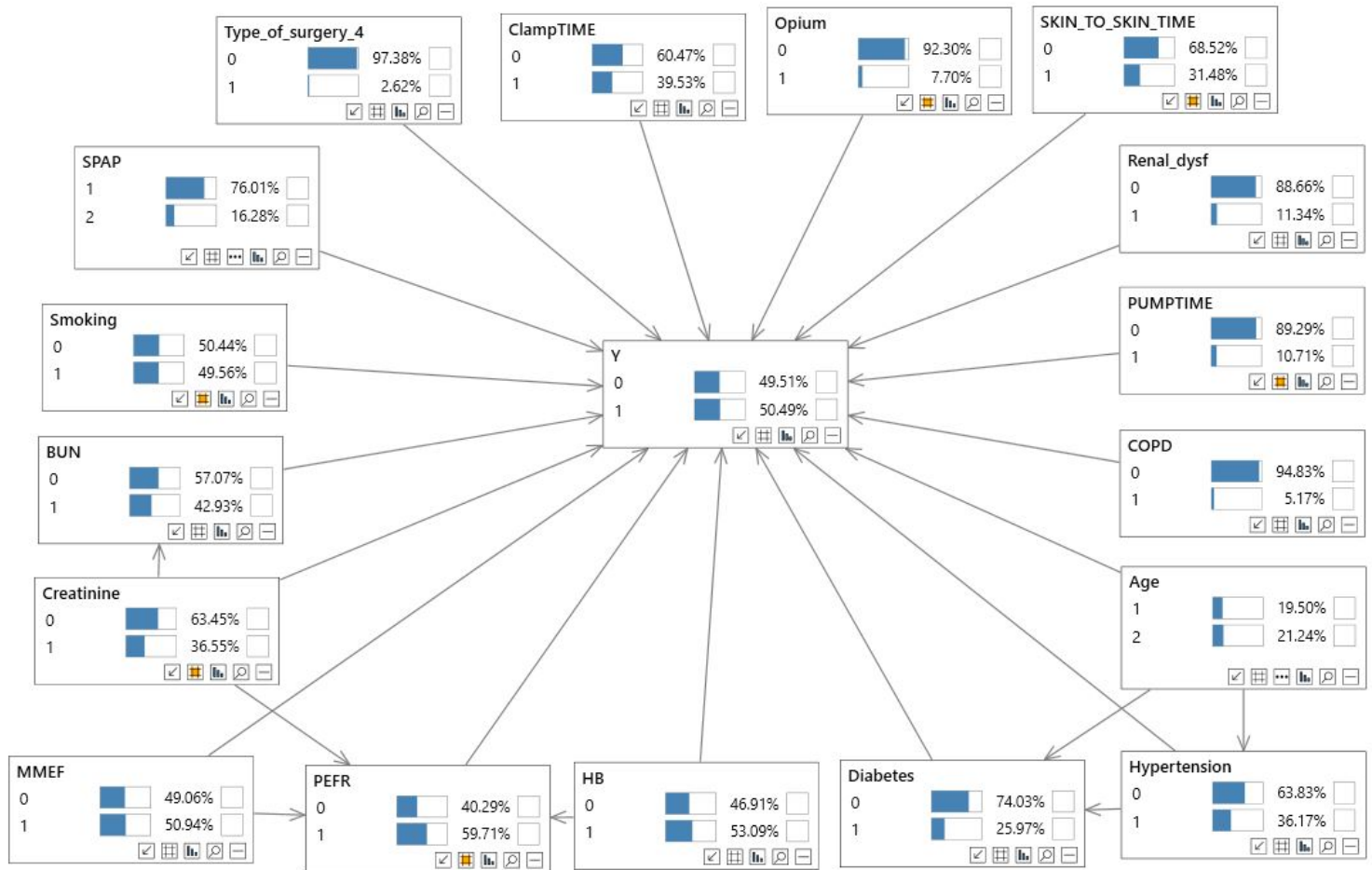
Comparison of the area under the ROC curve (AUC) between test and train datasets based on the selected features (P-value=0.449)



**Figure 2**

Results of Bayesian network classifier for the selected features in the training dataset. Abbreviations: BUN: blood urea nitrogen, COPD: chronic obstructive pulmonary disease, Hb: hemoglobin, MMEF: maximum expiratory flow rate, PEFR: peak expiratory flow rate, SPAP: systolic pulmonary artery pressure, Type of surgery 4: adult congenital heart surgery





**Figure 3**

Results of Bayesian network classifier for the selected features in the testing dataset. Abbreviations: BUN: blood urea nitrogen, COPD: chronic obstructive pulmonary disease, Hb: hemoglobin, MMEF: maximum expiratory flow rate, PEFR: peak expiratory flow rate, SPAP: systolic pulmonary artery pressure, Type of surgery 4: adult congenital heart surgery.

# Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Supp.docx](#)