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Copyright Year	2025	
Copyright HolderName	The Author(s), under exclusive license to Springer Nature Switzerland AG	
Author	Family Name	**Shakhgeldyan**
	Particle	
	Given Name	**Karina**
	Prefix	
	Suffix	
	Role	
	Division	
	Organization	Far Eastern Federal University
	Address	690922, Vladivostok, Russia
	Division	
	Organization	Vladivostok State University
	Address	690014, Vladivostok, Russia
	Email	
Corresponding Author	Family Name	**Kuksin**
	Particle	
	Given Name	**Nikita**
	Prefix	
	Suffix	
	Role	
	Division	
	Organization	Far Eastern Federal University
	Address	690922, Vladivostok, Russia
	Division	
	Organization	Vladivostok State University
	Address	690014, Vladivostok, Russia
	Email	kuksin.ns@dvfu.ru
Author	Family Name	**Domzhalov**
	Particle	
	Given Name	**Igor**
	Prefix	
	Suffix	
	Role	
	Division	
	Organization	Far Eastern Federal University
	Address	690922, Vladivostok, Russia

	Email	
Author	Family Name	**Pak**
	Particle	
	Given Name	**Regina**
	Prefix	
	Suffix	
	Role	
	Division	
	Organization	Far Eastern Federal University
	Address	690922, Vladivostok, Russia
	Email	
Author	Family Name	**Geltser**
	Particle	
	Given Name	**Boris**
	Prefix	
	Suffix	
	Role	
	Division	
	Organization	Far Eastern Federal University
	Address	690922, Vladivostok, Russia
	Division	
	Organization	Vladivostok State University
	Address	690014, Vladivostok, Russia
	Email	

Abstract	The aim of the study is to develop an ensemble machine learning (ML) method that enables the construction of interpretable prognostic models and to test it using the example of predicting in-hospital mortality (IHM) in patients with ST-segment elevation myocardial infarction (STEMI). A retrospective cohort study was conducted using data from 4673 electronic medical records of patients with STEMI who underwent percutaneous coronary intervention (PCI). Two groups of individuals were identified, the first of which consisted of 318 (6.8%) patients who died in hospital, the second - 4355 (93.2%) - with a favorable outcome of PCI. Using multimetric categorization methods (minimizing p-value, maximizing the area under the ROC curve-AUC and shap-value analysis results), the predictors were transformed into risk factors (RF) for IHM. To develop prognostic models of IHM, multivariate logistic regression, random forest RF (RandFRF), stochastic gradient boosting, random forest, Adaptive boosting, Gradient Boosting, Light Gradient-Boosting Machine and CatBoost were used. The authors developed the RandFRF method, which aggregates the predictions of modified decision trees, identifies key risk factors (RFs), and ranks them based on their contribution to the likelihood of the adverse outcome (IHM). The RandFRF method demonstrated a high prognostic capacity (AUC = 0.897), comparable to that of XGBoost (AUC = 0.891), Random Forest (AUC = 0.887), and CatBoost (AUC = 0.881). Importantly, RandFRF also enables clinical interpretation of the model outputs by quantifying the influence of each risk factor on the predicted probability of IHM. This method may serve as a reliable tool for developing interpretable ML models in clinical medicine.

Keywords (separated by '-')	ensemble machine learning methods - risk factors - continuous variable categorization - Shapley Additive Explanations - interpretable machine learning methods

Intelligent Service for Predicting Adverse Events in Cardiology Based on an Ensemble of Risk Factors

Karina Shakhgeldyan[1,2], Nikita Kuksin[1,2(✉)], Igor Domzhalov[1], Regina Pak[1], and Boris Geltser[1,2]

[1] Far Eastern Federal University, 690922 Vladivostok, Russia
kuksin.ns@dvfu.ru
[2] Vladivostok State University, 690014 Vladivostok, Russia

Abstract. The aim of the study is to develop an ensemble machine learning (ML) method that enables the construction of interpretable prognostic models and to test it using the example of predicting in-hospital mortality (IHM) in patients with ST-segment elevation myocardial infarction (STEMI).

A retrospective cohort study was conducted using data from 4673 electronic medical records of patients with STEMI who underwent percutaneous coronary intervention (PCI). Two groups of individuals were identified, the first of which consisted of 318 (6.8%) patients who died in hospital, the second - 4355 (93.2%) - with a favorable outcome of PCI. Using multimetric categorization methods (minimizing p-value, maximizing the area under the ROC curve-AUC and shap-value analysis results), the predictors were transformed into risk factors (RF) for IHM. To develop prognostic models of IHM, multivariate logistic regression, random forest RF (RandFRF), stochastic gradient boosting, random forest, Adaptive boosting, Gradient Boosting, Light Gradient-Boosting Machine and CatBoost were used.

The authors developed the RandFRF method, which aggregates the predictions of modified decision trees, identifies key risk factors (RFs), and ranks them based on their contribution to the likelihood of the adverse outcome (IHM). The RandFRF method demonstrated a high prognostic capacity (AUC = 0.897), comparable to that of XGBoost (AUC = 0.891), Random Forest (AUC = 0.887), and CatBoost (AUC = 0.881). Importantly, RandFRF also enables clinical interpretation of the model outputs by quantifying the influence of each risk factor on the predicted probability of IHM. This method may serve as a reliable tool for developing interpretable ML models in clinical medicine.

Keywords: ensemble machine learning methods · risk factors · continuous variable categorization · Shapley Additive Explanations · interpretable machine learning methods

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1 Introduction

Ischemic heart disease (IHD) remains the leading cause of mortality among cardiovascular conditions [18]. One of the most critical clinical manifestations of IHD is ST-elevation myocardial infarction (STEMI), which is typically managed with emergency myocardial revascularization through percutaneous coronary intervention (PCI) [8]. Despite advancements in PCI techniques, in-hospital mortality (IHM) following urgent PCI remains high, ranging from 4% to 7%, highlighting the urgent need for accurate prediction of adverse outcomes [11].

Traditionally, risk stratification tools—such as clinical scoring systems—have been used in practice. However, their performance often proves insufficient for guiding individualized treatment decisions. Recent advances in machine learning (ML) offer promising opportunities to improve prognostic performance by capturing complex, nonlinear relationships between predictors and clinical outcomes. Among ML approaches, ensemble methods such as Random Forest [20], Adaptive Boosting (AdaBoost) [2], Gradient Boosting [19], Light Gradient Boosting Machine (LightGBM) [9], Categorical Boosting (CatBoost) [4], and Extreme Gradient Boosting (XGBoost) [1] are frequently applied. These techniques combine the outputs of multiple weak learners—typically decision trees—through soft or hard voting mechanisms to enhance predictive performance [3, 22].

Nevertheless, ensemble methods often suffer from limited interpretability, which constrains their integration into clinical decision-making workflows [6]. To address this limitation, explainable artificial intelligence (XAI) algorithms have emerged as a promising solution. In the present study, we propose a novel ML approach—RandFRF—which combines high predictive performance with enhanced interpretability through clinically meaningful representations of risk

The aim of this study is to develop an interpretable ensemble machine learning approach—RandFRF—for predicting IHM in STEMI patients undergoing PCI.

2 Methods

The RandFRF approach is grounded in a multi-level categorization of continuous variables, transforming them into piecewise constant functions that describe the relationship between parameter values and the probability of an adverse event.

To construct these piecewise constant functions, we propose the use of modified decision trees [17]. Data splits are based on risk factors (RFs) identified through a combination of additive Shapley explanations, centroids, p-value minimization, area under the ROC curve (AUC) maximization, and multivariate logistic regression (MLR) weight coefficients [16]. Thus, the RandFRF model development involves identifying RFs and training a decision tree for each individual predictor.

The preliminary step for feature selection is described in Sect. 2.1. The RandFRF model architecture is presented in Sect. 2.2. The dataset and methodology for validating the model in predicting IHM among STEMI patients are detailed in Sects. 2.3 and 2.4.

2.1 Feature Selection

The study was designed as a binary classification task to distinguish between STEMI patients with favorable and unfavorable in-hospital outcomes following PCI. The feature selection process involved the following steps:

1. Comparisons of continuous predictors between outcome groups using the Mann–Whitney U test or Student's t-test, based on distribution normality.
2. Categorical variable comparisons using the chi-square (χ^2) test.
3. Recoding of multicategorical features into binary variables, followed by odds ratio (OR) estimation with 95% confidence intervals (CI).
4. Formation of a predictor pool, consisting of variables showing statistically significant differences ($p < 0.05$).
5. Ranking predictors within the pool based on their weight coefficients derived from univariate logistic regression (ULR) models, using normalized input values.
6. Model-based validation, in which predictors were sequentially introduced into MLR, Random Forest, and XGBoost models according to their rank. Predictors that did not improve AUC were excluded.

2.2 Description of the RandFRF Method

Traditional ensemble methods such as Random Forest, XGBoost, and AdaBoost improve predictive performance by constructing multiple weak classifiers trained on bootstrap or ranked subsets of the data. Although such models generally offer high performance, their interpretability is limited due to the structural complexity of the ensemble.

In contrast, RandFRF avoids partitioning data across observations and instead generates training subsets across predictors. Each subset includes only one predictor and the target variable, allowing continuous predictors to be transformed into piecewise constant functions. These transformations are performed using modified decision trees [17], "points of interest," and MLR models.

A distinctive feature of RandFRF is the use of predefined data-splitting thresholds—termed "points of interest"—which are derived using multimetric categorization [16]. These include centroid-based stratification, SHAP value analysis from an XGBoost model, p-value optimization (χ^2 test), and AUC maximization in ULR.

Each decision tree in RandFRF utilizes only a single parameter, and repeated data splits produce a piecewise constant function. The resulting intervals are encoded as separate binary features. Next, using these features, the MLR model is trained, and its weight coefficients (WC) $\in (-\infty; +\infty)$ are used to identify the RF. If WC $\in (-\infty; 0]$, then the values of the variable in the corresponding interval increase or do not affect the probability of a favorable outcome and cannot be interpreted as RF. The values of the piecewise constant function in this interval are equated to 0, thereby excluding this interval from the model. RF are intervals with WC > 0.

The output values of the piecewise functions can be represented as either the observed probability of adverse events within each subrange or the MLR weight coefficients. For improved interpretability, scores derived from these coefficients are standardized using Formula 1. The final prediction is obtained by aggregating the scores assigned by each

decision tree in the ensemble.

$$y\prime_i = \frac{f_i(x_i)}{\sum_{n=1}^{m} \max(f_n)} * 1000 \quad (1)$$

where, x_i is the value of parameter i;

f_i is the piecewise constant function corresponding to parameter i;

m is the total number of parameters

The values of the piecewise constant functions can also be represented by the probabilities of adverse events derived from decision trees. In this case, the aggregation of predictions from weak classifiers is performed using the formula for the sum of probabilities of independent and joint events (Eq. 2):

$$P'(A_1, A_2 \ldots A_n) = P(A_1) + P'(A_2, A_3 \ldots A_n) - P(A_1) * P'(A_2, A_3 \ldots A_n) \quad (2)$$

where P denotes the probability of an adverse event associated with a risk factor;

A_1,$A_1 \ldots A_n$ are the risk factors identified in a particular patient.

2.3 Dataset

The proposed RandFRF method was validated using a dataset obtained from a single-center retrospective cohort study. This study analyzed data extracted from the electronic medical records of patients treated at the Regional Vascular Center of "Primorsky Regional Clinical Hospital No. 1" in Vladivostok, Russia, from 2015 to 2021. Ethical approval was granted by the Ethics Committee of the School of Medicine at the Far Eastern Federal University.

To address the task of IHM prediction, the dataset included 4,673 patients diagnosed with STEMI who underwent PCI with infarct-related artery stenting within the first 24 h of hospitalization. Among these patients, IHM following PCI occurred in 318 individuals (6.8%).

In addition to demographic and clinical history data, the dataset comprised laboratory test results (complete blood count and biochemical analyses) and findings from instrumental investigations, including electrocardiography (ECG) and transthoracic echocardiography.

The primary study endpoint was all-cause IHM, recorded as a binary categorical outcome variable.

2.4 Machine Learning

Model training, cross-validation, and final testing were conducted according to the following protocol. The dataset was split into two subsets: a training and cross-validation set (80%) and a final test set (20%). Cross-validation was performed using a stratified K-folders approach. Performance metrics were averaged across folds and included AUC, Sen, and Sp. The AUC was used as the principal metric for model selection, predictor inclusion, and hyperparameter tuning.

The classification threshold for calculating sensitivity and specificity was determined by identifying the optimal balance between these two measures. Final model evaluation

involved training the best-performing models, with optimized parameters and hyperparameters, on the 80% training set and testing them on the held-out 20% test set. To ensure robustness, the entire training-testing split procedure was repeated 100 times using different random seeds.

Data preprocessing, model development and analysis were conducted using Python (version 3.9.16) with open-source libraries.

3 Results

3.1 Predictors of IHM

The RandFRF method was validated on a dataset of 4,673 STEMI patients aged 26 to 93 years (median age: 63 years; 95% CI: 62–63). Of these, 318 patients (6.8%) experienced IHM following PCI and were assigned to the adverse outcome group (Group 1), coded as "1". Patients who survived were assigned to the favorable outcome group (Group 2), coded as "0".

Comparative analysis of demographic, clinical, laboratory, and instrumental parameters between groups revealed that most variables differed significantly (Table 1). Patients who died in-hospital were more likely to be older and female (OR = 1.8, $p < 0.00001$). Group 1 also had a higher prevalence of acute heart failure (AHF) classified as Killip class III or IV (OR = 7.1), lower systolic blood pressure (SBP), and reduced left ventricular ejection fraction (LVEF). Additionally, this group exhibited elevated heart rates (HR), higher serum creatinine (Cr) and glucose (Glu) levels, increased relative neutrophil counts (NEUT), and plateletcrit (PCT), as well as decreased eosinophil (EOS) levels.

All predictors that demonstrated statistically significant intergroup differences were validated using predictive models of IHM in patients with STEMI following PCI. A predictor was considered validated for multivariate prognostic modeling if its inclusion in LR, Random Forest, or XGBoost models resulted in an increase in the AUC, as assessed via ten-fold cross-validation. Based on this criterion, the final set of validated predictors of IHM in STEMI patients post-PCI included: age, SBP, HR, Killip class of AHF, LVEF, Cr, NEUT, EOS, PCT, and Glu.

3.2 Application of the Modified Random Forest Method

Ensemble models were developed using several machine learning algorithms, including Random Forest, AdaBoost, Gradient Boosting, LightGBM, XGBoost, and CatBoost. Additionally, two models were developed based on the proposed RandFRF methodology. The first model employed multivariate logistic regression-derived weight coefficients (WC RandFRF) to rank the identified RFs, while the second model used predicted probabilities of IHM (Prob RandFRF) for this purpose. The performance metrics of these models are summarized in Table 2.

The comparative analysis of model performance metrics demonstrated the superiority of standard Random Forest and XGBoost models over AdaBoost and LightGBM (p-value <0.01). The performance of AdaBoost and LightGBM was comparable, with median AUC values of 0.871 and 0.870, respectively, and no statistically significant

Table 1. Comparison of basic characteristics between two groups

	Group 1 (n = 318)	Group 2 (n = 4355)	OR (95% CI)	p-value
Sex (female), n (%)	142 (44.65)	1332 (30.5)	1.8 [1.5; 2.3]	<0.000001
Age, y	71 (63; 78)	62 (55; 69)	–	<0.000001
SBP, mmHg	110 (90; 130)	130 (120; 150)	–	<0.000001
HR, bpm	86 (72; 100)	72 (65; 80)	–	<0.000001
Cr, µmol/L	130 (96; 193.3)	97 (81; 114.8)	–	<0.000001
Killip class for AHF				
I	71 (22.33%)	2726 (62.6%)	0.17 [0.13; 0.23]	<0.000001
II	58 (18.2%)	867 (19.9%)	0.9 [0.67; 1.20]	0.508052
III	66 (20.75)	479 (11)	2.1 [1.6; 2.8]	<0.000001
IV	123 (38.7)	269(6.18)	9.6 [7.4; 12.4]	<0.000001
III-IV	189 (59.4)	748 (17.2)	7.1 [5.6; 9]	<0.000001
LVEF, %	46.5 (38; 54.8)	56 (50; 61)	–	<0.000001
NEUT, %	81.3 (75.75; 86.5)	66.7 (59.1; 74.9)	–	<0.0001
PCT, %	0.22 (0.17; 0.28)	0.2 (0.16; 0.24)	–	0.0012
EOS, %	0.1 (0.00; 0.3)	0.9 (0.3; 1.9)	–	<0.000001
Glu, mmol/l	7.9 (6.3; 10.31)	5.8 (5.1; 7)	–	<0.000001

Abbreviations: *LVEF* left ventricular ejection fraction, *Glu* serum glucose, *SBP* systolic blood pressure, *HR* heart rate, *Cr* serum creatinine, *PCT* plateletcrit; *NEUT* neutrophil percentage, *EOS* eosinophil percentage, *AHF* acute heart failure

Table 2. Comparative analysis of IHM model performance

Model	AUC	Sen	Sp
LightGBM	0.870 [0.862; 0.878]	0.815 [0.811; 0.819]	0.810 [0.807; 0.814]
AdaBoost	0.871 [0.863; 0.880]	0.815 [0.811; 0.819]	0.810 [0.807; 0.814]
Gradient Boosting	0.875 [0.866; 0.884]	0.815 [0.805; 0.825]	0.812 [0.803; 0.822]
CatBoost	0.881 [0.873; 0.889]	0.815 [0.805; 0.825]	0.815 [0.806; 0.825]
WC RandFRF	0.881 [0.875; 0.887]	0.815 [0.805; 0.825]	0.809 [0.799; 0.818]
Random Forest	0.887 [0.883; 0.891]	0.833 [0.823; 0.844]	0.833 [0.822; 0.843]
XgBoost	0.891 [0.888; 0.895]	0.833 [0.829; 0.837]	0.840 [0.836; 0.844]
Prob RandFRF	0.897 [0.890; 0.904]	0.833 [0.824; 0.843]	0.837 [0.828; 0.846]

difference between them (p-value = 0.836). Although Random Forest and XGBoost models showed higher median AUC values compared to CatBoost and the WC RandFRF model, these differences were not statistically significant (p-values = 0.115 and 0.255, respectively).

Similarly, the performance of Gradient Boosting, CatBoost, and WC RandFRF models was comparable, with AUC values of 0.875, 0.881, and 0.881, respectively, and no statistically significant differences among them (p-values ranging from 0.088 to 0.396).

Based on the model trained on the entire dataset, a set of RFs associated with IHM was identified (Table 3). The most influential predictors of IHM included: Killip class IV heart failure (score: 0.446), Cr >195.4 μmol/L (0.386), HR >113 bpm (0.370), SBP ≤95 mmHg (0.367), and LVEF <35% (0.279). Additional but less influential RFs included: NEUT ≥88.4% (0.259), age > 82 years (0.234), Cr 164.1–195.4 μmol/L (0.178), and PCT ≥ 0.365% (0.169). Other predictor categories had a marginal impact on IHM probability, with influence scores ranging from 0 to 0.153.

Based on the extracted RFs, LR models were developed, and their performance characteristics are presented in Table 4. Models that relied solely on RFs showed inferior performance compared to models based exclusively on continuous variables. However, integrating both continuous variables and RFs into the LR models significantly improved predictive performance (p-value <0.01). This enhancement is attributed to the model's ability to account for nonlinear relationships between predictors and the outcome, which are otherwise not captured in purely linear models.

Table 4. IHM model performance

	Continuous variables	Risk factors	Both continuous variables and RFs
AUC	0.891 [0.888; 0.894]	0.877 [0.869; 0.885]	0.910 [0.908; 0.913]
Sen	0.833 [0.816; 0.851]	0.816 [0.807; 0.826]	0.834 [0.822; 0.844]
Sp	0.821 [0.82; 0.822]	0.819 [0.810; 0.828]	0.835 [0.831; 0.839]

4 Discussion

Ensemble-based ML models have demonstrated high predictive performance in clinical medicine and hold significant promise for risk stratification and decision support. However, their limited interpretability remains a major barrier to widespread adoption in clinical practice. To address this limitation, both global and local interpretability techniques have been introduced. Global interpretability methods aim to describe the overall logic of model behavior. These include Partial Dependence Plots (PDP) [14], Accumulated Local Effects Plots (ALEP) [12], SHAP [13], and RuleCOSI+ [10], etc. In contrast, local interpretability methods seek to explain individual predictions. Representative techniques in this category include Individual Conditional Expectation Plots (ICEP) [21] and Local Interpretable Model-Agnostic Explanations (LIME) [15], etc. A key limitation of these interpretability methods is that they are applied post hoc—after the model has been trained—which complicates the model development pipeline. The

Table 3. Risk factors of IHM

Predictor	Interval	IHM probability	Predictor	Interval	IHM Probability
Age, y	[70; 73] [73; 76] [76; 78] [78; 82] 82+	0.071 0.102 0.138 0.187 0.234	SBP, mmHg	−95 [95; 109] [109; 124] [124; 129]	0.367 0.143 0.074 0.043
HR, bpm	[82; 85] [85; 88] [88; 94] [94; 113] 113+	0.072 0.084 0.112 0.184 0.37	Killip Class of AHF	3 4	0.13 0.446
Cr, µmol/L	[122.8; 127.3] [127.3; 133.9] [133.9; 147.1] [147.1; 164.1] [164.1; 195.4] 195.4+	0.082 0.086 0.096 0.133 0.178 0.386	NEUT, %	[75.5; 76.7] [76.7; 78.9] [78.9; 81] [81; 83.3] [83.3; 85.5] [85.5; 88.4] 88.4+	0.099 0.106 0.116 0.153 0.177 0.206 0.259
EOS, %	−0.05 [0.05; 0.15] [0.15; 0.35]	0.186 0.114 0.064	LVEF, %	−35.5 [35.5; 40.5] [40.5; 44.3] [44.3; 46.7] [46.7; 49.8]	0.279 0.117 0.101 0.078 0.045
PCT, %	−0.135 [0.135; 0.14] [0.27; 0.285] [0.285; 0.32] [0.32; 0.365] 0.365+	0.082 0.077 0.065 0.055 0.084 0.169	Glu, mmol/L	−4.1 [6.79; 7.03] [7.03; 8.64] [8.64; 9.52] [9.52; 10.9] [10.9; 13.4] 13.4+	0.058 0.043 0.068 0.132 0.19 0.076 0.151

Abbreviations: *LVEF* left ventricular ejection fraction, *Glu* serum glucose, *SBP* systolic blood pressure, *HR* heart rate, *Cr* serum creatinine, *PCT* plateletcrit; *NEUT* neutrophil percentage, *EOS* eosinophil percentage, *AHF* acute heart failure

RandFRF method differs in that it incorporates feature RFs directly during the training process, thereby streamlining model development. In cardiology, established risk assessment tools such as the GRACE [5] and CADILLAC [7] scores use piecewise constant functions to stratify risk. Clinicians use these scoring systems to evaluate patient condition and guide treatment decisions based on categorical risk assessments. The proposed ensemble-based method builds on this paradigm by constructing models that transform continuous variables into piecewise constant functions. The cumulative value of these functions, together with a predefined decision threshold, enables binary classification into survival or in-hospital mortality categories. This design mirrors the decision logic

of widely accepted clinical risk scores, thereby enhancing transparency and clinician interpretability.

The piecewise constant function values can be represented either by the WC MLR or by the probability of an adverse outcome. In practice, the use of predicted probabilities slightly improved model performance (AUC 0.894 vs. 0.890). However, deriving WC MLR complicates the model development process. Thus, using WC as function values is not deemed practical.

The transformation of continuous variables into piecewise constant representations is driven by decision rules derived from feature RFs. These RFs encode knowledge about the relationships between predictors and the clinical outcome. They are identified through optimization procedures aimed at minimizing p-values or maximizing AUC, as well as through analysis of SHAP values derived from a multivariate XGBoost model. By evaluating SHAP value dynamics across predictor ranges, the method elucidates associations between predictor values and the outcome, supporting the use of this information for multilevel categorization.

The integration of these procedures enables the construction of RandFRF models with high interpretability and predictive performance that slightly exceeds that of conventional ensemble methods such as XGBoost and traditional random forests (AUC = 0.894 vs. 0.891 and 0.889, respectively).

Moreover, combining extracted RFs with original continuous variables improves the predictive performance of logistic regression models. This improvement arises from the ability of RFs to capture non-linear relationships with the outcome, while continuous variables retain additional information lost during categorization.

5 Conclusion

This study introduces a novel RandFRF methodology that leverages RFs to enhance model interpretability without compromising predictive accuracy. The approach was validated using a dataset of STEMI patients undergoing PCI to predict IHM. Predictive models based on RandFRF demonstrated performance comparable to that of state-of-the-art models developed using traditional random forests and XGBoost. Furthermore, the rule-based structure of the RandFRF model allows for interpretability of individual predictions and improves model performance when RFs are incorporated alongside continuous predictors in machine learning models.

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Chapter 30

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