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Keywords (separated by '-')	explainable artificial intelligence - risk factors - risk factor phenotypes - interpretable machine learning models

An Interpretable Predictive Model of In-Hospital Mortality in Patients with Myocardial Infarction Based on Risk Factor Phenotypes

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Abstract. The study addresses the problem of explaining the prediction results of machine learning models, developing methods for phenotyping risk factors, and predicting in-hospital mortality (IHM) in patients with ST-segment elevation myocardial infarction (STEMI) after percutaneous coronary intervention (PCI). For IHM prediction, risk factors were identified and their phenotypes were formed, providing not only transparency of decision-making but also improving prediction quality. Two methods were proposed for extracting risk factors and forming their phenotypes: entropy minimization and search for a separating curve based on AUC maximization. These methods were applied to a dataset of 4673 electronic health records of patients with STEMI and IHM prediction after emergency PCI. Risk factor phenotypes were identified, and IHM predictive models were developed based on them. The results demonstrated that the multifactor logistic regression (MLR) prediction model, with phenotypes identified by the entropy minimization method as predictors, was inferior in prediction accuracy to the MLR model with continuous predictors (AUC - 0.885 vs. 0.902, p-value = 0.036). The MLR model based on phenotypes formed by the separating lines method provided higher quality IHM prediction (AUC - 0.915 vs. 0.902 and 0.885, p-value = 0.029 and p-value $<$0.000001, respectively).

Keywords: explainable artificial intelligence · risk factors · risk factor phenotypes · interpretable machine learning models

1 Introduction

In clinical medicine, predictive and diagnostic models developed using logistic or linear regression are widely utilized, as they provide superior transparency in decision-making compared to other machine learning (ML) methods [1]. However, when dealing with

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nonlinear relationships between input features and the target variable, as well as when outcomes are influenced by combinations of predictors, these methods often fail to deliver the required predictive accuracy [5]. The lack of transparency and interpretability of ML models significantly limits their widespread adoption in clinical practice [2].

To address this issue, methods of explainable artificial intelligence (XAI) and interpretable ML models have been actively developed in recent years. A key component of these approaches is the categorization of predictors and the identification of risk factors (RFs) for adverse clinical events. Specifically, RFs refer to categorical predictors whose values exceed or fall below their threshold levels. Previous studies have demonstrated that identifying RF phenotypes—combinations of features with synergistic effects on the outcome—and incorporating them into model structures as predictors enhances prediction interpretability [4]. Nevertheless, methods for automated RF phenotyping have yet to be developed.

ST-segment elevation myocardial infarction (STEMI) represents the most severe clinical manifestation of ischemic heart disease and a leading cause of mortality in most countries worldwide. Percutaneous coronary intervention (PCI) with stenting of the infarct-related coronary arteries is the predominant strategy for myocardial revascularization in STEMI patients. However, when performed as an emergency procedure, in-hospital mortality (IHM) ranges from 4% to 9% [10], highlighting the need for reliable predictive tools to stratify the risk of adverse clinical outcomes.

The objective of this study is to develop novel methods for identifying RF phenotypes that ensure high interpretability and accuracy in predictive models of IHM in STEMI patients following PCI.

2 Data and Methods

2.1 Data

The retrospective study included data from 4,673 electronic medical records of patients admitted to the Regional Vascular Center of the Krai Clinical Hospital No. 1 in Vladivostok for emergency treatment of ST-segment elevation myocardial infarction between 2015 and 2021. All patients underwent emergency percutaneous coronary intervention with stenting of the infarct-related coronary arteries.

The patients were divided into two groups:

- Group 1 consisted of 159 patients (3.7%) who died during hospitalization (in-hospital mortality, IHM).
- Group 2 comprised 4,187 patients (96.3%) with successful treatment outcomes.

The data reflecting the clinical and functional status of the patients included continuous and categorical variables. The study's primary endpoint was a binary outcome: presence ("1") or absence ("0") of IHM.

The selection and validation of continuous predictors for IHM, as well as the development of a predictive model based on these factors, were previously performed by the authors [8].

In the current study, this model serves as the baseline and includes the following continuous predictors: Age – Patient age; HR – Heart rate; Killip class – Severity of

acute heart failure (Killip classification); Cr – Creatinine; EF LV – Left ventricular ejection fraction (Teichholz method); NEUT – Neutrophils; EOS – Eosinophils; PCT – Plateletcrit; Glu – Glucose; SBP – Systolic blood pressure.

2.2 The Methods Used

As we previously demonstrated, continuous predictors can be transformed into risk factors using various categorization methods [9]. An RF is a binary variable associated with a model predictor, which divides the data into two groups where the frequency of the adverse event exhibits a statistically significant difference. The RF is encoded as "1" for the group in which the adverse event (coded as "1") occurs significantly more often.

In prior work, the authors of this article introduced a multi-metric categorization method for continuous features, enabling the formation of an RF pool that explains machine learning model decisions in predicting adverse clinical events [9]. In the current study, we propose two methods for defining RF phenotypes with the following objective functions: entropy minimization and separating hyperplane identification based on AUC maximization.

Threshold values for continuous features and their corresponding RFs were determined using training (80%) and test (20%) datasets. Model performance was evaluated using: area under the ROC curve (AUC), sensitivity (Sen), specificity (Spec).

2.3 Entropy Minimization Method

The simultaneous presence of two RFs in a patient increases the probability of in-hospital mortality if they exhibit a combined effect on the outcome. Such pairs are termed RF phenotypes. In other cases, IHM probability depends solely on the individual impact of isolated RFs.

We formalize the rule for paired RFs and IHM as:

$$\text{IF } F_i \ \&F_j \ \text{THEN } Y = 1$$

where F_i, F_j are RFs corresponding to predictors X_i, X_j (with endpoint predictors $\mathbf{X} = \{X_i, i = 1, \ldots, K\}$), Y is the binary endpoint. An RF is a binary variable equal to 1 when X_i values significantly increase the probability of $Y = 1$. In clinical practice, this typically occurs when a predictor exceeds a "reference" interval boundary, defined as the RF's threshold value A_i.

Thresholds A_i are derived by minimizing entropy, expressed as Kullback-Leibler (KL) divergence [7]. For two discrete probability distributions p_j and q_j, KL divergence is:

$$D = -\sum_{j=0}^{n-1} p_j \ln q_j + \sum_{j=0}^{n-1} p_j \ln p_j, \tag{1}$$

where n is the number of possible values of the random variable.

Let: N = total observations, TP = true positives for F_i, FP = false positives, TN = true negatives, FN = false negatives.

Define p_j (actual distribution of Y) and q_j (predicted distribution under RF assessment) as:

$$p_1 = \frac{TP + FN}{N}, p_0 = \frac{TN + FP}{N}, \tag{2}$$

$$q_1 = \frac{TP + FP}{N}, q_0 = \frac{TN + FN}{N}\ . \tag{3}$$

Substituting (2) and (3) into (1) yields:

$$D = -\frac{TP + FN}{N} \ln \frac{TP + FP}{N} - \frac{TN + FP}{N} \ln \frac{TN + FN}{N} + \tag{4}$$

$$+\frac{TP + FN}{N} \ln \frac{TP + FN}{N} + \frac{TN + FP}{N} \ln \frac{TN + FP}{N}.$$

Thresholds A_i are identified via grid search over M points, minimizing D. For all predictors $\mathbf{X} = \{X_i, i = 1, ..., K\}$, this generates $K(K–1)/2$ possible RF pairs.

The above method treats RFs in isolation. To evaluate pairwise synergistic effects, fix a subset of the cohort where $F_i = 1$, and compute threshold A_{ij} for F_j by minimizing D within this subset.

2.4 Method for Maximizing the Area under ROC Curve (AUC) for Linear Combinations of Risk Factors

The method for identifying optimal linear combinations of paired risk factors is based on selecting the region with maximum AUC, achieved by partitioning the point cloud (X_i, X_j) with a straight line. The objective of this method is to find a separating line that predicts class "1" on one side, predicts class "0" on the other side, and provides optimal binary classification quality (maximized AUC). To optimize the line search algorithm, we only consider lines that pass through at least one point belonging to class "1".

The solution involves: enumerating all pairs of points (X_i, X_j) where at least one point belongs to class "1"; calculating AUC using the formula for single-factor dichotomous classification ($F_{ij} = aX_i < bX_j + c$), see [6]:

$$\text{AUC} = 0.5\left(1 + \frac{TP}{TP + FN} - \frac{FP}{TN + FP}\right). \tag{5}$$

The optimal separating line is determined by maximizing AUC for each pair of features (X_i, X_j). The algorithm complexity is $O(NM \log N)$, where: $N =$ total number of observations, $M =$ number of observations where $Y = 1$.

2.5 Study Design

The study design comprised four stages. At the first stage, we developed predictive models for in-hospital mortality in STEMI patients after PCI using continuous predictors identified in our previous research [4] and three machine learning methods: multiple

logistic regression (MLR), stochastic gradient boosting (SGB), random forest (RF). The best-performing model was selected as the baseline model. The second stage involved applying the entropy minimization method to identify: individual risk factors and RF phenotypes. The third stage implemented a classification line search method based on AUC maximization to identify phenotypes and derive linear combinations of RFs. The final stage developed IHM prediction models using MLR, where predictors consisted of RF phenotypes obtained through the proposed methods. Model accuracy was compared using the Mann-Whitney U test with AUC as the primary metric.

3 Results

Using the aforementioned continuous predictors (Age, HR, Killip class, Cr, EF LV, NEUT, EOS, PCT, Glu, SBP), baseline predictive models for in-hospital mortality in STEMI patients were developed (Table 1).

Table 1. Performance metrics of baseline IHM prediction models in STEMI patients based on continuous predictors.

	Cross-validation			Final testing		
	AUC	Sen	Spec	AUC	Sen	Spec
MLR	0.909 [0.905; 0.914]	0.86 [0.849; 0.871]	0.851 [0.848; 0.855]	0.897 [0.881; 0.913]	0.834 [0.804; 0.865]	0.848 [0.843; 0.853]
SGB	0.901 [0.899; 0.902]	0.826 [0.823; 0.83]	0.845 [0.844; 0.846]	0.902 [0.897; 0.907]	0.831 [0.819; 0.843]	0.846 [0.844; 0.849]
RF	0.896 [0.894; 0.897]	0.815 [0.811; 0.82]	0.818 [0.816; 0.819]	0.896 [0.891; 0.901]	0.824 [0.814; 0.835]	0.815 [0.812; 0.819]

During cross-validation, the MLR model demonstrated superior predictive accuracy (AUC 0.909 vs. 0.901 and 0.896, $p = 0.027$ and $p = 0.0014$, respectively). In final testing, all models showed comparable performance metrics ($p > 0.05$).

3.1 Entropy Minimization

Implementation of the first threshold search method for A_i enabled identification of risk factors (RFs) F_i, which were then paired through entropy minimization. These RF pairs were subsequently optimized by combining threshold values to maximize AUC during cross-validation. Several combination functions were employed for threshold integration: average(A_i), max(A_i), or min(A_i).

The seven primary risk factors (F_i), determined independently through entropy minimization, included: Heart rate $>$ 108 bpm; Killip class 3 or 4; Creatinine $>$190 umol/l;

Table 2. Risk factor phenotypes for in-hospital mortality derived using the entropy minimization method.

№	Primary RFs (F_i)	Secondary RFs (F_j)	OR [95% CI]	Cross-validation AUC	Final testing AUC
1	HR > 108 bpm	Killip class = 3, 4 or Cr > 190 umol/l or EF LV < 45% or EOS < 0.21% or Neut >85% or Glu > 10 mmol/l or SBP < 105 mmHg	10.15 [7.31; 14.1]	0.593 [0.592; 0.594]	0.591 [0.587; 0.595]
2	Killip class = 3, 4	Cr > 190 umol/l or EF LV < 45% or EOS < 0.21% or Neut >85% or Glu > 10 mmol/l or SBP < 105 mmHg or PCT > 0.28%	10.63 [8.29; 13.62]	0.716 [0.714; 0.717]	0.719 [0.714; 0.725]
3	Cr > 190 umol/l	EF LV < 45% or EOS < 0.21% or Neut >85% or Glu > 10 mmol/l or SBP < 105 mmHg or PCT > 0.28%	19.77 [13.77; 28.38]	0.617 [0.616; 0.618]	0.615 [0.611; 0.62]
4	EF LV < 45%	EOS < 0.21% or Neut >85% or Glu > 10 mmol/l or SBP < 105 mmHg or PCT > 0.28%	10.67 [7.88; 14.44]	0.673 [0.671; 0.675]	0.669 [0.662; 0.677]
5	Neut >85%	EOS < 0.21% or Glu > 10 mmol/l or SBP < 105 mmHg or PCT > 0.28%	8.27 [6; 11.4]	0.629 [0.628; 0.631]	0.624 [0.618; 0.631]
6	EOS < 0.21%	Glu > 10 mmol/l or SBP < 105 mmHg or PCT > 0.28%	10.83 [8.04; 14.58]	0.707 [0.706; 0.709]	0.7 [0.694; 0.707]
7	Age > 70 years	EF LV < 45% or Neut >85% or SBP < 105 mmHg	3 [2.35; 3.63]	0.613 [0.613; 0.615]	0.611 [0.606; 0.616]

LVEF <45%; Neutrophils >85%; Eosinophils <0.21%; Age > 70 years. Secondary RFs (F_j) were derived via conjunction with F_i and additional entropy minimization. Combining paired RFs (F_i and F_j) yielded 7 phenotypes (disjunctions of pairs), which

demonstrated prognostic value in logistic regression models (AUC range: 0.593–0.716; Table 2). Phenotypes (2) and (6) achieved the highest AUC values (0.716 and 0.707, respectively). Odds ratio (OR) calculations revealed highest IHM likelihood: Phenotype (3) (OR = 19.77); lowest IHM likelihood: Phenotype (7) (OR = 3.0); comparable ORs: Phenotypes (1), (2), (4), and (6) (range: 10.15–10.83).

3.2 Classification Boundary Optimization Via AUC Maximization

Implementation of the classification boundary method identified 10 risk factor phenotypes that effectively stratified STEMI patients into groups with either in-hospital mortality or favorable PCI outcomes (Table 3). Fig. 1 and 2 exemplify two derived phenotypes based on: age and eosinophil (EOS) count; age and heart rate (HR).

Table 3. In-hospital mortality risk factor phenotypes derived through optimal classification boundary analysis.

	Rule	OR [95% CI]	AUC (cross-validation)	AUC (final testing)
1	HR ≥ -1.778 * Age + 198	7.07 [5.49; 9.1]	0.726 [0.725; 0.728]	0.727 [0.722; 0.732]
2	EOS $\leq$ 0.039 * Age - 2	12.77 [8.65; 18.84]	0.773 [0.771; 0.774]	0.778 [0.772; 0.783]
3	EF LV $\leq$ 0.667 * HR - 4.28	9.04 [6.64; 12.3]	0.75 [0.748; 0.751]	0.746 [0.74; 0.752]
4	Glu ≥ -0.098 * HR + 14.84	6.81 [5.01; 9.26]	0.723 [0.722; 0.725]	0.72 [0.714; 0.726]
5	SBP $\leq$ 60 * Killip class +12.9	6.51 [5.07; 8.36]	0.719 [0.718; 0.72]	0.717 [0.712; 0.722]
6	EF LV $\leq$ 0.21 * Cr + 25.25	12.55 [9.05; 17.41]	0.78 [0.778, 0.781]	0.777 [0.771, 0.782]
7	SBP $\leq$ 0.963 * Cr - 0.423	7.88 [6.11; 10.17]	0.711 [0.71; 0.713]	0.715 [0.709, 0.721]
8	PCT $\geq$ 0.027 * EF LV - 1.139	5.97 [4.37; 8.16]	0.708 [0.706; 0.709]	0.715 [0.707, 0.722]
9	SBP $\leq$ 10.1 * NEUT - 646.8	12.17 [8.91; 16.63]	0.776 [0.775; 0.778]	0.771 [0.765; 0.777]
10	Glu ≥ -4.13 * PCT + 7.56	5.42 [3.96; 7.42]	0.699 [0.698, 0.701]	0.701 [0.695; 0.708]

The predictive accuracy of the identified risk factor phenotypes ranged from 0.701 to 0.778 during final testing, with odds ratios (OR) varying between 5.42 and 12.77. The highest AUC and OR values were observed for Phenotype (2), which incorporated

eosinophil count (Eos) and age as predictors (Fig. 1). Comparable predictive performance (AUC = 0.777, OR = 12.55) was demonstrated by Phenotype (2) combining left ventricular ejection fraction (EF LV) and creatinine (Cr). The lowest predictive values (AUC = 0.701, OR = 5.42) were associated with Phenotype (10), which included glucose (Glu) and plateletcrit (PCT) as predictive variables.

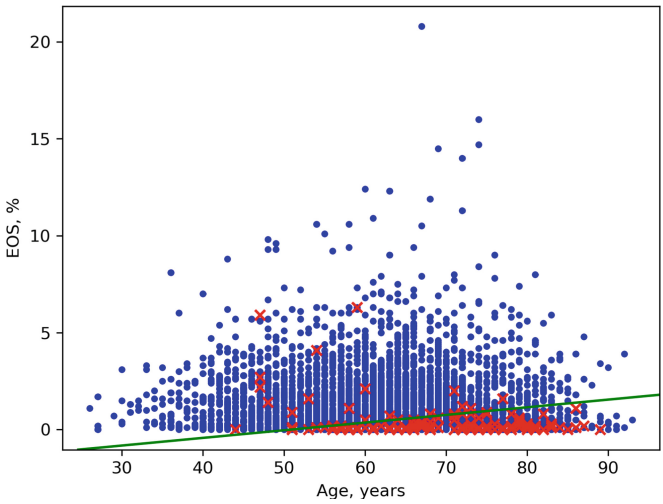

Fig. 1. Relationship between patient age and blood eosinophil count forming the risk factor phenotype (EOS $\leq 0.039 \times$ Age - 2). Patients with favorable treatment outcomes are shown in blue, while those with IHM are marked in red.

3.3 Development of Predictive Models and Comparative Analysis of their Accuracy

At this stage of the study, predictive models were developed using risk factor phenotypes derived via entropy minimization and AUC maximization (incorporating optimal classification boundaries). The performance characteristics of these models are presented in Table 4.

A comparative analysis of quality metrics revealed that the model with phenotypes formed by the classification line method demonstrated superior predictive properties compared to both the model with continuous predictors and the model with phenotypes identified using the entropy minimization method (p-value = 0.029 and p-value $<$0.000001, respectively).

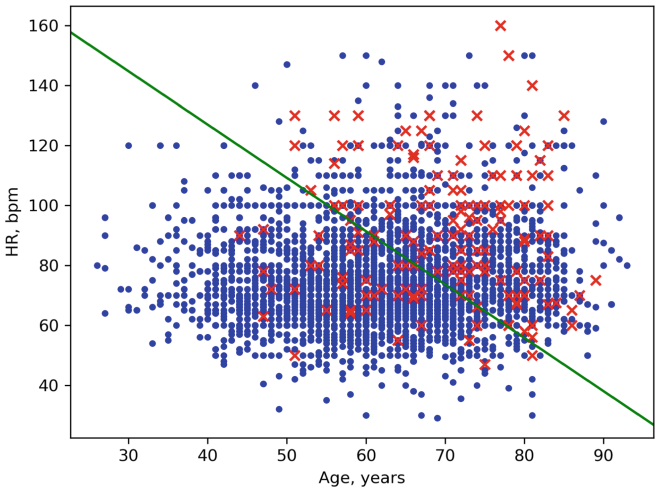

Fig. 2. Relationship between patient age and heart rate (HR) forming the risk factor phenotype ($HR \geq -1.778 \times Age + 198$). Patients with favorable treatment outcomes are shown in blue, while those with IHM are indicated in red.

Table 4. Predictive models of in-hospital mortality using continuous predictors and risk factor phenotypes

Predictors	AUC [95% CI]	Sensitivity [95% CI]	Specificity [95% CI]
Continuous, SGB Model	0.902 [0.897; 0.907]	0.831 [0.819; 0.843]	0.846 [0.844; 0.849]
Phenotypes of RFs based on entropy minimization	0.885 [0.88; 0.891]	0.813 [0.799; 0.826]	0.825 [0.819; 0.832]
Phenotypes of RFs based on classification line search	0.915 [0.911; 0.919]	0.853 [0.842; 0.863]	0.852 [0.849; 0.855]

4 Discussion

Clinical medicine is a field of knowledge where evidence of the predictive potential of analyzed factors is of particular importance. When there are linear relationships between predictors and the study endpoint, MLR models, which have the highest transparency, often demonstrate the best prediction results. However, when using continuous predictors, the conclusions they generate pose difficulties for clinical interpretation by practicing physicians.

The complexity of the relationships between adverse clinical events and their associated RFs is a reason to use ML methods (RF, SGB, CatBoost, artificial neural networks, etc.) capable of accounting for nonlinear relationships between the analyzed factors. The main disadvantage of these methods is the lack of transparency of the models developed on their basis. In such cases, the need for XAI and interpretable ML models significantly increases.

In this study, we used MLR, RF, and SGB methods to develop a baseline model with continuous predictors. These methods showed comparable results in predicting major adverse cardiovascular events (MACE) in patients with STEMI after PCI (AUC: 0.897–0.902), which may indicate the prevalence of linear relationships.

One approach to "whitening" the "black box" models is rule determination [5]. These rules typically have the form "predictor > = a", where "a" is a certain value, and the combination of rules ensures transparent decision-making. Rule extraction is a challenging task, and decision trees developed based on continuous predictors are most often used to solve it [5]. The main disadvantage of decision tree-based models is their low accuracy and a large number of extracted rules, which limit the transparency of decision-making.

Alternative approaches to rule extraction include categorization of continuous predictors with RFs verification. Several studies have pointed out problems with categorization, usually associated with information loss when converting continuous predictors into RFs, which was more noticeable in cases of dichotomization of variables [3]. To overcome this limitation, a multimetric categorization method of predictors was proposed, the use of which expands the possibilities for explaining and interpreting the generated conclusions [9].

An important feature of predictive research in clinical medicine is the presence of reference ranges for analyzed characteristics, deviations from which indicate violations of physiological functions of the body, the risk of developing diseases, or their complications. In these cases, categorization of continuous variables allows identifying numerical values of indicators related to the RF of the predicted adverse event, which increases the explainability of the forecast.

Promising areas for the development of predictive analytics in medicine include RF phenotyping [4]. RF phenotypes of adverse clinical events are a set of categorized characteristics (demographic, anamnestic, clinical, instrumental, laboratory, etc.), the combination of which based on conjunction and disjunction into separate pools can strengthen their relationship with the study endpoint and personalize the prediction.

Despite the typical nature of pathological processes, in real clinical practice, their implementation depends on the individual characteristics of the clinical and functional status of patients and the associated RF phenotypes that affect the outcome of the disease. Thus, RF phenotyping can be considered a useful ML tool that explains the relationships between RF and the endpoint.

Previously, it was shown that the accuracy of predicting MACE in patients with coronary heart disease after elective coronary artery bypass grafting was significantly higher when using an MLR model with RF phenotypes than the classical EuroSCORE II model [4]. In that study, RF phenotypes were formed using enumeration procedures requiring large computational resources.

In this work, the authors tested a new approach to RF phenotyping, which used two methods: entropy minimization and AUC maximization with search for a classification line. The first method identified 7 phenotypes, and the second identified 10 (Tables 2 and 3). Based on them, predictive models of MACE in patients with STEMI after PCI were developed (Table 4). The first model showed lower prediction accuracy than the model with continuous predictors (AUC - 0.885 vs. 0.902, p-value <0.000001). The second

model, using classification lines as predictors, demonstrated superior predictive accuracy (AUC - 0.915 vs. 0.902, p-value = 0.029 and 0.915 vs. 0.885, p-value <0.000001). It is important to note that the IHM prediction model developed based on phenotypes records the patient's relationship to one of them. The predictor takes the value 1 if the patient belongs to the corresponding phenotype and 0 if not. In cases where a patient is associated with several RF phenotypes, the predictors related to these phenotypes take the value 1. Thus, the main feature of this model is its structure, which is represented by a feature space where each feature demonstrates the patient's correspondence to a specific RFs phenotype. This approach significantly enhances the explainability and interpretability of ML predictive models.

The limitations of the study include phenotyping with the identification of only RFs pairs, as well as its single-center and retrospective nature.

5 Conclusion

In the present study, new approaches were used for identifying risk factors of adverse clinical events, forming RF phenotypes, and developing predictive models of major adverse cardiovascular events in patients with ST-elevation myocardial infarction after percutaneous coronary intervention. These models demonstrated high predictive accuracy, explainability, and interpretability of the generated conclusions.

The prospects for further development of this field are associated with the development of new methods for identifying phenotypes that include a larger number of RF, as well as validation of predictive models on datasets from multicenter studies.

Supplementary Material
The source code of the software implementation is available at the following link: https://github.com/lapkin25/XAI-Model.

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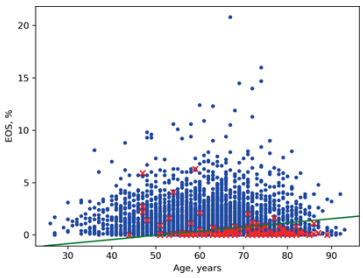
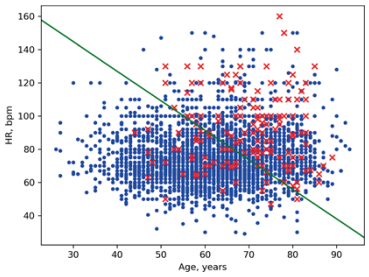
Declaration of Competing Interest. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Alowais, S.A., Alghamdi, S.S., Alsuhebany, N., Alqahtani, T., Alshaya, A.I., Almohareb, S.N., et al.: Revolutionizing healthcare: the role of artificial intelligence in clinical practice. BMC Med. Educ. **23**, 689 (2023)
2. Aravazhi, P.S., Gunasekaran, P., Benjamin, N.Z.Y., Thai, A., Chandrasekar, K.K., Kolanu, N.D., et al.: The integration of artificial intelligence into clinical medicine: trends, challenges, and future directions. Dis. Mon. **71**, 101882 (2025)
3. Collins, G.S., Ogundimu, E.O., Cook, J.A., Manach, Y.L., Altman, D.G.: Quantifying the impact of different approaches for handling continuous predictors on the performance of a prognostic model. Stat. Med. **35**, 4124–4135 (2016)

4. Geltser, B.I., Shakhgeldyan, K.I., Rublev, V.Y., Domzhalov, I.G., Tsivanyuk, M.M., Shekunova, O.I.: Phenotyping of risk factors and prediction of in hospital mortality in patients with coronary artery disease after coronary artery bypass grafting based on explainable artificial intelligence methods. Russian Journal of Cardiology. **28**, 5302 (2023)
5. Molnar, C.: Interpretable machine learning. A guide for making black box models explainable. (2025). https://christophm.github.io/interpretable-ml-book/
6. Muschelli, J.: ROC and AUC with a binary predictor: a potentially misleading metric. J. Classif. **37**, 696–708 (2020)
7. Samawi, H.M., Yin, J., Zhang, X., Yu, L., Rochani, H., Vogel, R., Mo, C.: Kullback-Leibler divergence for medical diagnostics accuracy and cut-point selection criterion: how it is related to the Youden index. J. Appl. Bioinform. Comput. Biol. **9** (2020)
8. Shakhgeldyan, K.J., Kuksin, N.S., Domzhalov, I.G., Geltser, B.I.: Methods of prognostic analysis for the prediction of in-hospital mortality in patients with acute ST-elevation myocardial infarction after percutaneous coronary interventions. Pattern Recognit. Image Anal. **34**, 786–796 (2024)
9. Shakhgeldyan, K.I., Kuksin, N.S., Domzhalov, I.G., Rublev, V.Y., Geltser, B.I.: Interpretable machine learning for in-hospital mortality risk prediction in patients with ST-elevation myocardial infarction after percutaneous coronary interventions. Comput. Biol. Med. **170**, 107953 (2024)
10. Thrane, P.G., Olesen, K.K.W., Thim, T., Gyldenkerne, C., Mortensen, M.B., Kristensen, S.D., Maeng, M.: Mortality trends after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. JACC. **82**, 999–1010 (2023)

Alternative Texts for Your Images, Please Check and Correct them if Required

Page no	Fig/Photo	Thumbnail	Alt-text Description
8	Fig1		Scatter plot showing the relationship between age (years) on the x-axis and EOS percentage on the y-axis. Blue dots represent data points, with a general trend of increasing EOS percentage with age. Red crosses indicate specific data points of interest. A green line suggests a trend or threshold across the data.
9	Fig2		Scatter plot showing heart rate (HR) in beats per minute (bpm) versus age in years. Blue dots represent individual data points, and red crosses indicate outliers. A green trend line shows a negative correlation between age and heart rate. The x-axis ranges from 30 to 90 years, and the y-axis ranges from 40 to 160 bpm.