

Prehospital Diagnostic Algorithm for Acute Coronary Syndrome Using Machine Learning: A Prospective Observational Study

Masahiko Takeda

Chiba University Graduate School of Medicine

Takehiko Oami

Chiba University Graduate School of Medicine

Yosuke Hayashi

Chiba University Graduate School of Medicine

Tadanaga Shimada

Chiba University Graduate School of Medicine

Noriyuki Hattori

Chiba University Graduate School of Medicine

Kazuya Tateishi

Chiba University Graduate School of Medicine

Rie E. Miura

Smart119 Inc

Yasuo Yamao

Smart119 Inc

Ryuzo Abe

Chiba University Graduate School of Medicine

Yoshio Kobayashi

Chiba University Graduate School of Medicine

Taka-aki Nakada (✉ taka.nakada@nifty.com)

Chiba University Graduate School of Medicine

Research Article

Keywords: prediction, acute coronary syndrome, acute myocardial infarction, ST-segment elevation myocardial infarction, STEMI, prehospital care, scoring system, XGBoost

Posted Date: February 21st, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1360222/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background

Rapid and precise prehospital recognition of acute coronary syndrome (ACS) is key to improving clinical outcomes. We tested the hypothesis that the machine learning-based prehospital algorithm shows a high predictive power for predicting ACS.

Methods

We conducted a multicenter observational prospective study that included 10 participating facilities in an urban area of Japan. The data from consecutive adult patients, identified by emergency medical service (EMS) personnel with suspected ACS, were analyzed. The primary outcomes were binary classification models for ACS prediction based on eXtreme Gradient Boosting (XGBoost). Secondary outcomes were classification models for subcategories of ACS, including acute myocardial infarction (AMI) and ST-segment elevation myocardial infarction (STEMI). We evaluated the model performance based on the area under the receiver operating curve (AUC).

Results

Of the 555 enrolled patients, 388 (70%) were randomly assigned to a training cohort, and 167 (30%) were placed in a test cohort. The XGBoost model for ACS using 43 features performed well (AUC 0.879 [95% CI 0.815–0.935]) in the test cohort. We repeated the analysis with a limited number of selected features, and the performance of the XGBoost model using 17 features remained high (AUC 0.883 [95% CI 0.820–0.939]) in the test cohort. The XGBoost model for ACS using 17 features had a higher AUC than the other four common prediction models: logistic regression, random forest, a linear support vector machine (SVM), and a radial basis function (RBF) kernel SVM. The XGBoost algorithm for prediction of AMI and STEMI using the same 17 features also resulted in high AUC scores of 0.857 [95% CI 0.788–0.919] and 0.871 [95% CI 0.819–0.925] in the test cohort, respectively.

Conclusions

We found that the machine learning-based prehospital algorithms showed a high predictive power for predicting ACS.

Background

Early therapeutic interventions are crucial for reducing the mortality of acute coronary syndrome (ACS) [1]. A substantial number of patients have initial symptoms of ACS outside hospitals; emergency medical service (EMS) personnel play a role as the first responders to patients. EMS personnel estimate the

possibility of ACS based on the symptoms of patients and transport them to the appropriate hospital for immediate treatment. Precise prediction of ACS in the prehospital setting may contribute to improving the quality of ACS care and clinical outcomes.

Several studies have investigated the prediction of ACS. Integrated components of patient history, vital signs, 12-lead electrocardiograms (ECG), and cardiac enzymes were studied to increase the accuracy of diagnosis in prehospital management [2]. Prehospital 12-lead ECG is recommended for early diagnosis in patients with suspected ST-segment elevation myocardial infarction (STEMI) [3]; however, costs and lack of training of 12-lead ECG limit its widespread use [4, 5]. Other diagnostic tools with cardiac biomarkers have demonstrated efficacy for risk stratification, but several concerns, including technical errors, high false-negative rates, and possible delays in transportation, cast a shadow on the generalization of promising results [6].

As a result of the low utility of 12-lead ECG and biochemical tests in the prehospital setting, a novel diagnostic tool with vital signs, 3-lead ECG monitoring, and symptoms is warranted to improve the diagnostic accuracy of EMS personnel. With the development of machine learning approaches, early prediction models for other diseases, including stroke and acute aortic syndrome, have demonstrated their accurate and stable performance [7, 8]. However, there are few studies using machine learning to predict the onset of ACS in a prehospital setting.

Therefore, we tested the hypothesis that the machine learning-based early prediction of ACS using vital signs, 3-lead ECG monitoring, and symptoms show a high predictive power. We used a large cohort of patients with suspected ACS.

Methods

Study population

This study was a multicenter observational study that was prospectively conducted in an urban area of Japan (Chiba city, population 1 million) between September 2018 and March 2021. Consecutive adult patients (≥ 20 years of age) identified by EMS personnel with suspected ACS who were transported to one of the twelve participating facilities were enrolled in the study. The symptoms indicating ACS to EMS personnel included pain, discomfort, or pressure in the chest, epigastric region, neck, jaw, or shoulder within 24 hours. Patients with other symptoms that were strongly suspected of having an onset of ACS were also enrolled in the study. Patients with cardiac arrest were excluded from the study because they could not be interviewed in a manner consistent with the other patients.

The study was approved by the Ethical Review Board of the Graduate School of Medicine, Chiba University (No.2733). In accordance with the Ethical Guidelines for Medical and Health Research Involving Human Subjects in Japan, the requirement for written informed consent was waived by the review board.

Data collection and definition

We collected data from 663 patients for 45 features used to predict ACS in a prehospital setting. These features included past medical history, vital signs, 3-lead ECG monitoring, and 21 symptoms (**Additional file1: Table S1**). However, we used only 43 features after excluding two low variance features that were constant in more than 95% of the sample, specifically, the past medical histories of “Prior coronary artery bypass grafting (CABG)” and “Intracranial hemorrhage.” The onset timing and meteorological conditions were considered, but discarded in the final analysis (see **Additional file1: Note S1** for contribution of onset timing and meteorological conditions).

ST changes were assessed with leads I, II, or III of ECG monitoring. ST changes included ST elevation and ST depression. Assessment of the ST changes were left to the discretion of EMS personnel. The contents of symptoms were determined based on previous studies [9–13]. Symptoms 1 and 2 were evaluated by palpation, and symptoms 3–21 were evaluated via interviews. Detailed interview data are shown in **Additional file1: Table S2**. The diagnosis of ACS was established by cardiologists with findings from a catheter angiography according to current guidelines [14]. ACS was defined as acute myocardial infarction (AMI) and unstable angina (UA).

Of the 663 screened patients, 555 patients were included in the final analysis after excluding 108 patients because of missing diagnostic data, multiple entries, and cardiac arrest (**Additional file2: Figure S1**).

Missing values

As our data had missing values for some features, we performed imputations before building the machine learning models. We used the imputed values as input even to the gradient boosting model, which can deal with missing values by treating them the same way as categorical values, because we found that our imputation approach written below had improved its performance compared to the implementation without imputation. Following the domain knowledge, we mutually imputed the missing values in some features: symptoms 4 to 21, except symptoms 19 and 20, and a pair of systolic and diastolic blood pressure. The vital signs, including body temperature, blood oxygen saturation, and breathing rate, were imputed with each median value. For any other categorical attribute, the missing values were replaced with a new subcategory “Unknown.”

Machine Learning model development

Enrolled patients were randomly divided into a training cohort (70%) or a test cohort (30%) for validation in a stratified fashion. There were no statistically significant differences in data distribution between the training and test cohorts ($P > 0.05$).

First, we developed binary classification models for ACS prediction as a primary outcome based on eXtreme Gradient Boosting (XGBoost). As a secondary outcome, we built binary classification models for AMI and STEMI prediction. Non-ST-segment elevation myocardial infarction (NSTEMI) was not included in the secondary analysis because of its small number. The parameters were optimized using the grid

search method with nested cross-validation (see **Additional file1: Note S2** for detailed descriptions of our nested cross-validation).

We assessed the feature importance in the machine learning model based on the Shapley Additive exPlanation (SHAP) value [15]. The SHAP value is a solution concept used in game theory and is computed by the difference in model output resulting from the inclusion of a feature in the algorithm, providing information on the impact of each feature on the output. The SHAP value is a method for its interpretability in machine learning models and is also used as a feature selection tool. A higher absolute SHAP value indicates a more important feature.

Feature selections

We also performed feature selection by discarding the redundant and irrelevant features for prediction to improve performance and the interpretability of the model using XGBoost. Feature selection was performed by the following steps, after we split the dataset into a training set and a test set to evaluate the final model. (1) We used the training set to optimize the hyperparameters using a grid search. (2) We then performed cross-validation on the training set using the optimized parameters and obtained the validation score. (3) We computed the SHAP values of the best model and excluded less important features with the lowest absolute SHAP values. (4) We repeated procedures (1)–(3) until the number of features became one. This process was repeated 10 times to avoid less important features appearing in the higher ranking by chance. As a result of the iterations, we determined the most plausible number of features (i.e., the most important features to be included) from the model that showed the best performance in the mean cross-validation scores. After feature selection, we evaluated a two-classification model for ACS prediction using four common machine learning algorithms other than XGBoost: logistic regression, random forest, a linear support vector machine (SVM), and a radial basis function (RBF) kernel SVM.

Statistical analysis

We expressed the data as median (interquartile range) values for continuous variables and absolute numbers and percentages for categorical variables. The model performance was evaluated using areas under the receiver operating characteristic curve (AUC), accuracy, sensitivity, specificity, and F1 score. Statistical significance was set at $P < 0.05$. We used Python 3.9.5 packages (NumPy 1.21.1, Pandas 1.3.0, XGBoost 1.4.0, and Scikit-learn 1.0) to construct the machine learning models and Prism (version 7.0, GraphPad Software, San Diego, CA) for statistical analysis.

Results

Baseline characteristics and outcomes

Among the training cohort, 134 (24%) patients were diagnosed with ACS (Table 1). ACS patients had significantly higher age, a higher proportion of males, lower frequency of past heart diseases (CAD and old myocardial infarction), lower heart rate, lower body temperature, higher blood oxygen saturation,

lower respiratory rate, and higher frequency of ST elevation or ST change than non-ACS patients. For the symptoms, ACS patients had greater pain severity and higher proportion of cold hands, hand moistening, pressing pain, cold sweat, pain radiating to jaw or shoulder, and persistent pain than non-ACS patients. In the test cohort, similar differences were confirmed between the ACS and non-ACS patients (**Additional file1: Table S3**).

Table 1
Baseline characteristics and clinical outcomes in the training cohort

	ACS (n = 134)	Non-ACS (n = 254)	P value
Age, years	68.5 (57–77)	73 (60–82)	0.010
Male sex, n (%)	105 (78.4)	147 (57.9)	< 0.001
Past medical history			
Diabetes mellitus, n (%)	27 (20.5)	46 (18.5)	0.304
Hypertension, n (%)	50 (38.2)	102 (41.0)	0.423
Dyslipidemia, n (%)	10 (7.8)	13 (5.3)	0.117
Known CAD, n (%)	11 (8.5)	47 (18.9)	0.007
Old myocardial infarction, n (%)	18 (13.6)	47 (19.1)	0.037
Prior PCI, n (%)	13 (10.1)	32 (13.4)	0.101
Prior CABG, n (%)	2 (1.6)	5 (2.1)	0.043
Intracranial hemorrhage, n (%)	1 (0.78)	1 (0.4)	0.237
Cerebral infarction, n (%)	9 (7.0)	13 (5.28)	0.347
Prior antiplatelet or anticoagulant therapy, n (%)	6 (5.0)	31 (13.6)	0.013
Vital signs			
Heart rate (beats/min)	74 (60–86)	90 (72–110)	< 0.001
Systolic blood pressure (mmHg)	143 (122–167)	147 (121–176)	0.413
Diastolic blood pressure (mmHg)	87 (76–102)	87 (72–103)	0.748
Body temperature (°C)	36.0 (35.8–36.4)	36.2 (36.0–36.6)	< 0.001
Blood oxygen saturation (%)	98 (97–99)	97 (93–99)	< 0.001
Respiratory rate (times/min)	20 (18–24)	24 (18–24)	0.014
Japan Coma Scale = 0, n (%)	117 (87.3)	202 (79.5)	0.057
Oxygen therapy, n (%)	50 (37.3)	98 (38.6)	0.807
ECG monitoring			

Data are presented as median and interquartile range for continuous features.

P-values were calculated using Pearson's chi-square test or Mann–Whitney U test.

CAD (coronary artery disease), PCI (percutaneous coronary intervention), CABG (coronary artery bypass grafting), ECG (electrocardiogram)

	ACS (n = 134)	Non-ACS (n = 254)	P value
ST elevation, n (%)	69 (51.5)	23 (9.1)	< 0.001
ST depression, n (%)	37 (27.6)	79 (31.1)	0.475
ST change, n (%)	106 (79.1)	102 (40.2)	< 0.001
Arrhythmia, n (%)	30 (22.4)	65 (25.6)	0.485
Symptoms			
1. Cold hands, n (%)	52 (38.8)	65 (25.6)	0.007
2. Hand moistening, n (%)	47 (35.1)	60 (23.6)	0.016
3. Dyspnea, n (%)	34 (25.4)	86 (33.9)	0.086
4. Palpitations, n (%)	25 (20.5)	66 (27.2)	0.300
5. Throbbing pain, n (%)	26 (21.1)	51 (20.9)	0.929
6. Sharp/stabbing pain, n (%)	13 (10.6)	18 (7.5)	0.614
7. Positional chest pain, n (%)	19 (17.0)	23 (10.0)	0.182
8. Reproduction of chest pain by palpation, n (%)	4 (3.7)	10 (4.4)	0.520
9. Chest pain with breathing or cough, n (%)	12 (5.5)	6 (5.94)	0.983
10. Pressing pain, n (%)	107 (82.3)	157 (64.3)	0.001
11. Nausea or vomiting, n (%)	34 (26.8)	43 (17.4)	0.098
12. Cold sweat, n (%)	74 (57.8)	83 (34.0)	< 0.001
13. Pain radiating to jaw or shoulder, n (%)	23 (19.3)	15 (6.6)	0.001
14. Similarity to previous ischemic episode, n (%)	18 (19.8)	53 (28.0)	0.205
15. Chest pain aggravated by walk, n (%)	16 (18.0)	40 (20.4)	0.745
16. Worsening pain, n (%)	35 (29.9)	74 (31.6)	0.844
17. Pain at rest, n (%)	101 (86.3)	185 (78.7)	0.173
18. Persistent pain, n (%)	123 (97.7)	199 (81.2)	< 0.001
19. Recurrent pain within 24 hours, n (%)	24 (20.9)	47 (21.4)	0.970
Data are presented as median and interquartile range for continuous features.			
<i>P</i> -values were calculated using Pearson's chi-square test or Mann–Whitney U test.			
CAD (coronary artery disease), PCI (percutaneous coronary intervention), CABG (coronary artery bypass grafting), ECG (electrocardiogram)			

	ACS (n = 134)	Non-ACS (n = 254)	P value
20. Chronic pain, n (%)	12 (10.4)	43 (19.2)	0.033
21. Pain severity (10-point scale)	7 (6–9)	6 (5–8)	< 0.001
Data are presented as median and interquartile range for continuous features.			
<i>P</i> -values were calculated using Pearson's chi-square test or Mann–Whitney U test.			
CAD (coronary artery disease), PCI (percutaneous coronary intervention), CABG (coronary artery bypass grafting), ECG (electrocardiogram)			

Prediction of ACS

The XGBoost model for ACS using 43 features showed a high predictive power (AUC 0.879 [95% CI 0.815–0.935]) in the test cohort (Fig. 1).

Feature selection for the prediction algorithm

We examined the relationship between the number of features and the change in predictive values (AUC, accuracy, sensitivity, specificity, and F1-score) using XGBoost (Fig. 2 **and Additional file3: figure S2**). While reducing the number of features from 43 to 17, the performance remained high. However, in decreasing the number of features from 16 to 1, the prediction algorithm with fewer features had lower predictive values. The model using 17 features had the highest AUC (17 features 0.883 [95% CI 0.820–0.939], 43 features 0.879 [95% CI 0.815–0.935]) in the test cohort (Fig. 1, **Additional file4: figure S3, and Additional file5: figure S4**). Of the five machine learning algorithms, XGBoost, logistic regression, random forest, SVM (RBF), and SVM (linear) with 17 features, XGBoost had the highest predictive value in the test cohort (Table 2 **and Additional file4: figure S3**).

Table 2
Prehospital diagnostic algorithms for acute coronary syndrome using 17 features

Models	AUC	Accuracy	Sensitivity	Specificity	F1-score
Training cohort					
XGBoost	0.898	0.827	0.791	0.846	0.760
Random forest	0.882	0.804	0.657	0.882	0.698
Logistic regression	0.884	0.835	0.664	0.925	0.736
SVM (Radial basis function)	0.893	0.827	0.694	0.898	0.735
SVM (Linear)	0.877	0.822	0.642	0.917	0.714
Test cohort					
XGBoost	0.883	0.832	0.810	0.844	0.770
Random forest	0.878	0.844	0.724	0.908	0.764
Logistic regression	0.860	0.808	0.638	0.899	0.698
SVM (Radial basis function)	0.869	0.832	0.707	0.899	0.745
SVM (Linear)	0.873	0.832	0.638	0.936	0.725
AUC (area under the receiver operating characteristic curve), XGBoost (eXtreme Gradient Boosting), SVM (support vector machine).					

The SHAP summary plot showed that the important predictors of ACS were “ST change,” “ST elevation,” “Heart rate,” “Cold sweat,” “Male,” and “Blood oxygen saturation” (Fig. 3 and Additional file6: figure S5).

Prediction of AMI or STEMI

Next, we built classification models for diagnosing subcategories of ACS, including AMI and STEMI, using XGBoost with 17 features. The prediction algorithm of AMI using XGBoost also had a high predictive value in the test cohort (AUC 0.857 [95% CI 0.788–0.919]). Likewise, the XGBoost model presented a high AUC for the prediction of STEMI (0.871 [95% CI 0.819–0.925]) in the test cohort (Table 3).

Table 3

Prehospital prediction algorithms for subcategories of acute coronary syndrome using XGBoost with 17 features

	AUC	Accuracy	Sensitivity	Specificity	F1-score
Training cohort					
AMI	0.883	0.820	0.790	0.833	0.737
STEMI	0.883	0.820	0.790	0.833	0.737
Test cohort					
AMI	0.857	0.802	0.792	0.807	0.718
STEMI	0.871	0.802	0.792	0.807	0.697
AUC (area under the receiver operating characteristic curve), XGBoost (eXtreme Gradient Boosting), AMI (acute myocardial infarction), STEMI (ST-segment elevation myocardial infarction)					

Discussion

In this study, we found that the machine learning-based prehospital model showed a high predictive power for predicting the diagnosis of ACS and subcategories of ACS using 17 features including vital signs, 3-lead ECG monitoring, and symptoms.

Although machine learning-based prediction algorithms have shown promising results with high accuracy in other fields, including stroke and acute aortic syndrome [7, 8], to the best of our knowledge, only one study has reported the efficacy of a machine learning-based prediction model for the prehospital onset of ACS using only 12-lead ECG [16]. In contrast, in our study, we built the models on the basis of 3-lead ECG monitoring, as well as vital signs and symptoms, which can be easily obtained without special equipment and technical training in a prehospital setting. The strength of this study is the remarkably high predictive values of our machine learning models, even when the model inputs are limited to easily obtainable features. Our XGBoost model showed superior predictive power (AUC = 0.883 in the test cohort) compared to those of the previously reported models using 12-lead ECG (AUC = 0.82) [16]. Furthermore, compared to the widely used standard scoring system (HEART score: AUC = 0.84) for patients with suspected ACS in the emergency department [16], our models had a higher predictive power even in the prehospital setting.

While several studies have demonstrated the efficacy and feasibility of risk stratification for ACS with combined modalities such as 12-lead ECG and biomarkers in the emergency department [11–13] and prehospital setting [2], there are few reports predicting the onset of ACS according to vital signs, ECG monitoring, and symptoms obtained by EMS personnel. A prehospital stroke scale with physical examination has been [17] designed to be accessible and applicable for EMS personnel initially triaging patients with limited information, but the conventional scoring system for suspected ACS requires 12-lead

ECG and cardiac troponin in addition to medical history [12]. A previous study [18], which compared diagnostic accuracy for ACS between an assessment of general practitioners and clinical decision rule (CDR) based on medical history and physical examination, reported that the AUC was 0.66 for the physicians' risk estimate and 0.75 for the CDR. This result implies that the diagnostic precision for ACS based on physical assessment reaches the ceiling when 12-lead ECG or cardiac enzymes are not available. In this context, our novel approach for predicting the onset of ACS with vital signs, ECG monitoring, and symptoms using machine learning would provide us with substantial advantages over traditional methods.

With the high predictive accuracy of the algorithm for the diagnosis of ACS, the SHAP analysis presented significant features contributing to the diagnosis of ACS: ST change, ST elevation, heart rate, cold sweat, sex (male), and blood oxygen saturation. While 12-lead ECG has been recognized as one of the most reliable tests for estimating the probability of diagnosis, ECG monitoring with leads I, II, or III demonstrated noteworthy findings for an assessment of the likelihood. Other features listed as contributing factors are potentially used as additional information to determine the possibility of ACS in a prehospital setting. Based on the extent of the contribution to the diagnosis, we successfully decreased the number of features for the prediction algorithm from 43 to 17 features. This can be explained by that the exclusion of the irrelevant and redundant features, and noises has improved the model performance. The advantages of the modified algorithm with a decreased number of features include reduction of workload and shorter duration of implementation, leading to potential feasibility of clinical application in the future. Such a diagnostic tool with a predicting algorithm is soon to be launched with validation in a prehospital setting.

Some limitations of this study need to be addressed. First, the specific study area, Chiba city, could be an obstacle for generalization of the results, although the study was conducted in multiple institutions. Second, patient background such as dyslipidemia in our study is different from that in previous studies [19]. Insufficient interviews with a limited time may be attributed to missing information. Third, the proportion of patients with STEMI in this study (83%) is higher than that in the Japanese registry data (approximately 70%) [20]. Selection bias is a potential reason for the lower percentage of patients with NSTEMI and UA. Fourth, the prediction algorithm for diagnosing NSTEMI was not developed in the analysis because of the lack of sufficient data. As ECG shows low sensitivity in NSTEMI [21] [22], our algorithm estimating the probability of ACS could improve the diagnostic accuracy of NSTEMI. Future studies should clarify the predictive value of NSTEMI, as well as the robustness of diagnostic accuracy for STEMI using the algorithm.

Conclusions

We found that the prehospital prediction algorithm had a high predictive power for diagnosing the onset of ACS using machine learning from the data of vital signs, 3-lead ECG monitoring, and symptoms obtained by EMS personnel. Further investigations are needed to validate the accuracy and feasibility of the algorithm in a prehospital setting.

Abbreviations

ACS

acute coronary syndrome

EMS

emergency medical services

ECG

electrocardiogram

STEMI

ST-segment elevation myocardial infarction

AMI

acute myocardial infarction

AUC

areas under the receiver operating characteristic curve

CI

Confidence interval

SHAP

SHapley Additive exPlanation

XGBoost

eXtreme Gradient Boosting

SVM

support vector machine

RBF

radial basis function

NSTEMI

non-ST-segment elevation myocardial infarction

UA

unstable angina

Declarations

Ethics approval and consent to participate

The study was approved by the Ethical Review Board of the Graduate School of Medicine, Chiba University. In accordance with the Ethical Guidelines for Medical and Health Research Involving Human Subjects in Japan, the requirement for written informed consent was waived by the review board.

Consent for publications

Not applicable

Data Availability Statement

The datasets used and analyzed during our study are available from the corresponding author upon reasonable request.

Competing interests

MT, TO, YH, TS, NH, and RA declare that they have no potential conflicts of interest. TN and YY are inventors and have submitted patents related to this work. TN and YY serve as directors and receive executive compensation and hold shares in Smart119 Inc. REM serves as a chief scientist in Smart119 Inc.

Funding

This research was supported by the Japan Agency for Medical Research and Development under Grant Number #JPhe1502001. The funder had no role in the study design, analysis of the data, or preparation of the manuscript.

Authors' contributions

Study concept and design: TN, RA, YY

Acquisition of data: TN, HN, TS, YH, MT

Drafting of the manuscript: TN, TO, MT, REM

Critical revision of the manuscript for important intellectual content: MT, TO, YH, TS, NH, KT, REM, YY, RA, YK, TN

Statistical analysis: TN, TO, MT, YY, REM

Supervision: TN

All authors have read and approved the final manuscript.

Acknowledgements

We thank all contributors to this study, especially the following investigators: Chiba Emergency Medical Center (Iwao Ishibashi), Chiba Medical Center (Yusuke Kageyama), Chiba Chuo Medical Center (Kazumasa Fukuda), National Hospital Organization Chiba Medical Center (Yukio Saito), Chiba Aoba Municipal Hospital (Kyohei Yamamoto), Chiba Kaihin Municipal Hospital (Masaru Terai), Mitsuwadai General Hospital (Yasuhiko Nakata), Japan Community Health Care Organization Chiba Hospital (Noriyoshi Murotani), Kashiwado Hospital (Toshihiro Saito), and Chiba City Fire Department (Hideki Shinhama).

References

1. Anderson JL, Morrow DA. Acute Myocardial Infarction. *N Engl J Med*. 2017; 376(21):2053–2064.
2. Knoery CR, Heaton J, Polson R, Bond R, Iftikhar A, Rjoob K, McGilligan V, Peace A, Leslie SJ. Systematic Review of Clinical Decision Support Systems for Prehospital Acute Coronary Syndrome Identification. *Crit Pathw Cardiol*. 2020; 19(3):119–125.
3. Welsford M, Nikolaou NI, Beygui F, Bossaert L, Ghaemmaghami C, Nonogi H, O'Connor RE, Pichel DR, Scott T, Walters DL et al. Part 5: Acute Coronary Syndromes: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation*. 2015;132(16 Suppl 1):S146-176.
4. Kimura K, Kimura T, Ishihara M, Nakagawa Y, Nakao K, Miyauchi K, Sakamoto T, Tsujita K, Hagiwara N, Miyazaki S et al. JCS 2018 Guideline on Diagnosis and Treatment of Acute Coronary Syndrome. *Circ J*. 2019;83(5):1085–1196.
5. Mori H, Maeda A, Akashi Y, Ako J, Ikari Y, Ebina T, Tamura K, Namiki A, Fukui K, Michishita I et al. The impact of pre-hospital 12-lead electrocardiogram and first contact by cardiologist in patients with ST-elevation myocardial infarction in Kanagawa, Japan. *J Cardiol*. 2021;78(3):183–192.
6. van Dongen DN, Tolsma RT, Fokkert MJ, Badings EA, van der Sluis A, Slingerland RJ, van 't Hof AW, Ottervanger JP. Pre-hospital risk assessment in suspected non-ST-elevation acute coronary syndrome: A prospective observational study. *Eur Heart J Acute Cardiovasc Care*. 2020;9(1_suppl):5–12.
7. Suzuki K, Nakajima N, Kunimoto K, Hatake S, Sakamoto Y, Hokama H, Nomura K, Hayashi T, Aoki J, Suda S et al. Emergent Large Vessel Occlusion Screen Is an Ideal Prehospital Scale to Avoid Missing Endovascular Therapy in Acute Stroke. *Stroke*. 2018;49(9):2096–2101.
8. Duceau B, Alsac JM, Bellenfant F, Mailloux A, Champigneulle B, Fave G, Neuschwander A, El Batti S, Cholley B, Achouh P et al. Prehospital triage of acute aortic syndrome using a machine learning algorithm. *Br J Surg*. 2020; 107(8):995–1003.
9. Swap CJ, Nagurney JT. Value and limitations of chest pain history in the evaluation of patients with suspected acute coronary syndromes. *JAMA*. 2005; 294(20):2623–2629.
10. Morrow DA, Antman EM, Charlesworth A, Cairns R, Murphy SA, de Lemos JA, Giugliano RP, McCabe CH, Braunwald E. TIMI risk score for ST-elevation myocardial infarction: A convenient, bedside, clinical score for risk assessment at presentation: An intravenous nPA for treatment of infarcting myocardium early II trial substudy. *Circulation*. 2000;102(17):2031–2037.
11. Antman EM, Cohen M, Bernink PJ, McCabe CH, Horacek T, Papuchis G, Mautner B, Corbalan R, Radley D, Braunwald E. The TIMI risk score for unstable angina/non-ST elevation MI: A method for prognostication and therapeutic decision making. *JAMA*. 2000;284(7):835–842.
12. Six AJ, Backus BE, Kelder JC. Chest pain in the emergency room: value of the HEART score. *Neth Heart J*. 2008;16(6):191–196.
13. Fox KA, Dabbous OH, Goldberg RJ, Pieper KS, Eagle KA, Van de Werf F, Avezum A, Goodman SG, Flather MD, Anderson FA, Jr. et al. Prediction of risk of death and myocardial infarction in the six

- months after presentation with acute coronary syndrome: prospective multinational observational study (GRACE). *BMJ*. 2006;333(7578):1091.
14. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD et al. Third universal definition of myocardial infarction. *Circulation*. 2012;126(16):2020–2035.
 15. Lundberg SM, Erion G, Chen H, DeGrave A, Prutkin JM, Nair B, Katz R, Himmelfarb J, Bansal N, Lee SI. From Local Explanations to Global Understanding with Explainable AI for Trees. *Nat Mach Intell*. 2020;2(1):56–67.
 16. Al-Zaiti S, Besomi L, Bouzid Z, Faramand Z, Frisch S, Martin-Gill C, Gregg R, Saba S, Callaway C, Sejdic E. Machine learning-based prediction of acute coronary syndrome using only the pre-hospital 12-lead electrocardiogram. *Nat Commun*. 2020;11(1):3966.
 17. Kothari RU, Pancioli A, Liu T, Brott T, Broderick J. Cincinnati Prehospital Stroke Scale: reproducibility and validity. *Ann Emerg Med*. 1999;33(4):373–378.
 18. Bruins Slot MH, Rutten FH, van der Heijden GJ, Geersing GJ, Glatz JF, Hoes AW. Diagnosing acute coronary syndrome in primary care: comparison of the physicians' risk estimation and a clinical decision rule. *Fam Pract*. 2011; 28(3):323–328.
 19. Ando H, Yamaji K, Kohsaka S, Ishii H, Wada H, Yamada S, Sawano M, Inohara T, Numasawa Y, Ikari Y et al. Japanese Nationwide PCI (J-PCI) Registry Annual Report 2019: patient demographics and in-hospital outcomes. *Cardiovasc Interv Ther*. 2022; doi: 10.1007/s12928-021-00832-0.
 20. Ishihara M, Fujino M, Ogawa H, Yasuda S, Noguchi T, Nakao K, Ozaki Y, Kimura K, Suwa S, Fujimoto K et al. Clinical Presentation, Management and Outcome of Japanese Patients With Acute Myocardial Infarction in the Troponin Era - Japanese Registry of Acute Myocardial Infarction Diagnosed by Universal Definition (J-MINUET). *Circ J*. 2015;79(6):1255–1262.
 21. Collet JP, Thiele H, Barbato E, Barthelémy O, Bauersachs J, Bhatt DL, Dendale P, Dorobantu M, Edvardsen T, Folliguet T et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J*. 2021;42(14):1289–1367.
 22. Amsterdam EA, Wenger NK, Brindis RG, Casey DE, Jr., Ganiats TG, Holmes DR, Jr., Jaffe AS, Jneid H, Kelly RF, Kontos MC et al. 2014 AHA/ACC Guideline for the Management of Patients with Non-ST-Elevation Acute Coronary Syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014; 64(24):e139-e228.

Figures

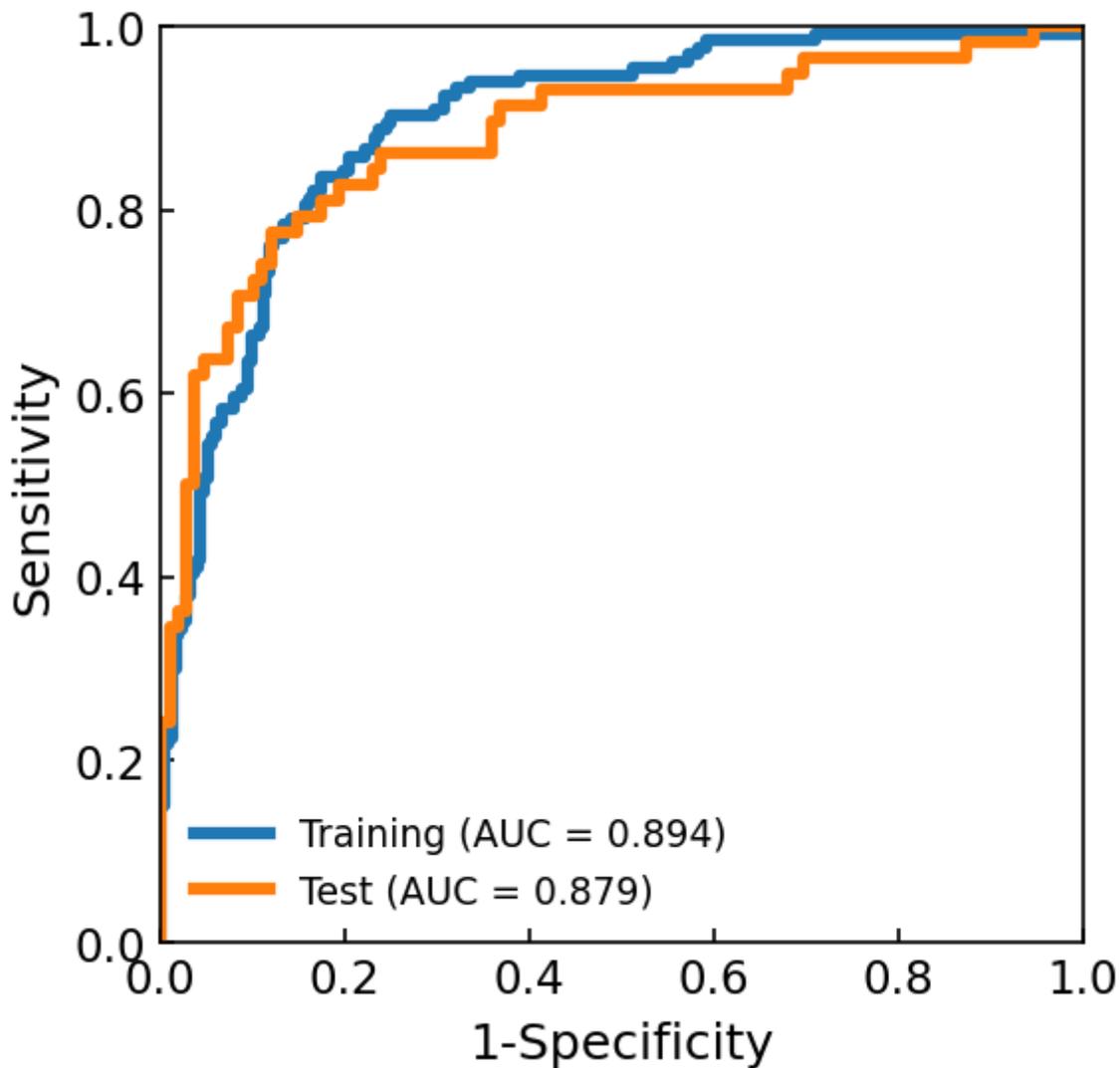


Figure 1

Receiver operating characteristic (ROC) curve of prehospital diagnostic algorithms for acute coronary syndrome using XGBoost with 43 features

The ROC curve of prehospital ACS prediction algorithms using 43 features were depicted at 1-specificity on the x-axis and sensitivity on the y-axis using the training cohort. The 95% confidence interval of AUC is shown as well.

AUC (area under the receiver operating characteristic curve), XGBoost (eXtreme Gradient Boosting)

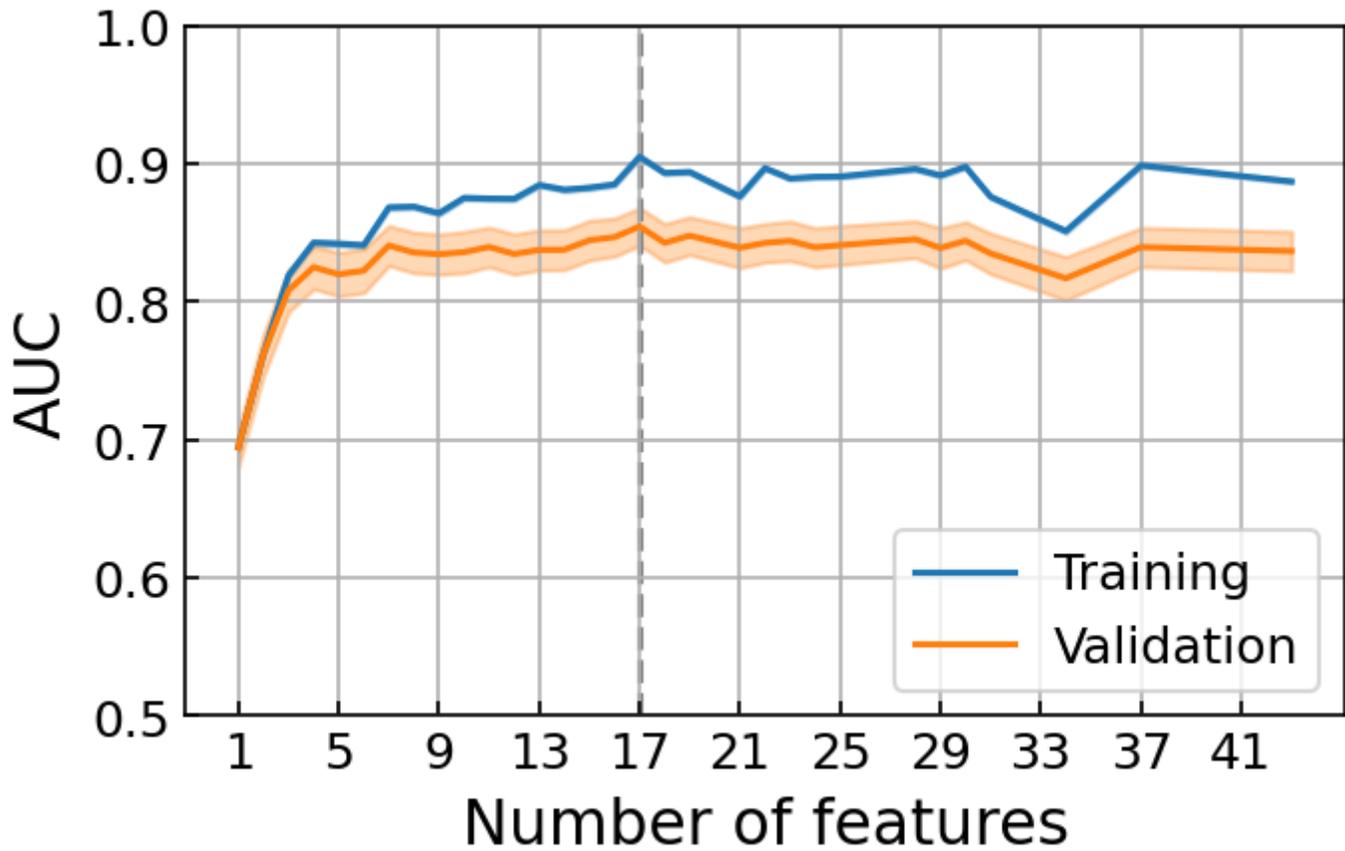


Figure 2

Relationship between the number of features and the area under the receiver operating characteristic curve for the prediction algorithm

The line plot depicts sequential changes in the AUC with the number of features for the prediction algorithm in (a) the training cohort (blue) and (b) the validation cohort (yellow). The dotted vertical line indicates the highest predictive value (n=17, AUC of the training cohort = 0.905, AUC of the validation cohort = 0.855). The error bars indicate 95% confidence intervals.

AUC (area under the receiver operating characteristic curve)

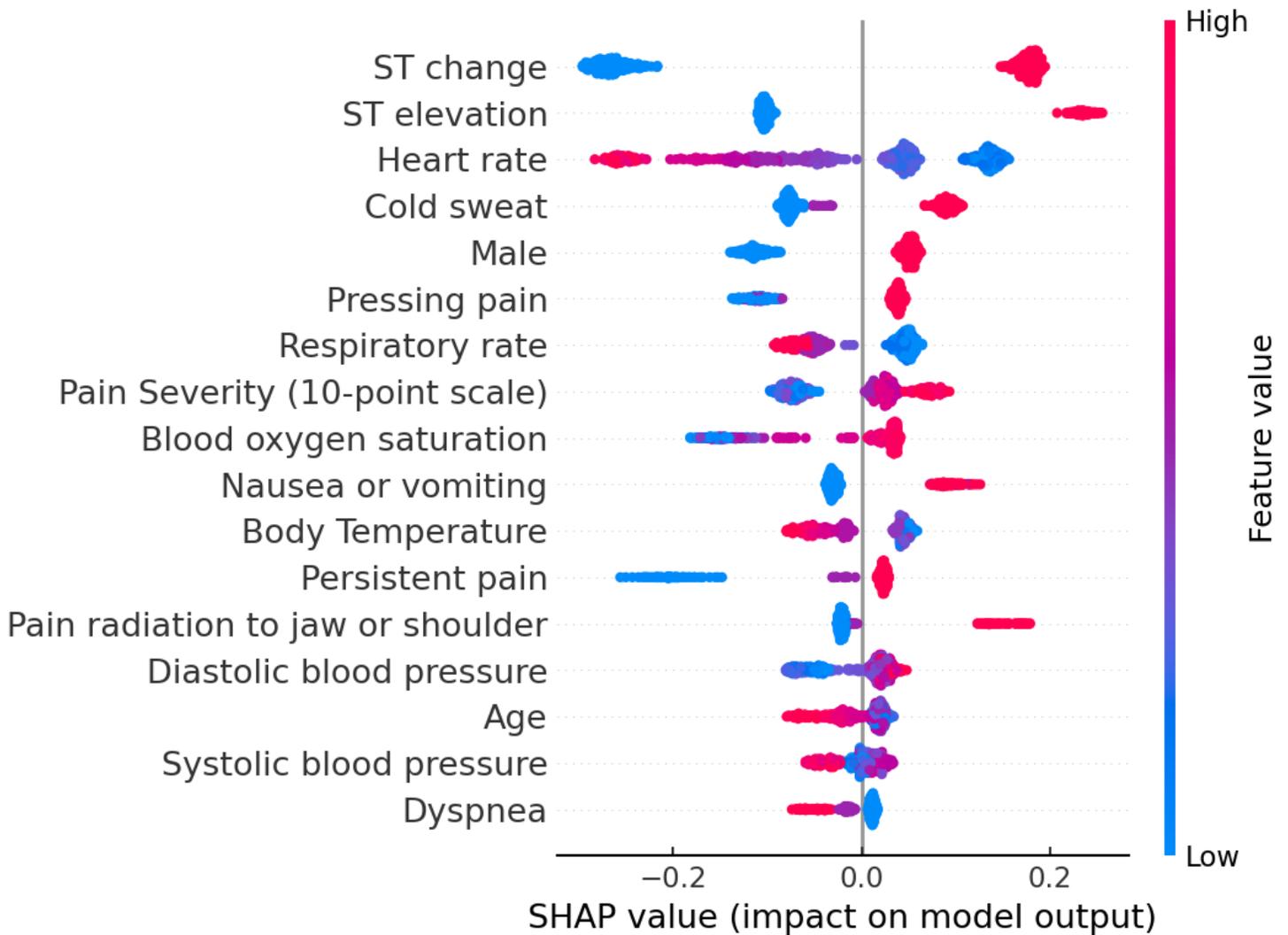


Figure 3

SHAP values of the prehospital diagnostic algorithm for acute coronary syndrome using 17 features

The impact of the features on the model output was expressed as the SHAP value. The features are placed in descending order according to their importance. The association between the feature value and SHAP value indicates a positive or negative impact of the predictors. The extent of the value is depicted as red (high) or blue (low) plots.

SHAP (SHapley Additive exPlanation)

Supplementary Files

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

- [Additionalfile1.docx](#)
- [Adittionalfile2.png](#)

- [Adittionalfile3.png](#)
- [Adittionalfile4.png](#)
- [Adittionalfile5.png](#)
- [Adittionalfile6.png](#)