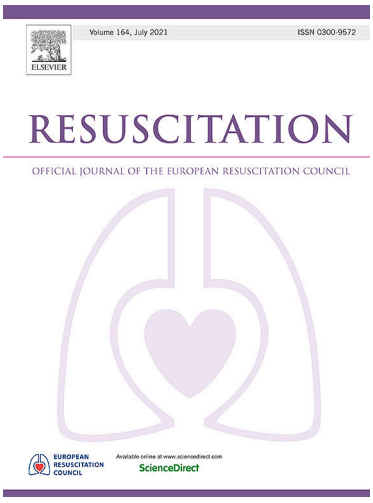
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Original paper

Artificial Intelligence-Assisted, Electrocardiogram-Derived, Sequential Rule-Based Decision Tree for Exclusion of Acute Coronary Syndrome as the Etiology of Out-of-Hospital Cardiac Arrest: A Single-Center Retrospective Cohort Study

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Artificial Intelligence-Assisted, Electrocardiogram-Derived, Sequential Rule-Based Decision Tree for Exclusion of Acute Coronary Syndrome as the Etiology of Out-of-Hospital Cardiac Arrest: A Single-Center Retrospective Cohort Study

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Highlights

- A sequential AI-ECG decision tree was developed to exclude ACS after cardiac arrest
- Zero false negatives were maintained across development and validation cohorts
- Approximately half of post-ROSC patients were classified as "ACS not likely"

- Five combined AI-ECG biomarkers outperformed any single biomarker alone
- Rhythm stratification concentrated rule-outs in the non-shockable subgroup

ABSTRACT

Background: After out-of-hospital cardiac arrest (OHCA) with return of spontaneous circulation (ROSC), deciding which patients without ST-segment elevation warrant emergency coronary angiography is difficult, as standard electrocardiogram (ECG), troponin, and echocardiography are limited in the early post-arrest window. We aimed to develop a sequential rule-based decision tree to identify post-ROSC patients in whom acute coronary syndrome (ACS) is unlikely to be the arrest etiology.

Methods: In this single-center retrospective study, adult patients with OHCA were divided into development (2020–2024; n=329) and temporal validation (2025; n=71) cohorts. Post-ROSC 12-lead ECGs were analyzed by a deep-learning platform generating ten digital biomarkers. Five candidate biomarkers were combined into a rhythm-stratified sequential decision tree under a zero false-negative constraint; its performance was compared with that of individual biomarkers and validated in the temporal cohort.

Results: The tree classified 171/329 (52.0%) and 32/71 (45.1%) patients in the development and validation cohorts, respectively, as "ACS not likely," with no adjudicated ACS case misclassified at any node. Yield concentrated in the non-shockable subgroup, in which the model excluded 169/261 (64.8%) non-ACS cases (area under the receiver operating characteristic curve [AUROC], 0.824), outperforming each individual biomarker. In the shockable subgroup, which carries a high pretest probability of ACS, 38/40 patients (95.0%) were retained as "ACS not excluded."

Conclusions: A rhythm-stratified, rule-based decision tree combining AI-assisted ECG-derived biomarkers classified approximately half of post-OHCA patients as "ACS not likely" with no adjudicated ACS case misclassified, principally in the non-shockable subgroup. This transparent, bedside-deployable framework warrants prospective multicenter evaluation.

Keywords: acute coronary syndrome, artificial intelligence, decision tree, electrocardiogram, out-of-hospital cardiac arrest, resource utilization

INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) remains a leading cause of mortality worldwide, with survival-to-discharge rates stagnating at approximately 8–9% despite decades of advancement in cardiopulmonary resuscitation (CPR) [1]. Even after return of spontaneous circulation (ROSC), post-cardiac arrest syndrome—a systemic ischemia-reperfusion injury—frequently precipitates clinical deterioration and multi-organ failure within the first 24 h [2]. In this early period, arguably the most consequential decision is whether emergency coronary angiography (CAG) is warranted or a period of observation is safe.

When ST-segment elevation (STE) is present on the post-ROSC electrocardiogram (ECG), immediate reperfusion is the established standard of care [3]. However, STE is absent in approximately 50–70% of patients with OHCA, and

within this non-STE population approximately 20% harbor acute coronary occlusive disease—increasingly recognized as "hidden occlusion myocardial infarction (OMI)" [4,5]. Such patients represent a diagnostic "gray zone": their lesions are silent on standard ECGs, yet delayed revascularization leads to progressive, irreversible myocardial necrosis.

Recent guidelines, informed by randomized trials such as COACT and TOMAHAWK, advise against routine immediate CAG in hemodynamically stable patients without STE after ROSC [6–9]. Although these recommendations support a selective approach, they provide no validated bedside tool to support patient selection for urgent coronary evaluation. Standard ECG interpretation, cardiac troponin, and echocardiography are each of limited reliability in the early post-arrest window [10–12].

Artificial intelligence (AI)-assisted ECG analysis may help by extracting quantitative information not apparent to the eye [13]. A single ECG feature may be insufficient after arrest, however, where arrest rhythm, resuscitation-related myocardial injury, conduction abnormalities, and post-arrest physiology all influence ECG signals. A useful decision-support framework should therefore integrate AI-derived biomarkers into a transparent workflow that reflects the clinical priority of identifying patients in whom acute coronary syndrome (ACS) can be reasonably excluded.

Therefore, we aimed to develop a sequential rule-based decision tree that prioritizes the exclusion of ACS as the cause of arrest, identifying which patients can be classified as "ACS not likely" and may be candidates for a deferred angiography strategy.

METHODS

Study Design and Ethics Approval

This retrospective observational study was conducted at a tertiary emergency medical center and approved by the Institutional Review Board of Severance Hospital (approval no. 4-2015-1162); informed consent was waived given the retrospective use of de-identified data. The study followed the Declaration of Helsinki.

Study Population

We screened patients aged ≥18 years presenting to the emergency department after OHCA during 2020–2025, including those with transient ROSC. As part of the Korean Cardiac Arrest Research Consortium (KoCARC) registry protocol, patients with obvious non-medical etiologies (e.g., trauma, drowning) were not enrolled. Patients were included if the arrest etiology could be determined and at least one post-ROSC 12-lead ECG was available for AI analysis. We excluded those (1) pronounced dead on arrival without resuscitation; (2) with prehospital ROSC in whom a true cardiac arrest could not be confirmed (e.g., suspected syncope or other transient loss of consciousness); (3) with do-not-resuscitate orders or withdrawal of treatment before workup completion; and (4) in whom sufficient clinical data were unavailable to determine arrest etiology. The cohort was divided into development (2020–2024) and temporal validation (2025) sets. The development set was used for training, biomarker selection, cutoff determination, and internal assessment.

Data Collection

Demographic and clinical data—age, sex, and prehospital arrest rhythm—were extracted from institutional data collected as part of the KoCARC registry. Prehospital rhythms were classified as shockable (ventricular fibrillation [VF] or pulseless ventricular tachycardia [pVT]) or non-shockable (pulseless electrical activity [PEA] or asystole).

All post-ROSC 12-lead ECGs were analyzed using ECG Buddy (ARPI Inc., Seoul, Korea), a deep learning-based platform approved by the Korean Ministry of Food and Drug Safety as a Class II device [14]. It converts ECG waveforms into two-dimensional spectrographic representations analyzed by convolutional neural networks to identify 11 types of cardiac rhythms along with their probabilities, and generate scores of 0–100 for 10 digital

biomarkers: (1) critical condition; (2) ACS; (3) ST-segment elevation myocardial infarction (STEMI); (4) myocardial injury (MyoInj); (5) pulmonary edema (PulmEdma); (6) large pericardial effusion or tamponade (PrcEff); (7) left ventricular dysfunction (LVDys); (8) right ventricular dysfunction (RVDys); (9) pulmonary hypertension (PulmHTN); and (10) severe hyperkalemia (HyperK) (K ≥6.0 mmol/L).

Each of these biomarkers is an independently developed AI-ECG score, reported on a 0–100 scale representing the estimated probability of the corresponding condition. Full definitions, reference standards, and external validation performance for all ten biomarkers are provided in Supplementary Table 1 [15–20]. The five incorporated into the decision tree were the ACS, STEMI, MyoInj, LVDys, and PulmHTN scores. These biomarkers were developed and validated primarily in general emergency-department and cardiac populations rather than in post-cardiac-arrest cohorts.

Outcome Definition

The primary outcome was arrest etiology, dichotomized as ACS versus non-ACS. The analytic cohort was not restricted to patients undergoing CAG, to avoid selection bias and to test whether ACS can be excluded before coronary anatomy is known. Etiology was determined by systematic electronic medical record review and independently adjudicated by two board-certified emergency physicians (8 and 15 years' experience), blinded to each other and to the AI biomarker scores; discordant cases were adjudicated by an independent interventional cardiologist (15 years' experience), whose determination was final.

ACS was defined as the etiology when an acute culprit lesion (thrombotic occlusion or ≥70% stenosis with acute plaque disruption) was identified on CAG, considered with troponin trends, wall-motion abnormalities, and clinical course. Without CAG, ACS was assigned if the managing cardiologist documented myocardial infarction, or if myocardial infarction was recorded as the cause of death and no alternative diagnosis emerged from the clinical evaluations performed. In all cases, a non-ACS classification required objective evidence of a definitive alternative etiology.

Rhythm-Based Stratification and Biomarker Selection

Given established differences in pathophysiology and ACS prevalence between shockable and non-shockable rhythms [21,22], all analyses were performed separately by prehospital initial rhythm. Shockable rhythms are strongly associated with acute coronary occlusion, whereas non-shockable rhythms are etiologically heterogeneous with a lower a priori probability of ACS. Separate decision trees were therefore developed for each rhythm group.

To corroborate feature selection and node hierarchy, variable importance was assessed across five machine learning models: least absolute shrinkage and selection operator regression, random forest, eXtreme Gradient Boosting (XGBoost), Gradient Boosting Machine (GBM), and component-wise gradient boosting (CGB). In the overall cohort, the ACS, STEMI, MyoInj, LVDys, and PulmHTN scores ranked first through fifth by average importance rank across all five models (Supplementary Table 2). These five biomarkers were selected and sequentially ordered within the decision tree based on these rankings and their established clinical relevance to acute coronary pathology. For each patient, the first ECG confirmed after ROSC served as the temporal reference point.

Decision Tree Development

The central innovation is a sequential rule-based decision tree that maximizes the exclusion of non-ACS patients while retaining all adjudicated ACS cases. Unlike standard classification trees that optimize accuracy or information gain at each split, ours was explicitly engineered for zero false negatives (FN=0)—a conservative approach that is intended to avoid missing an unrecognized coronary occlusion, while supporting deferral of angiography. At each node, a single biomarker score is compared with a predetermined cutoff. Patients below the cutoff (or above, for the inverted PulmHTN node) are classified "ACS not likely" and exit the tree—but only if no ACS-positive development-set patient falls below that cutoff at that node. Patients who do not exit proceed to the next biomarker; those traversing all nodes are designated "ACS not excluded" and considered for emergency CAG. Each cutoff was set to exclude the maximum number of non-ACS patients while maintaining ACS=0 among exiting patients.

When multiple serial post-ROSC ECGs were available, a change score (ΔACS) was calculated as the difference

between the score at approximately 2 h and the initial post-ROSC score. Given the greater heterogeneity and lower baseline ACS probability of non-shockable rhythms, ΔACS was added as an additional node only within the non-shockable tree; when only one ECG was available, this node was bypassed.

Comparison with Individual Biomarker Performance

To assess the added value of the tree over single biomarkers, the predictive performance of each biomarker for non-ACS classification was evaluated independently under the same FN=0 constraint and compared with the final combined model. Sensitivity, false-negative rate (FNR), false-positive rate (FPR), area under the receiver operating characteristic curve (AUROC), and the number classified "ACS not likely" were calculated for each biomarker and the sequential model.

Temporal Validation

The final tree was applied without modification to the temporal validation cohort. For each patient, the node at which they exited (or did not exit) the tree was recorded, and ACS status at each exit point was examined to confirm the FN=0 constraint held in the independent dataset. The proportion of non-ACS patients excluded and maintenance of the FN=0 constraint at each node were the primary validation metrics.

Sensitivity and Subgroup Analyses

To assess the robustness of the reference standard, we reported coronary angiography rates separately for adjudicated-ACS and adjudicated-non-ACS patients and repeated the analysis restricted to patients with an objectively (angiographically) verified reference standard. To examine the influence of ST-elevation, given that conventional STEMI already warrants immediate angiography, we additionally repeated the analysis excluding patients with definite ST-elevation on the post-ROSC ECG. Finally, because the interval from ROSC to the first ECG differed between cohorts, we stratified the development cohort by this interval (≤5, ≤10, and ≤15 min versus later) and reapplied the fixed tree.

Statistical Analysis

Continuous variables are presented as medians with quartiles 1–3 (Mann–Whitney U test); categorical variables as frequencies with percentages (chi-square or Fisher's exact test). Discrimination was assessed by AUROC. Sensitivity, FNR, and FPR were calculated with 95% confidence intervals (CIs) by the exact binomial method. A two-sided $P<0.05$ was significant. Analyses used R 4.4.0 (R Foundation for Statistical Computing, Vienna, Austria; packages "pROC" and "caret") and Python 3.10 (scikit-learn).

RESULTS

Study Population and Baseline Characteristics

We included 400 patients: 329 development and 71 validation (Figure 1). Baseline characteristics are summarized in Table 1 and were broadly similar between cohorts, with the exception of the timing of the first post-ROSC ECG, which was significantly earlier in the validation cohort (median 3 vs. 5 minutes, $P<0.001$). Prehospital initial rhythm did not differ ($P=0.303$), with non-shockable rhythms predominating (87.8% development, 93.0% validation); in-hospital first rhythm was similar ($P=0.591$). Adjudicated etiology did not differ ($P=0.055$); ACS was the cause in 53 patients (16.1%) in development and 8 (11.3%) in validation. ST-segment elevation meeting conventional STEMI criteria was present in 19 patients (5.8%) in the development cohort and 6 patients (8.5%) in the temporal validation cohort.

Decision Tree

In the development cohort, the tree (Figure 2a) classified 171/329 patients (52.0%) as "ACS not likely," with no FNs.

Yield was concentrated in the non-shockable subgroup (n=289; 28 with ACS): the initial ACS-score node (cutoff <15.2) excluded the largest fraction (134 non-ACS), and overall 169/261 non-ACS patients were classified "ACS not likely" while all 28 ACS patients were retained; the ΔACS node excluded one additional non-ACS patient. In the shockable subgroup (n=40; 25 with ACS), high pretest probability constrained exclusion: only 2/15 non-ACS patients were classified "ACS not likely," with all 25 ACS and 13 non-ACS retained as "ACS not excluded."

In the validation cohort (Figure 2b), the tree classified 32/71 patients (45.1%) as "ACS not likely." In the non-shockable subgroup (n=66, 5 with ACS), 31 non-ACS patients were classified "ACS not likely"—23 at the ACS-score node, 2 at MyoInj, and 6 at LVDys. In the shockable subgroup (n=5), one non-ACS patient was classified "ACS not likely."

Angiography rates differed markedly by adjudicated etiology, consistent with concordance between clinical adjudication and objective evaluation where available: CAG was performed in 32/53 (60.4%) patients adjudicated as ACS versus 16/276 (5.8%) adjudicated as non-ACS in the development cohort, and in 6/8 (75.0%) versus 2/63 (3.2%) in the validation cohort (Supplementary Table 3). Among patients with an angiographically verified reference standard, the zero false-negative property was preserved in both cohorts (Supplementary Table 4).

After excluding patients meeting conventional STEMI criteria (19 in development, 6 in validation), 39 and 5 adjudicated ACS cases remained, respectively; the rule-out yield (171/310, 55.2%; 32/65, 49.2%) and the zero false-negative property were preserved, indicating that the reported performance was not an artifact of including patients with overt STEMI (Supplementary Table 5). Stratifying the development cohort by the ROSC-to-ECG interval preserved the zero false-negative property in every stratum (Supplementary Table 6).

Comparison of Single-Biomarker Rules and the Decision Tree

Individual biomarkers were compared with the sequential tree (Table 2). In the non-shockable development subgroup, no single biomarker achieved adequate exclusion; the best, the ACS score, had an FPR of 0.487 (95% CI, 0.427–0.547) and AUROC of 0.757 (0.666–0.787). The decision tree achieved an FPR of 0.352 (0.297–0.412) and AUROC of 0.824 (0.795–0.853), superior to every individual biomarker. In the shockable subgroup, the tree also outperformed individual biomarkers (FPR=0.867; AUROC=0.567), though performance was much poorer than in the non-shockable subgroup.

DISCUSSION

In this single-center retrospective study of adults with OHCA, we developed and temporally validated a sequential rule-based decision tree using five AI-assisted ECG-derived biomarkers to identify patients unlikely to have ACS as the arrest etiology. Under an explicit FN=0 constraint, the tree classified 171/329 patients (52.0%) in development and 32/71 (45.1%) in validation as "ACS not likely," with no ACS case misclassified at any node in either cohort.

Guidelines shifted the standard of care for hemodynamically stable patients without STE after ROSC toward a delayed or selective angiography strategy in 2025 [3,6], informed by trials and meta-analyses showing no clear benefit of immediate angiography [7–9,23,24]. They offer no mechanism, however, to identify at the bedside which patients harbor occult coronary occlusion beneath a non-diagnostic ECG. Existing modalities cannot fill this gap in the first hours after ROSC: conventional STEMI-based interpretation detects acute coronary occlusion with a sensitivity of only 32.5% and is degraded further by tachycardia, noise, and conduction disturbances [10,13]; troponin may be normal or confounded by chest-compression-related release within the 0–2 h window [11]; and echocardiography cannot reliably distinguish global post-arrest stunning from focal ischemia [12,25]. The PROCAT II registry identified candidates for emergency percutaneous coronary intervention using clinical and demographic variables, but these required prolonged evaluation or laboratory testing [4].

Our framework operates at this decision point. Prior studies of post-ROSC ECG interpretation for OMI restricted the cohort to patients undergoing CAG, using angiographic findings as the reference [26], an approach applicable only to already-referred patients. Our framework instead addresses the earlier question of whether ACS can be excluded in

the broader post-ROSC population; accordingly, the reference standard was adjudicated arrest etiology, with non-ACS assigned only when a definitive alternative etiology was objectively supported. Whether angiography can be safely deferred in the "ACS not likely" group was not tested here and remains to be established prospectively.

The model prioritizes sensitivity over overall accuracy, reflecting markedly asymmetric harms: overlooking post-ROSC ACS may result in ongoing, irreversible myocardial loss and higher mortality [27], whereas subjecting an additional non-ACS patient to CAG carries procedural risk and resource burden. Enforcing FN=0 at every node meant accepting that a sizable fraction of non-ACS patients remain "ACS not excluded." The framework is also rhythm-stratified, reflecting the sequential workflow of OHCA management [28]: prehospital rhythm is among the earliest factors clinicians use to estimate ACS likelihood after ROSC [21,22,29], with shockable rhythms carrying a substantially higher a priori probability of acute coronary occlusion. As anticipated, yield concentrated in the non-shockable subgroup, in which the tree classified 31 of 66 validation patients (47.0%) as "ACS not likely." In the shockable subgroup, discrimination was poor (AUROC 0.567) and nearly all patients were retained as "ACS not excluded"; the clinical utility of the framework is therefore largely confined to the non-shockable subgroup.

The clinical impact of an AI-ECG biomarker depends not only on standalone discrimination but on integration into the decision workflow [30–32]. AI-ECG can detect conditions not visually apparent, such as left ventricular systolic dysfunction [33], and models for OMI detection [13,34] show strong discrimination in general chest-pain populations. These were developed as rule-in rather than rule-out classifiers, however, and have not been tested after arrest, where single-biomarker performance degrades. Combining five complementary biomarkers within a clinically constrained, rhythm-stratified structure substantially expanded the population classified as "ACS not likely." Although the biomarkers were generated by a deep-learning platform, the final decision layer was rule-based and transparent, providing auditable logic [35]; such platforms have reduced false-positive catheterization-laboratory activations in a multicenter registry [36].

This study has several limitations. It was single-center and retrospective, and the decision tree was not used to guide real-time CAG decisions, so the observed exclusion rates should be regarded as hypothesis-generating. The validation cohort was small (71 patients) and included only 5 shockable-rhythm cases, precluding firm conclusions for shockable arrests.

Because CAG was performed in a minority of patients, the non-ACS classification for the remainder relied on clinical adjudication rather than universal angiography, introducing possible verification bias; our zero false-negative result is therefore conditional on the adjudicated reference standard and does not exclude unrecognized occult ACS. Although we required objective evidence of a definitive alternative etiology and independent, blinded adjudication, adjudication cannot fully replace angiography, particularly where mechanisms overlap.

Addressing these limitations will require prospective, multicenter validation with protocolized serial ECG acquisition, structured follow-up, and prespecified adjudication. A multicenter study incorporating these elements is currently underway, which will also allow ΔACS to be evaluated as a dynamic marker of ischemic change over time.

CONCLUSION

By translating multiple AI-assisted ECG-derived biomarkers into a transparent, rhythm-aware, clinically prioritized rule-out model, our approach offers a candidate decision-support framework for the guideline-defined gray zone between routine immediate angiography and selective delay after cardiac arrest, particularly in patients with non-shockable rhythms. The present analysis demonstrates classification according to adjudicated etiology but does not establish the safety of deferring angiography. Prospective, multicenter studies with standardized ECG acquisition are needed to validate the framework and determine its impact on angiography decisions and downstream clinical outcomes before clinical deployment.

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CRediT authorship contribution statement

Arom Choi: Conceptualization, Funding acquisition, Formal analysis, Visualization, Supervision, Writing – original draft, Writing – review & editing, Hanna Yoon: Methodology, Writing – review & editing, Stephen Gyung Won Lee: Methodology, Writing – review & editing, Chaeryoung Park: Methodology, Writing – review & editing, Eunah Han: Methodology, Writing – review & editing, Yun Ho Roh: Data curation, Formal analysis, Ji Hoon Kim: Conceptualization, Formal analysis, Project administration, Writing – original draft, Writing – review & editing

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Table 1. Baseline characteristics of the development and temporal validation cohorts

Variable	Development set (n =	Temporal validation set (n	P-

	329)	= 71)	value
Demographics			
Age, years, median [Q1–3]	72 [60–82]	70 [64–82]	0.448
Male sex, n (%)	219 (66.6%)	42 (59.2%)	0.293
Arrest characteristics			
Bystander CPR, n (%)	206 (62.6%)	36 (50.7%)	0.084
Prehospital initial rhythm, n (%)			0.303
Shockable (VF/pulseless VT)	40 (12.2%)	5 (7.0%)	
Non-shockable (PEA/asystole)	289 (87.8%)	66 (93.0%)	
In-hospital first rhythm, n (%)			0.591
Asystole	201 (61.1%)	45 (63.4%)	
PEA	97 (29.5%)	22 (31.0%)	
VF/pulseless VT	31 (9.4%)	4 (5.6%)	
Arrest etiology, n (%)			0.055
ACS	53 (16.1%)	8 (11.3%)	
Non-ACS cardiogenic	46 (14.0%)	14 (19.7%)	
Metabolic	124 (37.7%)	19 (26.8%)	
Pulmonary	86 (26.1%)	20 (28.2%)	

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CNS	18 (5.5%)	10 (14.1%)	
Other	2 (0.6%)	0 (0.0%)	
Coronary angiography performed, n (%)	48 (14.6%)	8 (11.3%)	0.587
First ECG timing after ROSC, min, median [Q1–3]	5 [3–17]	3 [1–12]	<0.001
≥ 2 serial post-ROSC ECGs available, n (%)	251 (76.3%)	53 (74.6%)	0.888

CPR, cardiopulmonary resuscitation; VF, ventricular fibrillation; VT, ventricular tachycardia; PEA, pulseless electrical activity; ACS, acute coronary syndrome; CNS, central nervous system; ECG, electrocardiogram; ROSC, return of spontaneous circulation; Q, quartile.

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Table 2. Comparison of single-biomarker rules and the sequential rule-based decision tree under a zero false-negative constraint (development cohort)

Biomarker	Cutoff	ACS n (%)	non-ACS n (%)	Sensitivity (95% CI)	FNR (95% CI)	FPR (95% CI)	AUROC (95% CI)
Non-shockable rhythm subgroup (PEA/asystole), n = 289 (ACS = 28, non-ACS = 261)							
ACS score	≥ 15.2	28 (100.0%)	127 (48.7%)	1.000 (0.879–1.000)	—	0.487 (0.427–0.547)	0.757 (0.666–0.787)
	< 15.2	0 (0.0%)	134 (51.3%)	—	0.000 (0.000–0.121)	—	
ΔACS score	≥ −76.8 (or NA)	28 (100.0%)	260 (99.6%)	1.000 (0.879–1.000)	—	0.996 (0.979–0.999)	0.502 (0.440–0.511)
	< −76.8	0 (0.0%)	1 (0.4%)	—	0.000 (0.000–0.121)	—	
STEMI score	≥ 3.7	28 (100.0%)	142 (54.4%)	1.000 (0.879–1.000)	—	0.544 (0.483–0.603)	0.728 (0.638–0.758)
	< 3.7	0 (0.0%)	119 (45.6%)	—	0.000 (0.000–0.121)	—	
MyoInj score	≥ 36.0	28 (100.0%)	187 (71.6%)	1.000 (0.879–1.000)	—	0.716 (0.659–0.768)	0.642 (0.556–0.671)
	< 36.0	0 (0.0%)	74 (28.4%)	—	0.000 (0.000–0.121)	—	
LVDys score	≥ 35.7	28 (100.0%)	179 (68.6%)	1.000 (0.879–1.000)	—	0.686 (0.627–0.739)	0.657 (0.570–0.686)

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Biomarker	Cutoff	ACS n (%)	non-ACS n (%)	Sensitivity (95% CI)	FNR (95% CI)	FPR (95% CI)	AUROC (95% CI)
	< 35.7	0 (0.0%)	82 (31.4%)	—	0.000 (0.000–0.121)	—	
	≥ 42.0	28 (100.0%)	247 (94.6%)	1.000 (0.879–1.000)	—	0.946 (0.912–0.968)	
PulmHTN score							0.527 (0.456–0.544)
	< 42.0	0 (0.0%)	14 (5.4%)	—	0.000 (0.000–0.121)	—	
	ACS not excluded	28 (100.0%)	92 (35.2%)	1.000 (0.879–1.000)	—	0.352 (0.297–0.412)	
Sequential tree (final)							**0.824 (0.795–0.853)**
	ACS not likely	**0 (0.0%)**	**169 (64.8%)**	—	0.000 (0.000–0.121)	—	
Shockable rhythm subgroup (VF/pulseless VT), n = 40 (ACS = 25, non-ACS = 15)							
	≥ 2.5	25 (100.0%)	15 (100.0%)	1.000 (0.867–1.000)	—	1.000 (0.796–1.000)	
ACS score							0.500 (0.433–0.602)
	< 2.5	0 (0.0%)	0 (0.0%)	—	0.000 (0.000–0.133)	—	
	≥ 0.5	25 (100.0%)	15 (100.0%)	1.000 (0.867–1.000)	—	1.000 (0.796–1.000)	
STEMI score							0.500 (0.433–0.602)
	< 0.5	0 (0.0%)	0 (0.0%)	—	0.000 (0.000–0.133)	—	
MyoInj score	≥ 22.7	25 (100.0%)	15 (100.0%)	1.000 (0.867–1.000)	—	1.000 (0.796–1.000)	0.500 (0.433–0.602)

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Biomarker	Cutoff	ACS n (%)	non-ACS n (%)	Sensitivity (95% CI)	FNR (95% CI)	FPR (95% CI)	AUROC (95% CI)
	< 22.7	0 (0.0%)	0 (0.0%)	—	0.000 (0.000–0.133)	—	
	≥ 25.9	25 (100.0%)	14 (93.3%)	1.000 (0.867–1.000)	—	0.933 (0.702–0.988)	
LVDys score							0.533 (0.439–0.649)
	< 25.9	0 (0.0%)	1 (6.7%)	—	0.000 (0.000–0.133)	—	
	≥ 43.6	25 (100.0%)	14 (93.3%)	1.000 (0.867–1.000)	—	0.933 (0.702–0.988)	
PulmHTN score							0.533 (0.439–0.649)
	< 43.6	0 (0.0%)	1 (6.7%)	—	0.000 (0.000–0.133)	—	
	ACS not excluded	25 (100.0%)	13 (86.7%)	1.000 (0.867–1.000)	—	0.867 (0.621–0.963)	
Sequential tree (final)							**0.567 (0.478–0.656)**
	ACS not likely	**0 (0.0%)**	**2 (13.3%)**	—	0.000 (0.000–0.133)	—	

Each biomarker cutoff was fixed at the threshold yielding an FNR of zero (no patient with ACS classified as "ACS not likely"). Under this constraint all rules retain 100% sensitivity for ACS by design; the FPR therefore reflects the proportion of patients without ACS who could not be excluded and were retained in the "ACS not excluded" pathway. A lower FPR indicates a greater ability to rule out ACS without missing a true ACS case. For each biomarker, the upper row corresponds to the "ACS not excluded" classification (score at or above the cutoff; for PulmHTN, the opposite direction) and the lower row to the "ACS not likely" classification. The PulmHTN node is inverted, such that lower scores indicate "ACS not excluded."

ACS, acute coronary syndrome; STEMI, ST-segment elevation myocardial infarction; MyoInj, myocardial injury; LVDys, left ventricular dysfunction; PulmHTN, pulmonary hypertension; ΔACS, change in ACS prediction score between serial electrocardiograms after return of spontaneous circulation; FNR, false-negative rate; FPR, false-positive rate; AUROC, area under the receiver operating characteristic curve; CI, confidence interval; VF, ventricular fibrillation; VT, ventricular tachycardia; PEA, pulseless electrical activity.

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Figure legends

Figure 1 Participant flow diagram

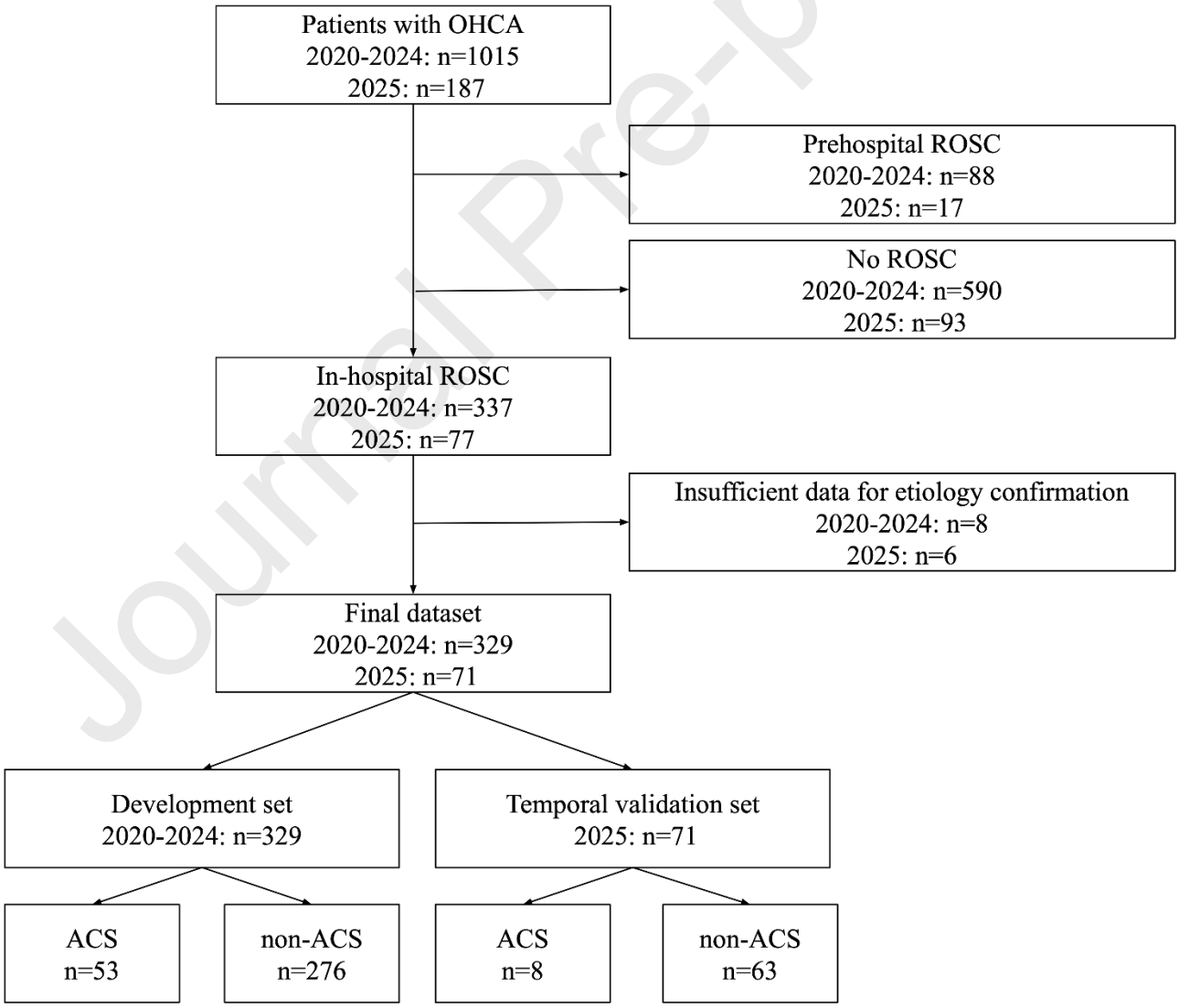
OHCA, out-of-hospital cardiac arrest; ACS, acute coronary syndrome; ROSC, return of spontaneous circulation

Figure 2 Decision trees

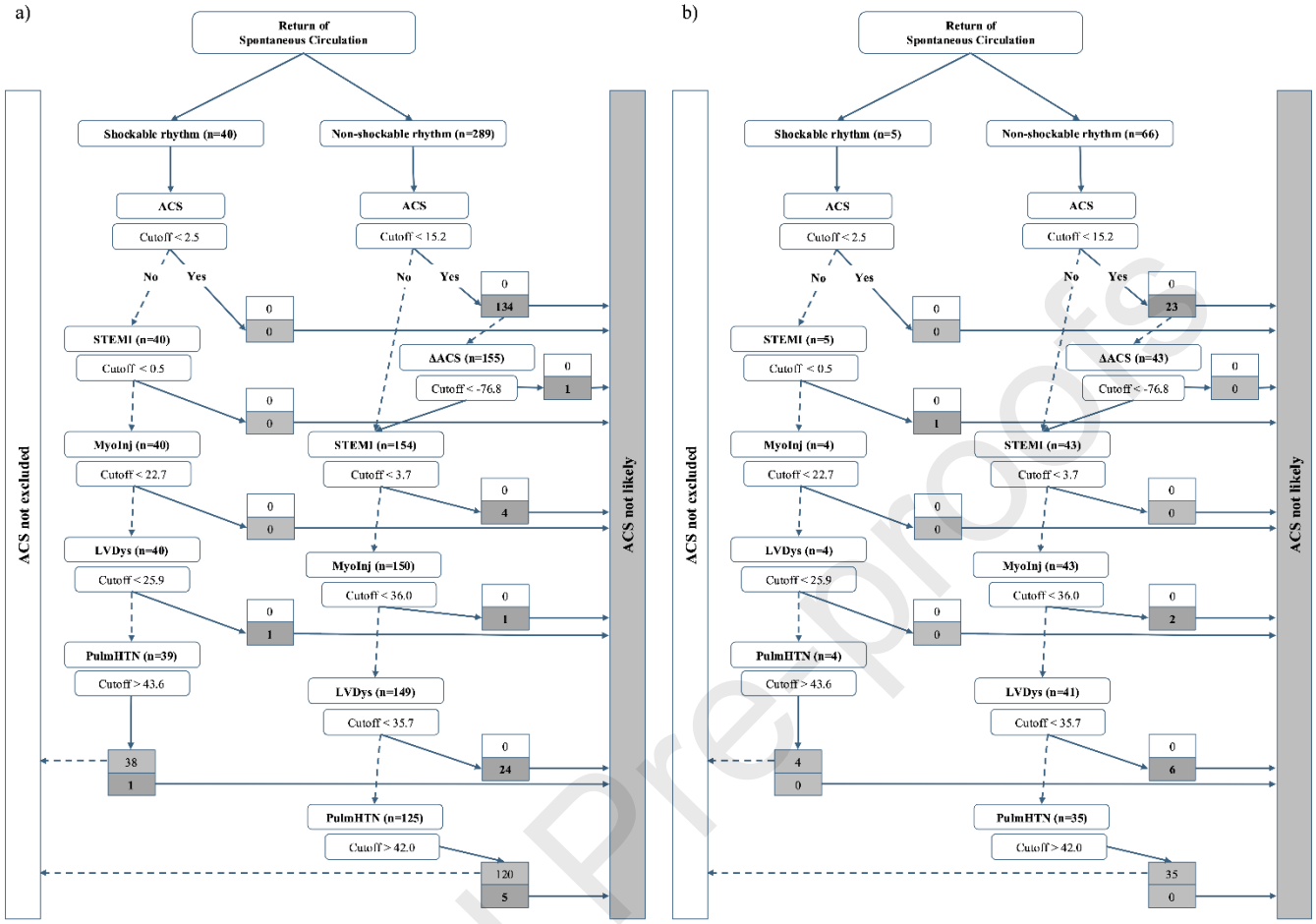
a) Development cohort. b) Validation cohort.

At each node, the upper cell shows the number of adjudicated ACS cases and the lower cell the number of non-ACS cases exiting as "ACS not likely"; at the terminal node, the upper cell shows patients retained as "ACS not excluded" and the lower cell those exiting as "ACS not likely."

ACS, acute coronary syndrome; LVDys, left ventricular dysfunction; MyoInj, myocardial injury; PulmHTN, pulmonary hypertension; STEMI, ST-segment elevation myocardial infarction



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Conflict of Interest Statement

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☒ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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