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ORIGINAL RESEARCH

CORONARY

AI-Enabled ECG Analysis Improves Diagnostic Accuracy and Reduces False STEMI Activations

A Multicenter U.S. Registry

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ABSTRACT

BACKGROUND Timely reperfusion is critical in reducing mortality in ST-segment elevation myocardial infarction (STEMI). Although electrocardiography-guided cardiac catheterization laboratory (CCL) activation on the basis of first medical contact recognition improves system-level response, diagnostic uncertainty, particularly in atypical presentations, contributes to false positive activations (FPAs) and reperfusion delays.

OBJECTIVES The aim of this study was to evaluate the diagnostic performance and operational impact of artificial intelligence (AI)-based electrocardiographic (ECG) analysis in real-world STEMI triage across a multicenter U.S. registry.

METHODS A total of 1,032 patients with suspected STEMI who triggered emergent CCL activation at 3 geographically diverse percutaneous coronary intervention centers (January 2020 to May 2024) were retrospectively analyzed. Index electrocardiograms underwent standard triage and blinded retrospective AI ECG analysis (Queen of Hearts, PMcardio) trained to detect acute coronary occlusion and benign mimics. The reference standard was an angiographically confirmed culprit lesion with positive enzymes. Diagnostic accuracy, subgroup analyses, and FPA reclassification were compared.

RESULTS Of 1,032 emergent CCL activations, 601 (58.2%) had confirmed STEMI. The AI ECG model outperformed standard triage, demonstrating higher index ECG sensitivity (553 of 601 [92.0%; 95% CI: 89.7%-94.1%] vs 427 of 601 [71.0%; 95% CI: 67.4%-74.6%]), reducing FPA rates (34 of 431 [7.9%; 95% CI: 6.4%-9.6%] vs 180 of 431 [41.8%; 95% CI: 38.9%-44.7%]), and improving specificity (431 of 531 [81.0%; 95% CI: 77.2%-84.5%] vs 154 of 531 [29.0%; 95% CI: 24.8%-33.4%]) ($P < 0.001$ for all). The AI ECG model's area under the receiver-operating characteristic curve was 0.94 (95% CI: 0.92-0.95), maintaining consistent performance across clinically challenging subgroups (eg, atrial fibrillation, bundle branch block, STEMI equivalents). The AI ECG model reclassified 277 of 306 (91%) biomarker-negative FPAs correctly.

CONCLUSIONS AI-based ECG analysis significantly improved STEMI detection, reduced FPAs, and enhanced the recognition of nonconventional presentations. This supports integration of AI-based ECG analysis into acute chest pain pathways. (JACC Cardiovasc Interv. 2026;19:145-156) © 2026 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

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ABBREVIATIONS AND ACRONYMS

AI = artificial intelligence

CCL = cardiac catheterization laboratory

D2B = door-to-balloon

DNN = deep neural network

ECG = electrocardiographic

EMS = emergency medical services

FMC = first medical contact

FPA = false positive activation

LBBB = left bundle branch block

PCI = percutaneous coronary intervention

QTc = corrected QT

SoC = standard of care

STEMI = ST-segment elevation myocardial infarction

Rapid reperfusion through primary percutaneous coronary intervention (PCI) remains the cornerstone of management for patients with ST-segment elevation myocardial infarction (STEMI).[1] Guided by the principle that "time is muscle," prompt identification and rapid activation of the cardiac catheterization laboratory (CCL) significantly reduce delays to intervention, improving clinical outcomes.[2] Recently, the American College of Cardiology guidelines broadened electrocardiographic (ECG) criteria for emergent CCL activation, emphasizing immediate invasive strategies for both conventional STEMI and critical STEMI-equivalent ECG patterns suggestive of acute coronary occlusion, such as isolated posterior infarction or hyperacute T waves.[3]

Despite advances in regional STEMI systems and prehospital CCL activation, delays in achieving guideline-recommended reperfusion times persist, especially at non-PCI centers and rural sites.[4,5] Intervention times longer than target are associated with 3-fold higher mortality for both STEMI and STEMI equivalents.[4] Standardized protocols and prearranged transfer pathways, often based on ECG interpretation by noncardiologist clinicians, have improved access to primary PCI.[6] However, these rapid activation strategies may increase the risk for false positive activation (FPA) rates, reported to be between 15% and 30%, leading to staff fatigue, unnecessary resource use, and potential patient harm.[7-9]

Artificial intelligence (AI)-driven ECG interpretation, using deep neural networks (DNNs) trained on angiographic outcomes in STEMI cohorts, has emerged as a promising tool to enhance triage accuracy at the first medical contact (FMC). Building on prior international evaluations demonstrating superior sensitivity and specificity with reduced misclassification and time to treatment,[10] this study assessed the clinical and operational impact of a newer version of the AI ECG model (Queen of Hearts, PMcardio, Powerful Medical) in a multicenter U.S. registry, with particular emphasis on diagnostic sensitivity using the index electrocardiogram, door-to-balloon (D2B) times, and FPA rates.

METHODS

STUDY SETTING AND POPULATION. Patients were identified from a prospective, electronic, consecutive STEMI catheterization laboratory activation logs maintained for reporting to the National Cardiovascular Data Registry Chest Pain-Myocardial Infarction and CathPCI Registry.[11] Consecutive adults (≥18 years of age) who had emergent CCL activation for suspected STEMI between January 2020 and May 2024 were screened at 3 geographically diverse, high-volume, urban U.S. PCI centers: Beth Israel Deaconess Medical Center (Boston, MA), the University of California Davis Medical Center (Sacramento, CA) and Memorial Hermann-Texas Medical Center (Houston, TX). Site-specific emergent CCL activation protocols are available in Supplemental Table 1. Each site contributed data from at least 12 continuous months of STEMI activations.

Inclusion criteria were: 1) emergent CCL activation during index hospitalization; 2) availability of the index 12-lead electrocardiogram; and 3) age ≥18 years. Exclusion criteria were 1) declined or deferred activation; 2) non-acute coronary syndrome CCL activation; 3) insufficient ECG quality; and 4) ventricular arrhythmia on index electrocardiography.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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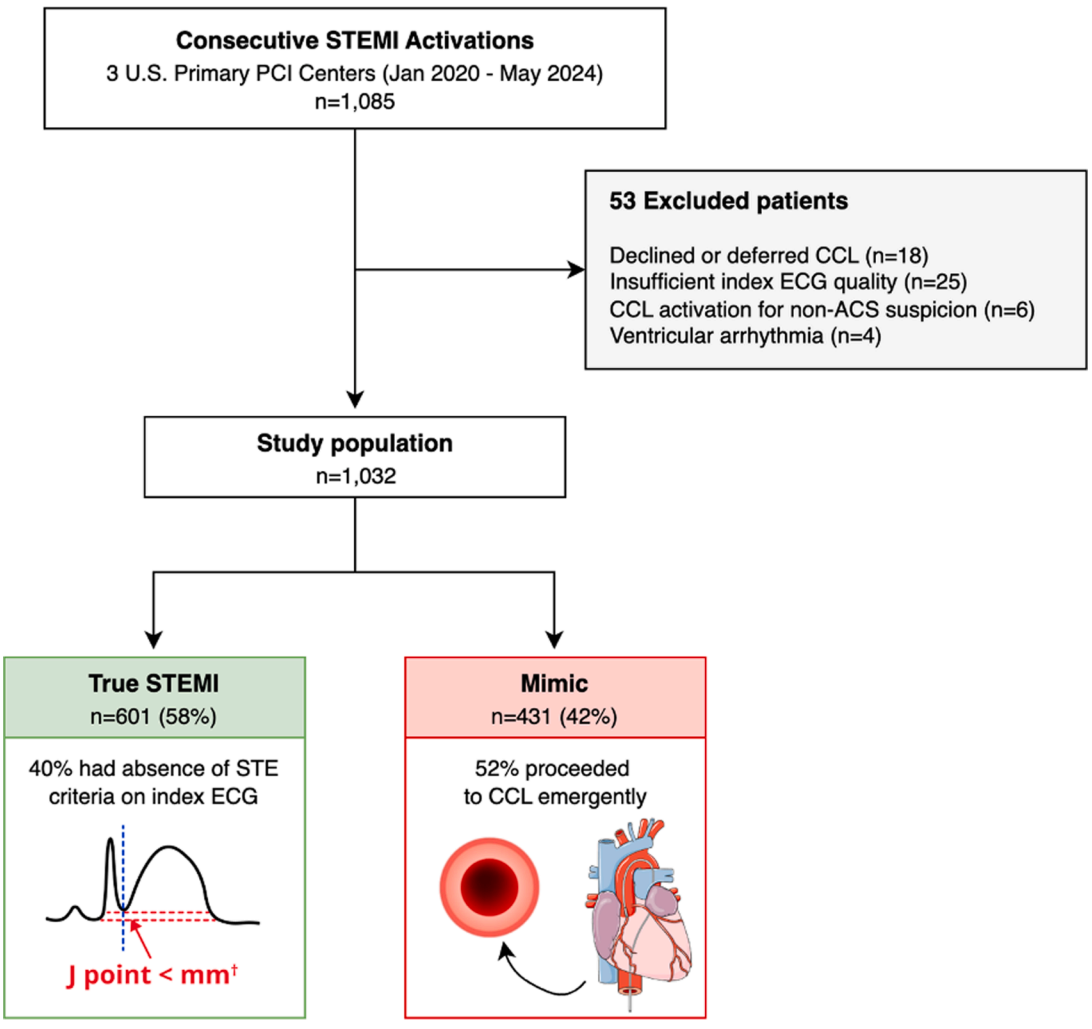
FIGURE 1 Study Flowchart



ACS = acute coronary syndrome; CCL = cardiac catheterization laboratory; ECG = electrocardiographic/electrocardiography; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

After exclusions, 1,032 patients (of an initial 1,085) were retained in the study (Figure 1). The study was approved by the Institutional Review Board or quality improvement committee at each center and complied with the Declaration of Helsinki.

DATA COLLECTION AND ECG MEASUREMENTS. Demographic, procedural, management, and outcome data were collected through the National Cardiovascular Data Registry Chest Pain-Myocardial Infarction and CathPCI Registry. Deidentified index electrocardiograms, including those acquired by emergency medical services (EMS) or non-PCI hospitals, were retrospectively collected by trained specialists. Standard-of-care (SoC) triage performance reflected real-time clinician judgment, defined as whether the CCL was activated within 10 minutes of index electrocardiogram availability.

Formal STEMI millimeter criteria were assessed on all electrocardiograms by independent blinded expert reviewers (S.W.S., H.P.M.) according to the fourth universal definition of myocardial infarction. ST-segment elevation was measured at the J point in ≥2 contiguous leads, using age- and sex-specific thresholds: ≥2 mm in leads V_2 and V_3 for men ≥40 years of age, ≥2.5 mm for men <40 years of age, ≥1.5 mm in women, and ≥1 mm in all other leads.[12]

Key ECG parameters, including heart rate, rhythm, corrected QT (QTc) interval, QRS complex duration,

TABLE 1 Baseline Demographics and Index ECG Characteristics

	Overall (N = 1,032)	True STEMI (n = 601)	Mimics (n = 431)	*P* Value
Age, y	63.1 ± 14.1	62.7 ± 13.5	63.6 ± 14.9	0.299
≤45	114 (11.0)	56 (9.3)	58 (13.5)	**0.005**
45-60	312 (30.2)	203 (33.8)	109 (25.3)	
>60	606 (58.7)	342 (56.9)	264 (61.3)	
Male	729 (70.6)	428 (71.2)	301 (69.8)	0.682
Site				
A	278 (26.9)	141 (23.5)	137 (31.8)	**0.007**
B	455 (44.1)	271 (45.1)	184 (42.7)	
C	299 (29.0)	189 (31.4)	110 (25.5)	
Arrival method				
EMS	640 (62.0)	387 (64.4)	253 (58.7)	0.024
Walk-in	219 (21.2)	110 (18.3)	109 (25.3)	
Transfer	131 (12.7)	83 (13.8)	48 (11.1)	
Inpatient	35 (3.4)	19 (3.2)	16 (3.7)	
Other	7 (0.7)	2 (0.3)	5 (1.2)	
Index ECG characteristics				
STEMI criteria	486 (47.1)	363 (60.4)	123 (28.5)	**≤0.001**
Sinus rhythm	850 (82.4)	513 (85.4)	337 (78.2)	**0.004**
AF rhythm	99 (9.6)	53 (8.8)	46 (10.7)	0.373
Heart rate ≥100 beats/min	284 (27.5)	144 (24.0)	140 (32.5)	**0.006**
QRS complex duration ≥120 ms	179 (17.3)	71 (11.8)	108 (25.1)	**≤0.001**
QTc interval duration ≥440 ms	256 (24.8)	110 (18.3)	146 (33.9)	**≤0.001**
LBBB	83 (8.0)	22 (3.7)	61 (14.2)	**≤0.001**
RBBB	67 (6.5)	37 (6.2)	30 (7.0)	0.697
Management				
ICA performed	796 (77.1)	572 (95.2)	224 (52.0)	**≤0.001**

Values are mean ± SD or n (%). *P* values in **bold** denote statistical significance.

AF = atrial fibrillation; ECG = electrocardiographic; EMS = emergency medical services; ICA = invasive coronary angiography; LBBB = left bundle branch block; QTc = corrected QT (Framingham Heart Study); RBBB = right bundle branch block; STEMI = ST-segment elevation myocardial infarction.

and ST/T-wave measurements, were extracted automatically using a Conformité Européenne-certified AI platform (PMcardio, application programming interface version 2.5, Powerful Medical).[13]

AI-BASED ECG ANALYSIS. All deidentified 12-lead electrocardiograms were retrospectively analyzed using the Conformité Européenne-certified PMcardio AI platform, which accepts raw waveform data or converts ECG images (PDF, PNG, or JPEG) to digitized waveforms (retaining a sampling frequency of 320 Hz). The ECG digitization methodology has been described elsewhere.[14] The primary DNN model (Queen of Hearts [aOMI version 1], "STEMI/STEMI Equivalent Detected") identifies acute coronary occlusion at the time of ECG acquisition. This model requires ≥2.5 seconds of waveform data per lead and produces a continuous probability score from 0 to 1. A prior version (eOMI version 1, "Occlusive Myocardial Infarction [OMI] Detected") of this DNN model has been previously described and validated.[10] Both versions share the same deep learning architecture and training methodology, but the current model (aOMI version 1) was recalibrated with an emphasis on higher specificity for STEMI and STEMI-equivalent patterns (high probability of active coronary occlusion at time of ECG recording). This U.S. multicenter registry cohort was entirely independent of the data sets used for model development and calibration, with no overlap in patients or institutions.

DEFINITION OF TRUE STEMI. The primary outcome (reference standard), angiographically confirmed "true STEMI," was adjudicated on the basis of the presence of positive high-sensitivity cardiac troponin and angiographic identification of a culprit vessel using all available clinical data. Positivity was defined as any high-sensitivity cardiac troponin value above the assay-specific 99th percentile upper reference limit, with a serial rise and/or fall required. The culprit vessel was defined as the infarct-related artery, identified by the operator on the basis of angiographic features (≥70% stenosis or TIMI [Thrombolysis In Myocardial Infarction] flow grade 0 or 1). True STEMI also included myocardial infarction with nonobstructive coronary arteries due to mechanisms including, but not limited to, vasospasm, coronary embolization, or spontaneous coronary artery dissection. True STEMI was further stratified on the basis of whether the index electrocardiogram met conventional millimeter ST-segment elevation criteria adjudicated by independent expert reviewers (S.W.S., H.P.M.), classifying cases as either "conventional STEMI" or "STEMI equivalents."

Patients for whom the catheterization laboratory was initially activated but subsequently canceled by cardiology were adjudicated as "STEMI mimics" only if serial troponin testing and discharge diagnosis excluded acute myocardial infarction. We verified that none of these patients later underwent delayed coronary angiography for evolving STEMI during the index hospitalization. Additionally, biomarker-positive patients who underwent coronary angiography but lacked an identifiable culprit vessel (eg, subendocardial ischemia due to type 2 myocardial infarction, takotsubo cardiomyopathy, and myocarditis) were also classified as STEMI mimics. The final determination of STEMI mimic phenotype was performed by 2 independent expert reviewers (S.W.S., H.P.M.), incorporating ECG features and the full clinical context.

STATISTICAL ANALYSIS. All statistical analyses were conducted using Python. Continuous variables with normal distribution are expressed as mean ± SD and were compared using Student's *t*-tests. Categorical variables are reported as frequency (percentage) and were compared using chi-square or Fisher exact tests. Diagnostic performance of the AI ECG model vs SoC in detecting angiographically confirmed STEMI

was evaluated using area under the receiver-operating characteristic curve, sensitivity, specificity, positive predictive value, negative predictive value, and FPA rates. Paired comparisons of diagnostic accuracy between the AI ECG model and SoC were assessed using the McNemar test, with discordant-pair ORs. For binary metrics, the AI ECG model was applied using a fixed threshold of 0.5, reflecting the on-label cutoff for the general chest pain population. Additional threshold optimization (eg, Youden index) was not applied. A 95% CI was calculated for each metric. Forest plots were constructed to assess model performance across predefined subgroups. All statistical tests were 2-sided, with significance defined as a *P* value <0.05.

RESULTS

STUDY POPULATION. Between January 2020 and May 2024, a total of 1,032 consecutive patients underwent CCL activation for suspected STEMI (Figure 1). Of these, 601 activations (58.2%) were confirmed as true STEMI (positive cardiac troponin[s] with an acute coronary culprit), whereas 431 activations (41.7%) proved to be FPAs due to STEMI mimics. Among 431 FPAs, 306 (71.0%) were troponin negative.

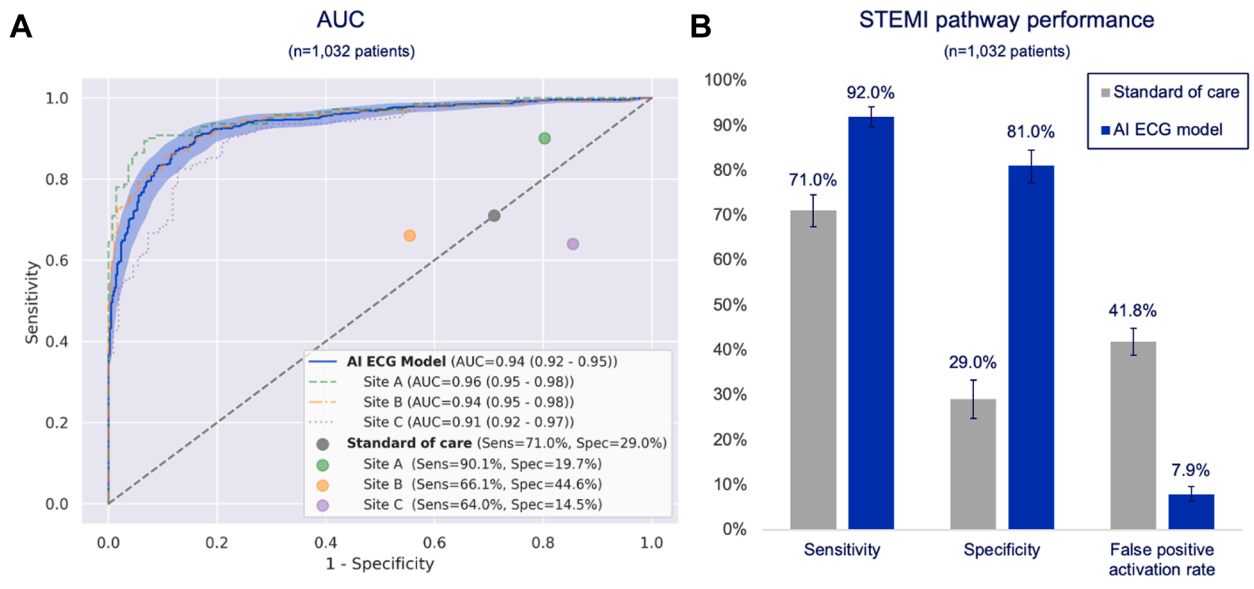
TABLE 2 Invasive Coronary Angiographic Findings of True STEMI Patients Stratified by the Presence of Formal STEMI t on Index ECG

	Overall (N = 601)	STEMI Equivalent (n = 238)	Conventional STEMI (n = 363)	*P* Value
Activated on initial ECG	427 (71.0)	138 (58.0)	289 (79.6)	**≤0.001**
Evolved into conventional STEMI	442 (73.5)	79 (33.2)	–	–
D2B time, min	75 (55-115)	88 (62-162)	69 (52-98)	**≤0.001**
D2B time <90 min	482 (80.2)	175 (73.5)	307 (84.6)	**0.001**
Culprit artery				
Culprit main branch	502 (83.5)	196 (82.4)	306 (84.3)	0.606
Left main coronary artery	10 (1.9)	5 (2.4)	5 (1.5)	**≤0.001**
LAD (including diagonal)	238 (44.7)	82 (39.6)	156 (47.9)	
LCx (including marginal)	64 (12.6)	45 (21.7)	22 (6.7)	
RCA	214 (40.2)	74 (35.7)	140 (42.9)	
Multivessel	4 (0.8)	1 (0.5)	3 (0.9)	
Culprit lesion segment				
Proximal	238 (51.3)	88 (51.5)	150 (51.2)	0.976
Mid	178 (38.4)	66 (38.6)	112 (38.2)	
Distal	48 (10.3)	17 (9.9)	31 (10.6)	
Culprit stenosis				
≥90%	241 (94.9)	102 (92.7)	139 (96.5)	0.285
70%-90%	12 (4.7)	7 (6.4)	5 (3.5)	
<70%	1 (0.4)	1 (0.9)	0	
Management				
PCI performed	512 (85.2)	200 (84.0)	312 (86.0)	0.596

Values are n (%) or median (Q1-Q3). *P* values in **bold** denote statistical significance.

D2B = door-to-balloon time; ECG = electrocardiography; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; PCI = percutaneous coronary intervention; RCA = right coronary artery; STEMI = ST-segment elevation myocardial infarction.

FIGURE 2 Performance Comparison of Standard-of-Care Triage vs AI ECG Model



(A) Receiver-operating characteristic curve of the artificial intelligence (AI) electrocardiographic (ECG) model, with an area under the curve (AUC) of 0.94 (n = 1,032 patients), significantly outperforming standard of care interpretation (sensitivity [Sens], 71.0%; specificity [Spec], 29%). Site-specific AI ECG model and standard-of-care performance is shown. (B) Bar plot comparing ST-segment elevation myocardial infarction (STEMI) pathway sensitivity (71.0% with standard of care vs 92% with the AI ECG model) and specificity using the index electrocardiogram alone (29.0% with standard of care vs 81.0% with the AI ECG model) and false positive activation rate (41.8% with standard of care vs 7.9% with the AI ECG model).

TABLE 3 Diagnostic Performance of the AI ECG Model at Different Raw Output Thresholds Ranging From 0 to 1

AI ECG Model Threshold	Accuracy, %	Sensitivity, %	Specificity, %	FPA, %	PPV, %	NPV, %
≥0.05	80.6	95.5	59.9	16.8	76.8	90.5
≥0.10	82.5	94.7	65.4	14.4	79.2	89.8
≥0.15	83.7	94.5	68.7	13.1	80.8	90.0
≥0.20	85.1	94.3	72.2	11.6	82.5	90.1
≥0.25	85.6	94.0	73.8	10.9	83.3	89.8
≥0.30	85.9	93.5	75.4	10.3	84.1	89.3
≥0.35	86.3	93.0	77.0	9.6	85.0	88.8
≥0.40	86.3	92.5	77.7	9.3	85.3	88.2
≥0.45	87.4	92.3	80.5	8.1	86.9	88.3
≥0.50	**87.4**	**92.0**	**81.0**	**7.9**	**87.1**	**87.9**
≥0.55	87.7	91.2	82.8	7.2	88.1	87.1
≥0.60	87.6	90.5	83.5	6.9	88.5	86.3
≥0.65	87.2	89.4	84.2	6.6	88.8	85.0
≥0.70	86.8	88.0	85.2	6.2	89.2	83.6
≥0.75	87.2	87.4	87.0	5.4	90.4	83.1
≥0.80	86.9	86.0	88.2	4.9	91.0	81.9
≥0.85	85.9	83.9	88.6	4.7	91.1	79.7
≥0.90	85.8	81.7	91.4	3.6	93.0	78.2
≥0.95	84.3	77.7	93.5	2.7	94.3	75.0

The threshold of 0.50 (in **bold**) was selected for the primary analysis.

AI = artificial intelligence; ECG = electrocardiographic; FPA = false positive activation; NPV = negative predictive value; PPV = positive predictive value.

BASELINE DEMOGRAPHICS AND INDEX ELECTROCARDIOGRAPHY. Baseline characteristics are shown in Table 1. The mean age was 63.1 ± 14.1 years, similar between true STEMI and mimics (62.7 ± 13.5 years vs 63.6 ± 14.9 years; $P = 0.30$). Women constituted 304 of 1,032 patients (29.4%) overall. FPAs were more often walk-ins (109 of 431 [25.3%] vs 110 of 601 [18.3%]; $P = 0.02$) and less often EMS arrivals (253 of 431 [58.7%] vs 387 of 601 [64.4%]; $P = 0.02$). Heart rate ≥100 beats/min, QRS complex duration ≥120 ms, QTc interval ≥440 ms, and left bundle branch block (LBBB) were all significantly more common in STEMI mimics ($P < 0.004$ for all).

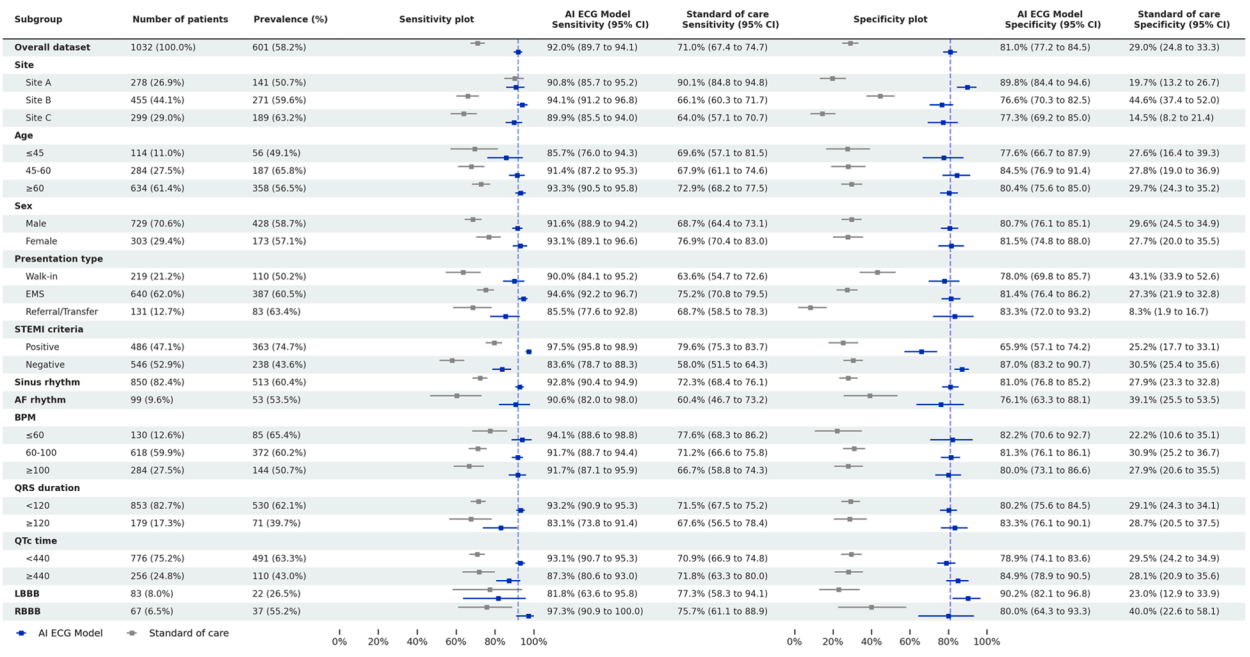
PROCEDURAL AND ANGIOGRAPHIC FINDINGS. Coronary angiography was performed in 796 of 1,032 patients (77.1%), including 572 of 601 (95.2%) of those with true STEMI vs 224 of 431 (52.0%) of those with FPAs ($P < 0.001$). Among patients with true STEMI, 363 of 601 (60.4%) met STEMI millimeter criteria on the index electrocardiogram (conventional STEMI), whereas 238 of 601 (39.6%) did not (STEMI equivalents). Patients presenting with STEMI equivalents were less frequently activated within 10 minutes of index electrocardiography (138 of 238 [58.0%] vs 289 of 363 [79.6%]; $P < 0.001$) and evolved into conventional STEMI prior to coronary angiography in only 79 of 238 (33.2%) (Table 2). STEMI equivalents experienced significantly longer median D2B times (88 minutes [Q1-Q3: 62-162 minutes] vs 69 minutes [Q1-Q3: 52-98 minutes]; $P < 0.001$) and were less likely to achieve D2Bs <90 minutes (173 of 238 [72.7%] vs 305 of 363 [84.0%]; $P = 0.002$).

Culprit artery distribution differed significantly ($P < 0.001$); STEMI equivalents involved more left main (2.4% vs 1.5%), left circumflex (21.7% vs 6.7%), and less frequent left anterior descending (39.6% vs 47.9%), right coronary artery culprits (35.7% vs 42.9%), and multivessel culprits (0.5% vs 0.9%). Culprit lesion segments (proximal, mid, distal), stenosis severity (≥90%, 70%-90%, <70%) and PCI rates (85.2% vs 84.0%) were comparable between groups ($P > 0.28$ for all).

DIAGNOSTIC PERFORMANCE OF AI VS SoC. Using only the index electrocardiogram, the AI ECG model significantly outperformed SoC in detecting angiographically confirmed STEMI ($P < 0.001$ for all comparisons) (Figure 2). The area under the receiver-operating characteristic curve for the AI ECG model was 0.937 (95% CI: 0.923-0.951). AI demonstrated markedly higher sensitivity: 553 of 601 (92.0%; 95% CI: 89.7%-94.1%) vs 427 of 601 (71.0%; 95% CI: 67.4%-74.6%). Specificity was also superior with AI: 431 of 531 (81.0%; 95% CI: 77.2%-84.5%) vs 154 of 531 (29.0%; 95% CI: 24.8%-33.4%). The FPA rate was substantially lower with AI: 34 of 431 (7.9%; 95% CI: 6.4%-9.6%) vs 180 of 431 (41.8%; 95% CI: 38.9%-44.7%). Positive and negative predictive values were also superior with AI: 553 of 635 (87.1%; 95% CI: 84.5%-89.6%) vs 427 of 732 (58.3%; 95% CI: 54.6%-61.8%) and 349 of 397 (87.9%; 95% CI: 84.7%-91.0%) vs 125 of 299 (41.8%; 95% CI: 36.4%-47.4%), respectively (Supplemental Table 2). Paired comparison confirmed significantly greater diagnostic accuracy with AI compared to SoC (chi-square = 264.8; $P < 0.001$, McNemar test; discordant-pair OR: 7.36; 95% CI: 5.56-9.76) (Supplemental Table 3). AI ECG model performance across varying raw output thresholds is presented in Table 3. At the highest specificity threshold (AI score ≥0.95, corresponding to an FPA rate of 12 of 431 [2.7%; 95% CI: 1.5%-4.9%]), the AI model still maintained higher sensitivity using the index electrocardiogram only compared with SoC: 467 of 601 (77.7%; 95% CI: 72.8%-82.3%) vs 427 of 601 (71.0%; 95% CI: 67.4%-74.6%).

SUBGROUP ANALYSIS. The AI ECG model demonstrated consistent superiority across clinical and ECG subgroups (Figure 3; all comparisons showing

FIGURE 3 Index ECG Interpretation Performance Comparison of Standard of Care and AI ECG Model Across Demographic and Electrocardiographic Subgroups



AF = atrial fibrillation; EMS = emergency medical services; LBBB = left bundle branch block; QTc = corrected QT interval (Framingham Heart Study); RBBB = right bundle branch block; other abbreviations as in Figures 1 and 2.

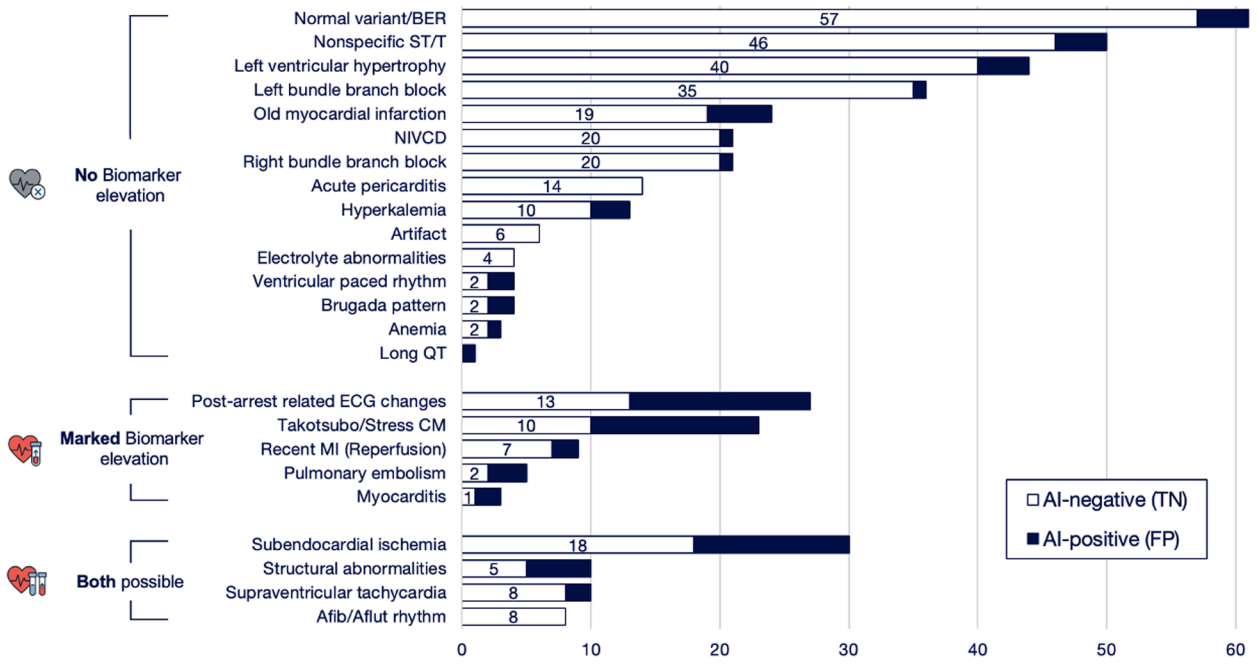
$P < 0.001$). Among STEMI equivalents, AI ECG model sensitivity was 199 of 238 (83.6%; 95% CI: 78.9%-88.1%) vs 138 of 238 (58.0%; 95% CI: 51.7%-64.3%) for SoC. In patients with atrial fibrillation, sensitivity was 48 of 53 (90.6%; 95% CI: 81.8%-98.0%) vs 32 of 53 (60.4%; 95% CI: 47.1%-73.3%). Among those transferred from non-PCI centers, sensitivity reached 71 of 83 (85.5%; 95% CI: 77.8%-92.7%) vs 57 of 83 (68.7%; 95% CI: 58.5%-78.4%). Specificity also favored the AI ECG model in key subgroups: in patients with wide QRS intervals (≥120 ms), specificity was 90 of 108 (83.3%; 95% CI: 75.9%-90.0%) vs 31 of 108 (28.7%; 95% CI: 20.5%-37.5%), and in those with prolonged QTc intervals (≥440 ms), specificity was 124 of 146 (84.9%; 95% CI: 78.8%-90.6%) vs 41 of 146 (28.1%; 95% CI: 20.9%-35.5%).

STEMI MIMIC ANALYSIS. AI correctly reclassified the majority of the 431 FPAs by SoC (Figure 4). The 5 most common STEMI mimics without biomarker elevation included benign early repolarization (AI reclassified 57 of 61 [93%]), nonspecific ST/T-wave changes (AI reclassified 46 of 50 [92%]), left ventricular hypertrophy (AI reclassified 40 of 44 [91%]), LBBB (AI reclassified 35 of 40 [88%]), and old myocardial infarction (AI reclassified 19 of 24 [79%]). Reclassification was lower in more challenging cases mimicking acute coronary occlusion due to myocardial tissue injury: subendocardial ischemia (AI reclassified 18 of 30 [60%]), post-cardiac arrest changes (AI reclassified 13 of 27 [48%]), and takotsubo cardiomyopathy (AI reclassified 10 of 23 [43%]).

DISCUSSION

In this multicenter study we evaluated the clinical performance and quality improvement potential of AI-based ECG triage in patients with suspected STEMI. The key findings are as follows: 1) substantial diagnostic challenges persist within conventional STEMI pathways, evidenced by treatment delays and high FPA rates; 2) AI-based ECG interpretation significantly outperformed SoC by reducing FPAs more than 4-fold while significantly improving the sensitivity for detecting angiographically confirmed STEMI solely using the index ECG; and 3) robust performance of AI was observed across diverse patient subgroups, including those with diagnostically challenging ECG features such as atrial fibrillation, prolonged QTc intervals, wide QRS complexes, LBBB, and STEMI-equivalent patterns (Central Illustration).

FIGURE 4 False Positive Activations by STEMI Mimic Stratified According to AI ECG Model Interpretation

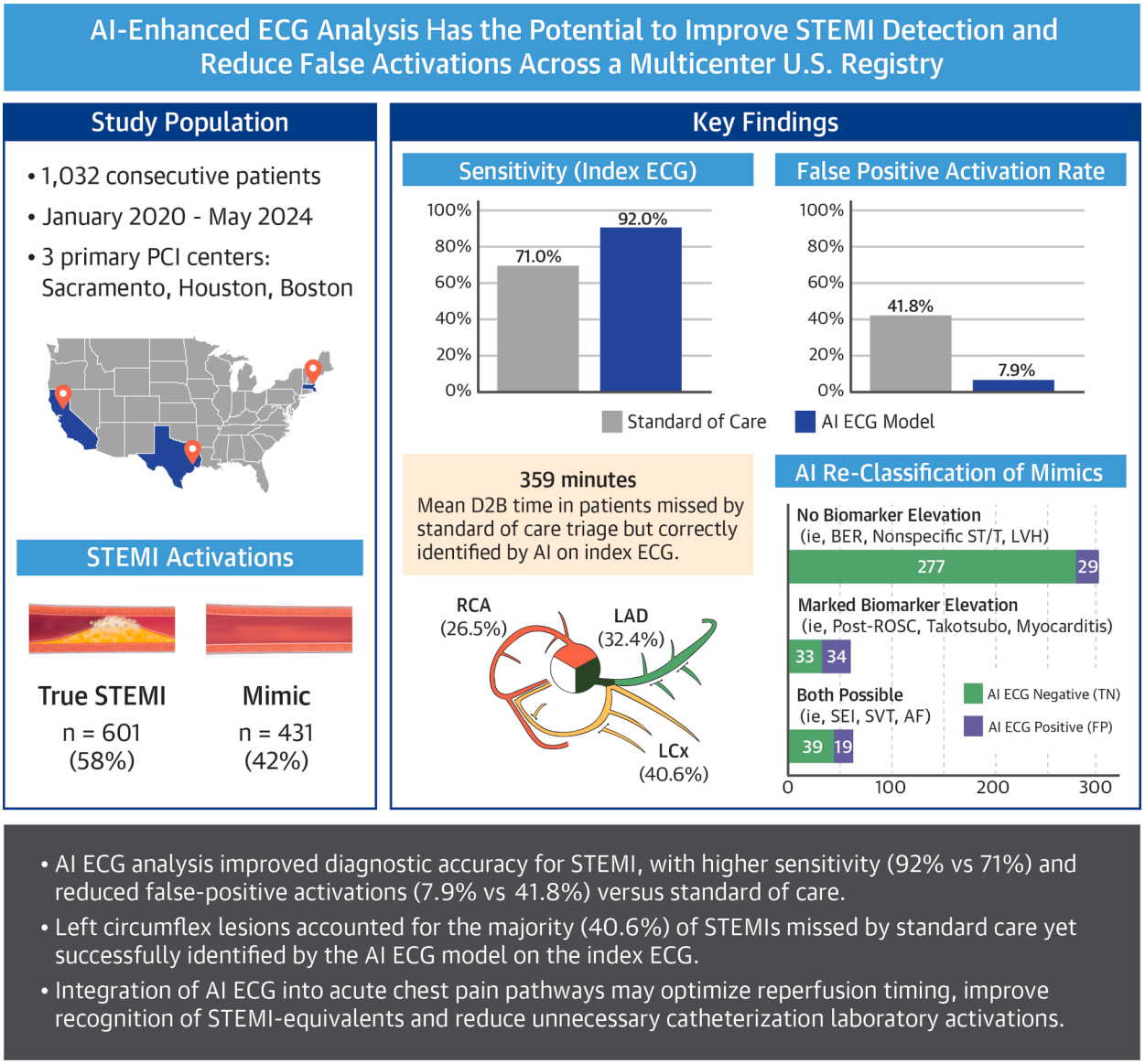


Standard-of-care false positives (FPs; n = 431), categorized by mimic type and biomarker profile. White bars represent cases correctly identified as negative by the AI ECG model (true negatives [TNs]), while shaded bars indicate STEMI mimics not reclassified by AI. Afib = atrial fibrillation; Aflut = atrial flutter; BER = benign early repolarization; CM = cardiomyopathy; ECG = electrocardiogram; MI = myocardial infarction; NIVCD = nonspecific intraventricular conduction delay; other abbreviations as in Figures 1 and 2.

Despite international guidelines emphasizing the recognition of STEMI-equivalent ECG patterns, current clinical pathways rely on millimeter-based thresholds for STEMI diagnosis.[1,3,15] This approach inherently limits sensitivity, particularly among a growing number of patients presenting with nonconventional ST-segment elevation. In our study, only fewer than two-thirds of angiographically confirmed STEMI cases met conventional STEMI criteria on index electrocardiography. Among those presenting with STEMI equivalents, more than one-half experienced delayed CCL activation, and only one-third progressed to conventional STEMI millimeter criteria prior to coronary angiography. This is consistent with recent findings in cases of total occlusions of the left anterior descending artery[16] associated with prolonged D2B times due to unrecognized STEMI equivalent, pointing to critical deficiencies in existing triage protocols. In contrast, a currently used AI ECG model, trained specifically on electrocardiograms of angiographically confirmed STEMI patients regardless of millimeters of ST-segment elevation,[10] demonstrated favorable accuracy to detect more subtle STEMI patterns using the index electrocardiogram alone. These findings extend prior reports of AI-based ECG interpretation for timely STEMI detection.[17-19] Although a recent randomized trial demonstrated reductions in time to treatment for conventional STEMI by a median of only 5.6 minutes,[17] our analysis suggests that detection of STEMI equivalents can shorten reperfusion delays by several hours. Earlier non-deep learning approaches relied on handcrafted features and additional clinical information beyond the waveform, which limited scalability at the point of care.[18] Moreover, they were not validated in broad in-hospital and prehospital cohorts or lacked 12-lead waveforms to detect infarcts in every territory.[18,19] In contrast, our model operates using single 12-lead ECG waveforms and can be deployed through a smartphone-based infrastructure,[14] enabling use across diverse and resource-limited settings.

To our knowledge, this is the first large-scale multicenter analysis to systematically characterize ECG phenotypes associated with STEMI mimics. In our cohort, only 6 of 10 emergent CCL activations resulted in confirmed STEMI, with a higher FPA rate than in previous studies, typically ranging between

CENTRAL ILLUSTRATION **Use of Artificial Intelligence to Improve Coronary Occlusion Detection**

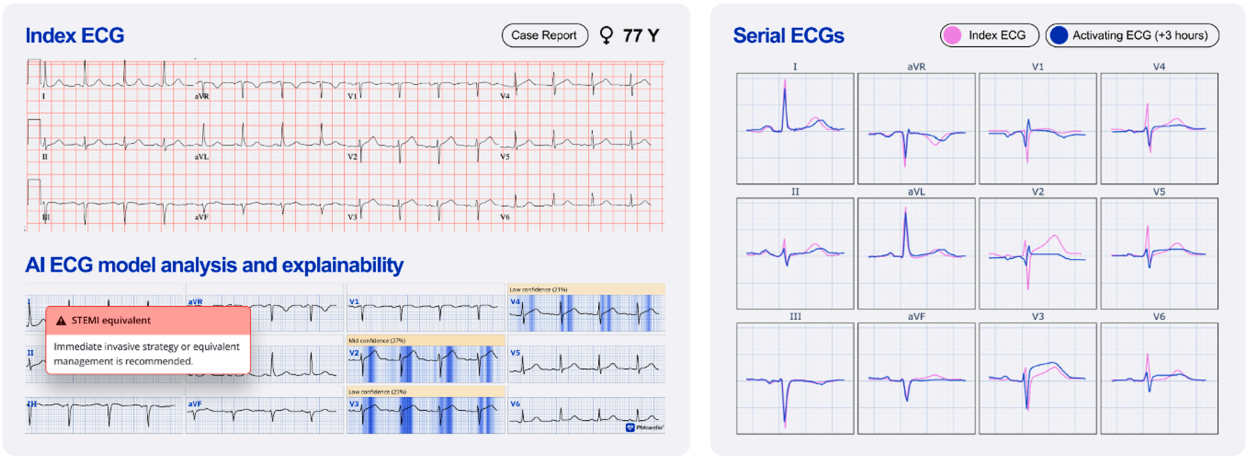


Herman R, et al. JACC Cardiovasc Interv. 2026;19(2):145–156.

AF = atrial fibrillation; AI = artificial intelligence; BER = benign early repolarization; D2B = door-to-balloon; ECG = electrocardiographic/electrocardiography; FP = false positive; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LVH = left ventricular hypertrophy; PCI = percutaneous coronary intervention; RCA = right coronary artery; ROSC = return of spontaneous circulation; SEI = subendocardial ischemia; STEMI = ST-segment elevation myocardial infarction; SVT = supraventricular tachycardia; TN = true negative.

15% and 30%.[7-9] This discrepancy is attributable to 2 methodological distinctions: 1) our reference standard was biomarker elevation with strict angiographic confirmation of a culprit lesion, classifying clinically relevant myocardial infarction with nonobstructive coronary arteries mimics[20] with marked biomarker elevation requiring early diagnostic coronary angiography such as takotsubo cardiomyopathy or myocarditis as false positives; and 2) our analysis included all initial activation attempts, including canceled activations ("call-offs"), reflecting real-world clinical practice and resource use.

FIGURE 5 A Real Clinical Case From the Study Cohort



A female patient with an ostial 100% thrombotic LAD occlusion who experienced a 368-minute catheterization delay. The AI electrocardiographic model correctly identified this STEMI equivalent on the index electrocardiogram (ECG).

Minimizing unnecessary urgent coronary angiography in patients without biomarker elevation is a priority for acute chest pain pathway quality improvement. In our study, one-half of patients who underwent emergent invasive angiography had negative cardiac enzymes. The AI ECG model correctly reclassified 91% of these cases as negatives, including benign mimics such as early repolarization, nonspecific ST/T-wave changes, left ventricular hypertrophy, and nonischemic LBBB, conditions that do not warrant emergent catheterization.

CLINICAL IMPLICATIONS. The AI ECG model demonstrated significantly higher diagnostic accuracy based solely on the index ECG at the FMC without using additional clinical information. In direct paired comparison, when the AI ECG model and SoC disagreed, AI was approximately 7 times more often correct than SoC and reduced site-level variability, suggesting potential to harmonize triage performance across institutions. Importantly, patients missed by SoC triage but successfully detected by the AI on index electrocardiography presented frequently with left circumflex coronary artery occlusions and in more than one-half of the cases with either left anterior descending or right coronary artery culprits. Consequently, failure to detect these culprits at FMC was associated with a markedly prolonged mean D2B time of more than 6 hours, pointing to critical shortcomings of current standard care pathways.

For example, a female patient with a 100% thrombotic ostial left anterior descending coronary artery occlusion experienced a 368-minute delay to revascularization, yet the AI ECG model correctly flagged the case at presentation on index electrocardiography (Figure 5). The accompanying AI explainability heatmap highlighted hyperacute T waves, a STEMI-equivalent finding recently validated as 98% specific for STEMI and present in one-fifth of cases without ST-segment elevation millimeter criteria.[21] These findings directly address recent guidelines emphasizing the role of AI in supporting streamlined, single-page STEMI activation pathways. In practice, the AI ECG model can function as a stand-alone decision support for EMS providers or emergency department physicians via smartphone-based ECG analysis or be fully integrated with ECG devices and hospital information technology systems, accelerating STEMI notification while minimizing workflow disruption. This feasibility has already been demonstrated in a prospective AI-powered STEMI network implementation,[22] and its impact on clinical outcomes is currently being investigated in ongoing randomized trials (NCT07077057).[23,24] Importantly, only 25 electrocardiograms (<3%) were excluded because of insufficient quality, which demonstrates the broad applicability of the model across diverse emergency care settings. This offers several practical advantages, including rapid point-of-care inference and compatibility with any ECG format, enabling real-time triage even in resource-limited settings, such as prehospital or non-PCI centers.

STUDY LIMITATIONS. First, retrospective ECG analysis may introduce selection or ascertainment bias. Second, although angiographic identification of a culprit vessel is a reproducible standard, we did not assess the impact of rapid STEMI detection on clinical outcomes such as infarct size, left ventricular function, and mortality. Third, operational aspects of integrating AI into emergency workflows (eg, interpretability, alert thresholds, clinician interface) warrant further exploration. Last, although our analysis was focused on a rigorously defined STEMI population from standardized registries, findings need to be prospectively validated in all-comers cohorts.

CONCLUSIONS

In this large, multicenter registry of patients undergoing emergent CCL activation for suspected STEMI, AI-based ECG analysis significantly outperformed conventional clinical triage of the index electrocardiogram in identifying angiographically confirmed STEMI. It reduced FPA rates while maintaining high sensitivity, particularly among patients with nonclassic ECG presentations. These findings support the integration of AI ECG models into acute chest pain pathways to optimize triage, reduce unnecessary interventions, and enhance timely reperfusion.

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PERSPECTIVES

WHAT IS KNOWN? Rapid reperfusion using primary PCI remains the cornerstone of STEMI management, but FMC ECG interpretation misidentifies STEMI equivalents, leading to frequent FPAs.

WHAT IS NEW? In this multicenter U.S. registry, AI-based ECG analysis (Queen of Hearts, PMcardio) significantly outperformed SoC by improving index ECG sensitivity for detecting angiographically confirmed STEMI and reducing false positive catheterization laboratory activations more than 4-fold.

WHAT IS NEXT? Prospective implementation studies are needed to evaluate whether integrating AI-based ECG interpretation at FMC can optimize resource use and shorten time to reperfusion.

REFERENCES

1. Rao SV, O'Donoghue ML, Ruel M, et al. 2025 ACC/AHA/ACEP/NAEMSP/SCAI guideline for the management of patients with acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2025;85:2135–2237.

2. De Luca G, Suryapranata H, Ottervanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: every minute of delay counts. *Circulation*. 2004;109:1223–1225.

3. Kontos MC, de Lemos JA, Deitelzweig SB, et al. 2022 ACC expert consensus decision pathway on the evaluation and disposition of acute chest pain in the emergency department: a report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol*. 2022;80:1925–1960.

4. Jollis JG, Granger CB, Zègre-Hemsey JK, et al. Treatment time and in-hospital mortality among patients with ST-segment elevation myocardial infarction, 2018-2021. *JAMA*. 2022;328:2033–2040.

5. Sammour YM, Khan SU, Hong H, et al. Institutional variability in processes of care and outcomes among patients with STEMI in the US. *JAMA Cardiol*. 2025;10(8):787–796.

6. Kontos MC, Gunderson MR, Zegre-Hemsey JK, et al. Prehospital Activation of Hospital Resources (PreAct) ST-Segment–Elevation Myocardial Infarction (STEMI): a standardized approach to prehospital activation and direct to the catheterization laboratory for STEMI recommendations from the American Heart Association's Mission: Lifeline Program. *J Am Heart Assoc*. 2020;9:e011963.

7. Larson DM, Menssen KM, Sharkey SW, et al. "False-positive" cardiac catheterization laboratory activation among patients with suspected ST-segment elevation myocardial infarction. *JAMA*. 2007;298:2754–2760.

8. Lange DC, Rokos IC, Garvey JL, Larson DM, Henry TD. False activations for ST-segment elevation myocardial infarction. *Interv Cardiol Clin*. 2016;5:451–469.

9. Garvey JL, Monk L, Granger CB, et al. Rates of cardiac catheterization cancelation for ST-segment elevation myocardial infarction after activation by emergency medical services or emergency physicians: results from the North Carolina Catheterization Laboratory Activation Registry. *Circulation*. 2012;125:308–313.

10. Herman R, Meyers HP, Smith SW, et al. International evaluation of an artificial intelligence–powered electrocardiogram model detecting acute coronary occlusion myocardial infarction. *Eur Heart J Digit Health*. 2024;5:123–133.

11. Kontos MC, Gandhi S, Garrett KN, et al. The NCDR's Chest Pain Myocardial Infarction Registry: 15 years of myocardial infarction quality improvement. *JACC Adv*. 2023;2:100712.

12. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction (2018). *J Am Coll Cardiol*. 2018;72:2231–2264.

13. Herman R, Demolder A, Vavrik B, et al. Validation of an automated artificial intelligence system for 12-lead ECG interpretation. *J Electrocardiol*. 2024;82:147–154.

14. Demolder A, Kresnakova V, Hojcka M, et al. High precision ECG digitization using artificial intelligence. *J Electrocardiol*. 2025;90:153900.

15. Byrne RA, Rossello X, Coughlan J, et al. 2023 ESC guidelines for the management of acute coronary syndromes: developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC). *Eur Heart J Acute Cardiovasc Care*. 2024;13:55–161.

16. Meyers HP, Sharkey SW, Herman R, et al. Failure of standard contemporary ST-elevation myocardial infarction electrocardiogram criteria to reliably identify acute occlusion of the left anterior descending coronary artery. *Eur Heart J Acute Cardiovasc Care*. 2025;14(7):403–411.

17. Lin C, Liu W-T, Chang C-H, et al. Artificial intelligence–powered rapid identification of ST-elevation myocardial infarction via electrocardiogram (ARISE)—a pragmatic randomized controlled trial. *NEJM AI*. 2024;1:AIoa2400190.

18. Al-Zaiti SS, Martin-Gill C, Zègre-Hemsey JK, et al. Machine learning for ECG diagnosis and risk stratification of occlusion myocardial infarction. *Nat Med*. 2023;29(7):1804–1813.

19. Li J, Pang SP, Xu F, Ji P, Zhou S, Shu M. Two-dimensional ECG-based cardiac arrhythmia classification using DSE-ResNet. *Sci Rep*. 2022;12:14485.

20. Yildiz M, Ashokprabhu N, Shewale A, Pico M, Henry TD, Quesada O. Myocardial infarction with non-obstructive coronary arteries (MINOCA). *Front Cardiovasc Med*. 2022;9:1032436.

21. Meyers HP, Simančík F, Herman R, et al. Hyperacute T waves are specific for occlusion myocardial infarction, even without diagnostic ST elevation. *JACC Adv*. 2025;4(10P2):102120.

22. Herman R, Schelfault D, Lauwers R, et al. TCT-594 AI-powered STEMI Network: first prospective implementation of smartphone-based ECG interpretation system assisting emergent cathlab activation. *J Am Coll Cardiol*. 2024;84:B219.

23. Herman R, Kisova T, Belmonte M, et al. Artificial intelligence–powered electrocardiogram detecting culprit vessel blood flow abnormality: AI-ECG TIMI study design and rationale. *J Soc Cardiovasc Angiogr Interv*. 2025;4:102494.

24. Aslanger EK, Aggul B, Yildirimturk O, et al. A diagnostic paradigm shift in acute myocardial infarction: rationale and design of the DIFOCCULT-3 trial. *JACC Adv*. 2025;4:102227.

KEY WORDS acute coronary syndrome, artificial intelligence, electrocardiography, percutaneous coronary intervention, ST-segment elevation myocardial infarction

APPENDIX For supplemental tables, please see the online version of this paper.