NEJM AI

NEJM AI 2024; 1 (7)
DOI: 10.1056/AIoa2400190

ORIGINAL ARTICLE

Artificial Intelligence–Powered Rapid Identification of ST-Elevation Myocardial Infarction via Electrocardiogram (ARISE) — A Pragmatic Randomized Controlled Trial

Chin Lin, Ph.D.,[1,2,3,4] Wei-Ting Liu, M.D.,[5] Chiao-Hsiang Chang, M.D.,[5] Chiao-Chin Lee, M.D.,[5] Shi-Chue Hsing, M.D.,[5] Wen-Hui Fang, M.D.,[2,6] Dung-Jang Tsai, Ph.D.,[1,2,7] Kai-Chieh Chen, M.S.,[8] Chun-Ho Lee, M.S.,[3] Cheng-Chung Cheng, M.D.,[5] Yi-Jen Hung, M.D.,[9] Shih-Hua Lin, M.D.,[10] Chien-Sung Tsai, M.D.,[11] and Chin-Sheng Lin, M.D., Ph.D.[1,5]

Received: February 21, 2024; Revised: April 7, 2024; Accepted: April 30, 2024; Published: June 27, 2024

Abstract

BACKGROUND Timely diagnosis of ST-elevation myocardial infarction (STEMI) is crucial for the treatment of patients with acute coronary syndrome. Artificial intelligence–enabled electrocardiogram (AI-ECG) has shown potential for the accurate and timely detection of STEMI on 12-lead electrocardiograms (ECGs). However, its impact on clinical treatment times is unknown.

METHODS To evaluate the potential of AI-ECG–assisted detection of STEMI to reduce treatment delays for patients with STEMI, we conducted an open-label, cluster randomized controlled trial involving 43,234 eligible patients (mean age, 60 years; 49.5% male) without a history of coronary angiography within 3 days in the emergency department or inpatient wards at Tri-Service General Hospital, Taipei, Taiwan between May 1, 2022, and April 31, 2023. Patients were randomly assigned 1:1 to AI-ECG–assisted detection of STEMI (intervention group) or to standard of care (control group). The primary end point was door-to-balloon time; ECG-to-balloon time was also evaluated as a branch of the primary analysis. Secondary end points included incidence of new-onset low ejection fraction, cardiac death, and all-cause mortality.

RESULTS Among the 43,234 patients, 77 in the intervention group and 68 in the control group were diagnosed with STEMI with occluded vessel(s) based on coronary angiography. The use of AI-ECG demonstrated a positive predictive value of 89.5% (95% confidence interval [CI], 85.3 to 93.6%) and a negative predictive value of 99.9% (95% CI, 99.9 to 100.0%). For patients in the emergency department, the median door-to-balloon time was 82.0 minutes (interquartile range, 62.5 to 89.5) in the intervention group compared with

The author affiliations are listed at the end of the article.

Dr. Chin-Sheng Lin can be contacted at littlelincs@gmail.com or at the Division of Cardiology, Tri-Service General Hospital, No. 325, Sec. 2, Cheng-Kung Rd., Neihu 114, Taipei, Taiwan.

96.0 minutes (interquartile range, 78.0 to 137.0) in the control group (P=0.002). When analyzing both emergency and inpatient cases, the median ECG-to-balloon time was 78.0 minutes (interquartile range, 56.9 to 88.2 minutes) in the intervention group compared with 83.6 minutes (interquartile range, 72.7 to 127.8 minutes) in the control group (P=0.011). In the intervention group versus the control group, there were 340 versus 304 cases, respectively, of new-onset heart failure with reduced ejection fraction (odds ratio, 1.12; P=0.151), 85 versus 116 cases of cardiac death (odds ratio, 0.73; P=0.029), and 1153 versus 1127 cases of all-cause mortality (odds ratio, 1.02; P=0.568).

CONCLUSIONS In patients with STEMI, AI-ECG–assisted triage of STEMI decreased the door-to-balloon time for patients presenting to the emergency department and decreased the ECG-to-balloon time for patients in the emergency room and inpatients. (Funded by the National Science and Technology Council, Taiwan and others; ClinicalTrials.gov number, NCT05118009.)

Introduction

Acute coronary syndrome, particularly ST-segment elevation myocardial infarction (STEMI), represents a substantial health care burden and contributes to global morbidity and mortality.[1] Timely diagnosis and immediate initiation of primary percutaneous coronary intervention (PPCI) are essential for improving the prognosis of patients with STEMI.[2] However, distinguishing patients with STEMI from those with undifferentiated chest pain remains a clinical challenge in acute settings. Inexperienced physicians may exhibit reduced accuracy in diagnosing STEMI, potentially leading to misdiagnoses,[3,4] which are observed in approximately 20.5% of STEMI cases and are related to poorer prognoses.[5] Providing clinical support to frontline physicians is of paramount importance for optimizing the management of STEMI.

Delayed treatment, stemming from a combination of systematic and nonsystematic factors, is independently associated with increased mortality in PPCI-treated patients with STEMI.[6] Because nonsystematic issues, such as cardiac arrests and endotracheal tube intubation, are challenging to address,[7] minimizing systematic errors is essential for improving health care quality.[8]

Clinical decision support systems (CDSSs) are extensively used to optimize workflows and improve patient outcomes.[9] However, although commercial electrocardiogram (ECG) machines typically encompass an automatic analysis system, which includes a diagnostic function for STEMI, diagnostic accuracy is usually poor.[10] Incorporating such low positive predictive values into an automatic alarm system may pose a risk to patient safety because of the potential for alert fatigue.[11,12]

With the advent of deep learning techniques, artificial intelligence (AI) systems have demonstrated significant benefits in ECG interpretation.[13,14] The integration of artificial intelligence–enabled electrocardiogram (AI-ECG) into CDSS has been confirmed through a randomized controlled trial (RCT), highlighting its potential for diagnosing asymptomatic left ventricular dysfunction and reducing mortality.[15,16] We hypothesize that AI-ECG–based CDSS can also be applied to enhance STEMI management.

Previous studies have shown that the performance of AI-ECGs developed for STEMI identification has generally reached or exceeded the expertise of cardiologists.[10,17,18] Subsequent before-and-after analyses have demonstrated the effectiveness of AI-ECG–based CDSS in reducing door-to-balloon time.[19,20] It has been suggested that health care quality improvement over time could potentially influence the findings from before-and-after analyses.[21,22] In addition, patients with STEMI in the inpatient department exhibit a higher risk of mortality compared with those experiencing STEMI outside of the hospital setting.[23,24] This finding could potentially be attributed to greater delays in treatment activation in the inpatient department than in the emergency department.[25] Currently, few RCTs have evaluated the impact of AI-ECG systems in STEMI management,[26] whether in the emergency or inpatient department. We designed the Artificial Intelligence–Powered Rapid Identification of ST-Elevation Myocardial Infarction via Electrocardiogram (ARISE) trial to assess the impact of AI-ECG in facilitating STEMI diagnosis and management.

Methods

TRIAL DESIGN

The two-center, open-label, cluster randomized controlled ARISE trial (NCT05118009) followed the A/B testing methodology, whereby different software versions are

randomly assigned to users, which aligns with the pragmatic RCT approach.[27] The study adhered to Consolidated Standards of Reporting Trials (CONSORT)-AI Extension guidelines for reporting (CONSORT-AI Extension checklist)[28] and was approved by the institutional review board (IRB) at Tri-Service General Hospital, Taipei, Taiwan (IRB A202105120). Informed consent was obtained from all 20 on-duty cardiologists in the hospital's catheterization laboratory who participated in the study. The ethical committee permitted the enrollment of patients during the trial period without consent given the need for timeliness of emergent procedures. Additional information is available in the protocol provided with the full text of this article at ai.nejm.org.

The ARISE trial was conducted at both an academic medical center and a community hospital in Taiwan, both of which shared the catheterization laboratory. Patients with STEMI visiting the community hospital were required to be referred to the academic medical center. Although these patients were not considered to be study participants, patient-level data from electronic health records (EHRs) were analyzed to investigate the impact of AI-ECG support on on-duty cardiologists. The ethical committee concluded that AI-ECG software qualified as a medical device with minimal risk, in accordance with the announcement by the Taiwan Food and Drug Administration (Taiwan Food and Drug Administration document 1101603684).

PATIENT DATA AND RANDOMIZATION

The ARISE trial involved a total of 43,994 patients without a history of coronary angiography who received an ECG in the emergency department or inpatient department at Tri-Service General Hospital between May 1, 2022, and April 31, 2023 (Fig. 1). Patients were randomly assigned 1:1 to AI-ECG–assisted detection of STEMI (intervention group) or standard of care (control group) according to the date of their first ECG such that those who had their first ECG on odd dates were assigned to one group and those with first their ECG on even dates were assigned to the other group. The simple randomization method ensured that only a single sequence of random assignments,[29] which was generated by an independent database programmer before the trial, was used to ensure blindness from the previous day.

For the on-duty cardiologists participating in the trial, the specific assignment to either the intervention or control group was revealed at 8 a.m. on the respective day. Only the first ECG of each patient during the study period was included for analysis. Initially, the intervention and control groups consisted of 21,989 and 22,005 patients, respectively. After excluding 760 patients younger than 18 years of age, the final analysis included 21,612 patients in the intervention group and 21,622 patients in the control group.

AI-ECG INTERVENTION

The AI algorithm used 12-lead ECG waveform data to identify STEMI.[10] The algorithm was reported to have a positive predictive value of 93.2% in a preliminary prospective study in an emergency department.[20] In the current study, cardiologists on duty were assigned to either the AI-assisted group or the control group daily, and all were aware of whether or not they would receive support from the AI-ECG system. Frontline physicians did not participate in the study and were blinded to the daily randomization.

In the intervention group, real-time analysis was performed by the AI-ECG system on all ECGs completed that day (details are shown in Supplementary Method 1 in the Supplementary Appendix). Immediate short message service (SMS) notifications, including ECG images, were sent to the on-duty cardiologists when the AI-ECG system detected potential STEMI cases to allow for review and confirmation. Given the lack of real-time documentation of ischemic-related symptoms in EHRs, on-duty cardiologists needed to assess patient symptoms upon receiving the AI-ECG alert. When STEMI was confirmed, the cardiologists could then activate the catheterization laboratory for PPCI.

In the control group, potential patients with STEMI were initially assessed by frontline physicians, who then notified the on-duty cardiologists for confirmation. Regardless of whether the AI-ECG system was used, frontline physicians were able to request consultation from the on-duty cardiologists. All frontline physicians could see the interpretation from a Philips automatic ECG analysis system for ECG interpretation, although the Philips system did not trigger subsequent SMS notifications to on-duty cardiologists because of concerns of alert fatigue.[11,12] Only on-duty cardiologists had the authority for catheterization laboratory activation, according to our national policy.

STEMI DIAGNOSIS AND BASELINE CHARACTERISTICS

The diagnosis of STEMI in this trial was made according to ischemic-related symptoms and ST-segment elevation

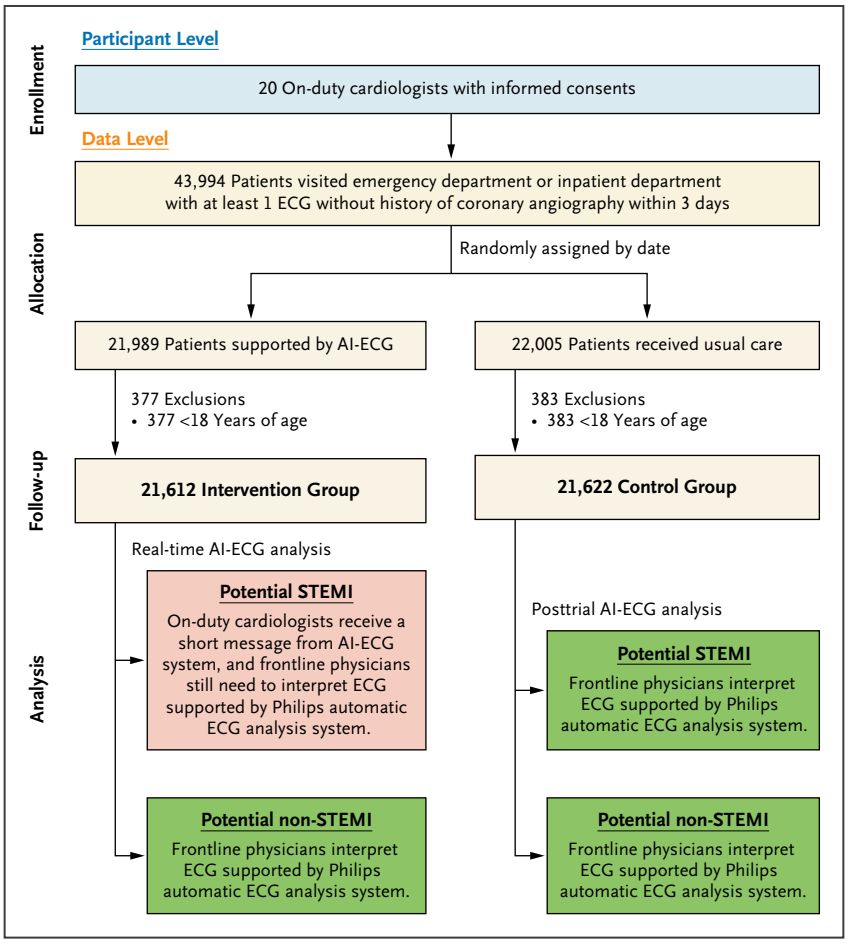

Figure 1. CONSORT-AI Flow Diagram.

Of note, in the intervention group, there were 57 patients (0.3%) who underwent ECG examination while our AI-ECG system was inoperative (postanalysis revealed that they were all classified as AI-ECG–potential non-STEMI). Although they were not covered by the AI-ECG–based clinical decision support systems, we still included them in the analysis based on the intention-to-treat design. AI denotes artificial intelligence; AI-ECG, artificial intelligence–enabled electrocardiogram; CONSORT, Consolidated Standards of Reporting Trials; ECG, electrocardiogram; and STEMI, ST-segment myocardial infarction.

on ECGs without considering the value of cardiac troponin level[30,31] (details are shown in Supplementary Method 2). Our EHR recorded all STEMI cases confirmed by urgent coronary angiography, independent of this trial.

For patients with STEMI who underwent urgent coronary angiography, four cardiologists reviewed the patients after the trial to further divide them into two groups: STEMI with occluded vessel(s) or STEMI with nonobstructive coronary arteries. For patients without urgent coronary angiography, the cardiologists reviewed 45 AI-ECG–identified potential STEMI cases and categorized them into two groups: STEMI without coronary angiography or without STEMI. Because of the large number of cases identified as potentially without STEMI by AI-ECG, a case-by-case review was deemed impractical, and all of these patients were categorized as without STEMI. For the primary analysis, only patients with STEMI with occluded vessel(s) were used. For event and accuracy analyses, all patients with STEMI were included. We acknowledge that this pragmatic approach might miss some patients with STEMI without urgent coronary angiography.

The index time in our study was defined as the time of ECG conduction. The baseline characteristics of each patient were collected from the EHR before the index time. The presence of coronary artery disease, diabetes mellitus, hypertension, hyperlipidemia, and chronic kidney disease was identified by the appropriate International Classification of Diseases codes. Patient information in

the emergency department was acquired during the triage process, focusing on typical chest pain symptoms at the triage station to enable subsequent stratified analysis (details are shown in Supplementary Method 2).

PRESPECIFIED END POINTS AND POST HOC ANALYSIS

The prespecified primary end point was door-to-balloon time in patients with STEMI with occluded vessel(s). Because the door-to-balloon time may not represent the first medical contact time for patients in the inpatient department, the primary analysis considered only patients in the emergency department. We also analyzed the ECG-to-balloon time for both patients in the emergency department and inpatient patients simultaneously. The AI-ECG intervention was expected to be the most beneficial for patients identified as potentially having STEMI. Therefore, we conducted prespecified stratified analyses of the primary end point based on the AI-ECG results. For the prespecified exploratory analysis, we conducted additional stratified analyses and further analyses for each period of the treatment waiting time. In sensitivity analyses, patients with STEMI with occluded vessel(s) without ST elevation in the first ECG, patients with instances of intubation or resuscitation before coronary angiography, and patients who refused PPCI treatment were excluded in adherence to established quality indicator policies.[32]

The prespecified secondary end points were all-cause mortality within 365 days from the first ECG, cardiac death within 365 days, new-onset low ejection fraction within 90 days, hospitalization for patients in the emergency department, and STEMI-related diagnoses. STEMI-related diagnoses encompassed the following: STEMI with occluded vessel(s); urgent coronary angiography: STEMI with occluded vessel(s) plus STEMI with nonobstructive coronary arteries; all patients with STEMI: STEMI with occluded vessel(s) plus STEMI with nonobstructive coronary arteries plus STEMI without coronary angiography; and STEMI without coronary angiography. For patients with STEMI with occluded vessel(s), the ejection fraction, the highest level of high-sensitivity cardiac troponin I (hscTnI), the highest level of creatine kinase (CK), and the length of hospitalization were compared in post hoc analyses. An accuracy analysis of the AI-ECG system was also performed (details are shown in Supplementary Method 3).

SAMPLE SIZE

Prior to the ARISE trial, we conducted a pilot study of 25,002 patients and observed that AI-ECG intervention had the potential to reduce the door-to-balloon time from 70.0 ± 13.6 minutes to 64.1 ± 12.4 minutes.[20] Based on a significance level of $P<0.05$, a statistical power of 0.80, and a sample size ratio of 1.0 between the intervention and control groups, we concluded that we would require 77 patients with STEMI in each group. Considering that the incidence of STEMI among patients undergoing ECG examinations in our hospital is around 0.4%,[20] approximately 19,250 patients in each group (intervention and control) were required. That figure corresponds roughly to the total number of patients who underwent ECG examinations in our hospital annually. Therefore, the trial was conducted for 1 year to achieve a total of 21,612 and 21,622 cases in the intervention and control groups, respectively.

STATISTICAL ANALYSIS

The detailed statistical plan was based on an intention-to-treat design (details are shown in Supplementary Method 4). The statistical analysis was performed using R version 3.4.4. For time difference analysis, the Mann–Whitney U test using the wilcox.test function was chosen primarily because of the skewed distribution of treatment waiting time,[33] and raov function in R package Rfit version 0.24.2 was used to support stratified analysis for interaction terms. Logistic regression was used to estimate the odds ratios for event analyses. The prespecified stratified analysis was conducted by adding interaction terms to the logistic regression model for testing. For numeric prognosis analyses, the same statistical method of time difference analysis was used. For the accuracy analyses, we calculated the confidence intervals (CIs) for each percentage using the Z distribution and used chi-square tests for conducting stratified analyses.

Results

PATIENTS' CHARACTERISTICS STRATIFIED BY RANDOMIZATION

Table 1 presents the baseline characteristics of patients stratified by randomization (details regarding the participating cardiologists are shown in Supplementary Result 1). The average age of patients was 60 years, 49.5% were male, and 7.2% were from the community hospital, of whom 36.8% were from the inpatient department. Of the 21,612 patients in the intervention group, 77 (0.4%), 23 (0.1%), and 7 (0.0%) were classified as having STEMI

with occluded vessel(s), STEMI with nonobstructive coronary arteries, and STEMI without coronary angiography, respectively. Of the 21,621 patients in the control group, 68 (0.3%), 18 (0.1%), and 16 (0.1%) were classified into the corresponding subgroups, respectively. The average age of patients with STEMI with occluded vessel(s) was 65 years, and 80% were male. Notably, in the inpatient department, there were seven patients with STEMI with occluded vessel(s) in the intervention group and only one in the control group. No significant differences in baseline characteristics were observed between the intervention and control groups for both the entire patient population and specifically, among patients with STEMI with occluded vessel(s) (details are shown in Supplementary Result 2).

PRIMARY ANALYSIS FOR STEMI WITH OCCLUDED VESSEL(S)

In the emergency department, the median door-to-balloon time was 82.0 minutes (interquartile range, 62.5 to 89.5 minutes) in the intervention group compared with 96.0 minutes (interquartile range, 78.0 to 137.0 minutes) in the control group (P=0.002). When analyzing both emergency and inpatient cases, the median ECG-to-balloon time was 78.0 minutes (interquartile range, 56.9 to 88.2 minutes)

Table 1. Baseline Characteristics and Diagnostic Group in Intervention and Control Groups.*

	All Patients			STEMI with Occluded Vessel(s)		
Characteristic	Intervention (n=21,612)	Control (n=21,622)	P Value†	Intervention (n=77)	Control (n=68)	P Value†
AI-ECG result			0.625			0.965
Potential STEMI	108 (0.5%)	101 (0.5%)		67 (87.0%)	59 (86.8%)	
Potential non-STEMI	21,504 (99.5%)	21,521 (99.5%)		10 (13.0%)	9 (13.2%)	
Hospital			0.568			1.000
Academic medical center	20,040 (92.7%)	20,080 (92.9%)		73 (94.8%)	64 (94.1%)	
Community hospital	1,572 (7.3%)	1,542 (7.1%)		4 (5.2%)	4 (5.9%)	
Department			0.451			0.067
Emergency department	13,606 (63.0%)	13,688 (63.3%)		70 (90.9%)	67 (98.5%)	
Inpatient department	8,006 (37.0%)	7,934 (36.7%)		7 (9.1%)	1 (1.5%)	
Time frame			0.328			0.055
Regular hours	12,384 (57.3%)	12,289 (56.8%)		37 (48.1%)	22 (32.4%)	
Off hours	9,228 (42.7%)	9,333 (43.2%)		40 (51.9%)	46 (67.6%)	
Gender (male)	10,722 (49.6%)	10,675 (49.4%)	0.617	64 (83.1%)	52 (76.5%)	0.318
Age — yr, mean (±SD)	60.3±18.4	60.2±18.3	0.601	64.8±13.2	65.1±11.3	0.899
Age group — yr			0.449			0.780
<65	12,056 (55.8%)	12,191 (56.4%)		40 (51.9%)	33 (48.5%)	
65–74	4,881 (22.6%)	4,829 (22.3%)		23 (29.9%)	24 (35.3%)	
≥75	4,675 (21.6%)	4,602 (21.3%)		14 (18.2%)	11 (16.2%)	
Coronary artery disease	4,616 (21.4%)	4,677 (21.6%)	0.491	49 (63.6%)	48 (70.6%)	0.375
Diabetes mellitus	4,970 (23.0%)	5,080 (23.5%)	0.220	23 (29.9%)	24 (35.3%)	0.486
Hypertension	7,864 (36.4%)	8,037 (37.2%)	0.091	26 (33.8%)	27 (39.7%)	0.459
Hyperlipidemia	7,826 (36.2%)	8,004 (37.0%)	0.082	30 (39.0%)	30 (44.1%)	0.529
Chronic kidney disease	4,400 (20.4%)	4,560 (21.1%)	0.061	19 (24.7%)	11 (16.2%)	0.207
Diagnostic group			0.196			
STEMI with occluded vessel(s)	77 (0.4%)	68 (0.3%)				
STEMI without occluded vessel(s)	23 (0.1%)	18 (0.1%)				
STEMI without coronary angiography	7 (0.0%)	16 (0.1%)				
Probably non-STEMI	21,505 (99.5%)	21,520 (99.5%)				

* Values are numbers (percentages) unless indicated otherwise. AI-ECG denotes artificial intelligence–assisted electrocardiogram; SD, standard deviation; and STEMI, ST-segment myocardial infarction.

† The P values are two sided, with no adjustment for multiple comparison.

in the intervention group compared with 83.6 minutes (interquartile range, 72.7 to 127.8 minutes) in the control group (P=0.011). The overall trend was consistent in the sensitivity analysis that excluded patients with nonsystematic delayed factors, in adherence to established quality indicator policies.[32]

Because of the limited sample size, the stratified analysis based on AI-ECG results did not confirm the prespecified hypothesis (P for intervention group × AI-ECG group interaction >0.05) (details are shown in Supplementary Result 3). For ECG-to-balloon time, the AI-ECG intervention demonstrated a consistent pattern across all stratified analyses (Fig. 2).

PRESPECIFIED SECONDARY ANALYSIS

Figure 3 presents the event analysis of the AI-ECG intervention in the diagnosis and management of STEMI. Cardiac death was significantly different between the groups (0.4% in the intervention group vs. 0.5% in the control group; odds ratio, 0.73; 95% CI, 0.55 to 0.97). The only significant result in STEMI-related diagnoses was a lower incidence of STEMI without coronary angiography in the intervention group (odds ratio, 0.37; 95% CI, 0.14 to 0.94). There was no significant difference in all patients with STEMI between the two groups (odds ratio, 1.05; 95% CI, 0.80 to 1.38), indicating that more patients in the intervention group were scheduled for urgent coronary angiography (Supplementary Result 4 shows the

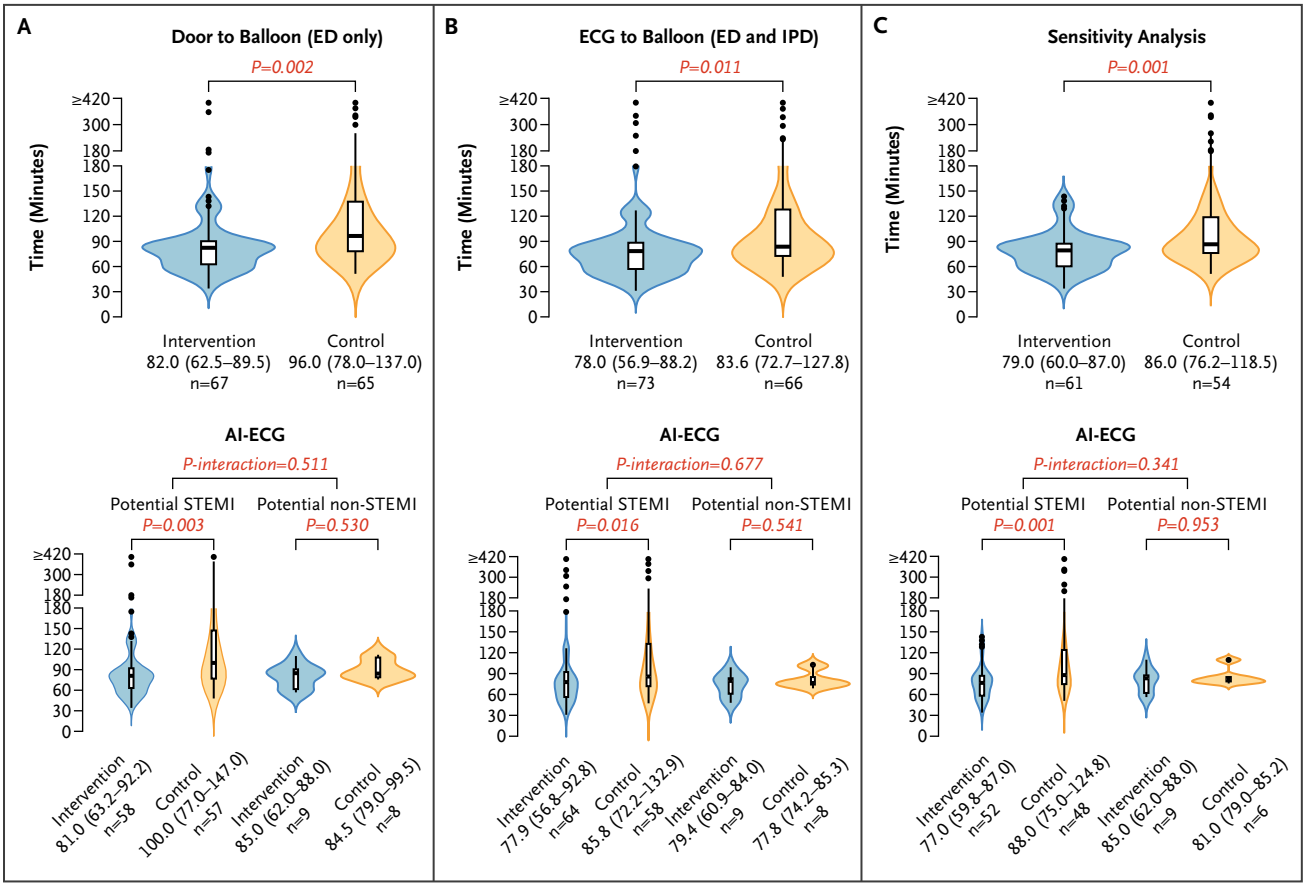

Figure 2. Time Difference Analysis for STEMI with Occluded Vessel(s).

Panel A shows the intention-to-treat analysis on door-to-balloon time. Because the door time was unavailable for patients in the IPD, the prespecified primary analysis included only the patients in the ED. There were three and two STEMIs with occluded vessel(s) without balloon time in the intervention and control groups, respectively, because they were found to be ineligible for primary percutaneous coronary intervention during coronary angiography. Panel B shows the ECG-to-balloon time for patients in the ED and IPD. One additional STEMI with occluded vessel(s) without balloon time in the intervention group in IPD was excluded in this analysis. Panel C shows the door-to-balloon time comparison in patients without nonsystematic delayed factors (nondiagnostic ECG, intubation/resuscitation, and patient declined). The stratified analysis in the lower panel was the only prespecified stratified analysis. AI-ECG denotes artificial intelligence–electrocardiogram; ECG, electrocardiogram; ED, emergency department; IPD, inpatient department; and STEMI, ST-segment myocardial infarction.

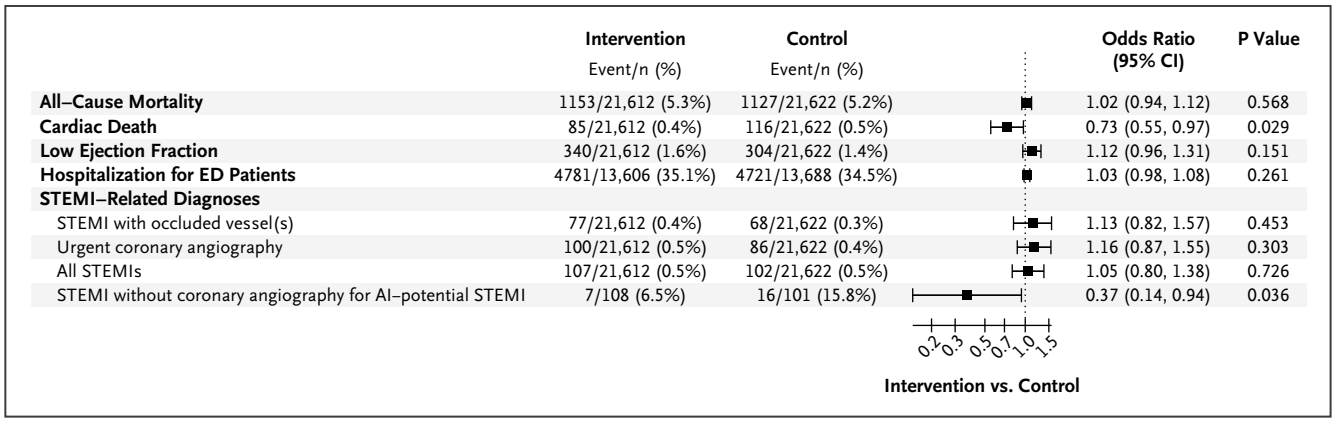

Figure 3. Analyses of Prespecified Secondary End Points.

The analysis of hospitalization was only for patients in the ED. The detailed definitions of each STEMI-related diagnosis are STEMI with occluded vessel(s); urgent coronary angiography (STEMI with occluded vessel[s] + STEMI with nonobstructive coronary arteries); all STEMI patients (STEMI with occluded vessel[s] + STEMI with nonobstructive coronary arteries + STEMI without coronary angiography); and STEMI without coronary angiography. Because there was no STEMI without coronary angiography in AI-potential non-STEMI group due to the pragmatic data collection strategy, the analysis for this event included only the AI-potential STEMI subgroup. AI denotes artificial intelligence; CI, confidence interval; ED, emergency department; and STEMI, ST-segment myocardial infarction.

prespecified stratified analysis and other detailed analyses). The reduction in cardiac death might not come from AI-ECG alerts in the AI-potential STEMI subgroup because we observed a nonsignificant increasing trend of cardiac death in the intervention group compared with the control group (odds ratio, 1.36; 95% CI, 0.57 to 3.21). A noteworthy but nonsignificant trend was the increased identification of STEMI with occluded vessel(s) in the intervention group compared with the control group from the inpatient department (odds ratio, 6.94; 95% CI, 0.85 to 56.42).

POST HOC ANALYSIS FOR CLINICAL OUTCOMES IN STEMI WITH OCCLUDED VESSEL(S)

We analyzed the differences in several important prognostic indicators during hospitalization for STEMI with occluded vessel(s) between the intervention and control groups (details are shown in Supplementary Result 5). The results showed no significant differences in these measures, including ejection fraction, highest level of hscTnI, highest level of CK, and length of hospitalization. Further subgroup analyses did not reveal any significant findings.

PROSPECTIVE ACCURACY OF AI-ECG

Table 2 shows the diagnostic accuracy of AI-ECG in the trial, with a positive predictive value of 89.5% (95% CI, 85.3 to 93.6%), a negative predictive value of 99.9% (95% CI, 99.9 to 100.0%), a sensitivity of 89.5% (95% CI, 85.3 to 93.6%), and a specificity of 99.9% (95% CI, 99.9 to 100.0%), significantly better than the Philips automatic ECG analysis system (a stratified analysis and a false-positive analysis are shown in Supplementary Result 6).

Discussion

The ARISE trial is a pragmatic RCT that compared the implementation of the AI-ECG versus standard of care for STEMI management. We found that the integration of AI-ECG into the EHR as a CDSS significantly reduced the door-to-balloon time in the emergency department setting and the ECG-to-balloon time in patients in the emergency department and inpatients. There was modest to no difference between the intervention and control groups in rates of new-onset heart failure with reduced ejection fraction or all-cause mortality.

Reducing door-to-balloon time in STEMI, a key performance indicator, is crucial for improving prognosis. However, timely diagnosis and treatment are challenging in the clinical setting.[34] Strategies have entailed improvement in catheterization laboratory activation, rapid team preparedness, data feedback, and administrative support.[35] All of these interventions have demonstrated significant reductions in treatment waiting times, but they often incur

Table 2. The Accuracy of the Deep Learning Model and the Philips Automatic System.*						
	Deep Learning Model			Philips Automatic System		
Case/Control	Potential STEMI (n=209)	Potential Non-STEMI (n=43,025)	Sensitivity/ Specificity	AMI (n=1,001)	Not AMI (n=42,233)	Sensitivity/ Specificity
Case						
STEMI with occluded vessel(s)	126 (60.3%)	19 (0.0%)		99 (9.9%)	46 (0.1%)	
STEMI without occluded vessel(s)	38 (18.2%)	3 (0.0%)		14 (1.4%)	27 (0.1%)	
STEMI without coronary angiography	23 (11.0%)	0 (0.0%)		16 (1.6%)	7 (0.0%)	
All STEMI cases	187 (89.5%)†	22 (0.1%)	Sensitivity 89.5% (187/209)	129 (12.9%)†	80 (0.2%)	Sensitivity 61.7% (129/209)
Control						
Probably non-STEMI	22 (10.5%)	43,003 (99.9%)‡	Specificity 99.9% (187/209)	872 (87.1%)	42,153 (99.8%)‡	Specificity 98.0% (187/209)

* Values are numbers (percentages) unless indicated otherwise. The "case" group encompassed the combination of STEMI with occluded vessel(s), STEMI without occluded vessel(s), and STEMI without coronary angiography groups, whereas the "control" group consisted of the remaining "probably non-STEMI" group. AMI denotes acute myocardial infarction; and STEMI, ST-segment myocardial infarction.

† This indicates positive predictive values.

‡ This indicates negative predictive values.

high costs. In contrast, low-cost interventions, such as AI-ECG–based CDSS, have potential by expediting communication between frontline physicians and on-duty cardiologists. Numerous studies have shown the effectiveness of AI-ECG–based CDSS in reducing treatment delay.[19,20] The ARISE trial, the first RCT evaluating the efficacy of AI-ECG–based CDSS, provides compelling evidence for future large-scale implementation of this technology to further reduce ECG-to-catheterization laboratory time.

We show that the median door-to-balloon time in the emergency department was 86.0 minutes in the control group (excluding patients with nonsystematic delays in adherence to established quality indicator policies[32]), a time that was higher than in our previous study (70 minutes).[20] It had been proposed that the median door-to-balloon time was 78 minutes (interquartile range, 62 to 106 minutes).[36] Other research reported a median door-to-balloon time of 86 minutes without prehospital activation, similar to the results in this study.[37] Upon a comprehensive retrospective analysis of the study population, it became evident that the time delay during the pandemic era was partially attributable to the screening for coronavirus disease 2019 (Covid-19) before PPCI. However, because both groups in the RCT were equally affected by the Covid-19 pandemic, we believe that the time difference between the intervention and control groups in the ARISE trial remains credible.

AI-ECG–based CDSS provides an additional advantage by minimizing the risk of misdiagnosis. Misdiagnoses among patients with STEMI are frequently reported,[5] and the constraints of observational studies impede the precise identification of such cases because they typically focus on patients with a confirmed final diagnosis of STEMI. Furthermore, regarding the rate of occluded vessels among patients with STEMI who underwent urgent coronary angiography, we observed that the proportions were comparable in the intervention group (77/100, 77%) and the control group (68/86, 79%). It is more plausible that the decrease in patients with STEMI without urgent coronary angiography identified in posttrial review in the intervention group, compared with the control group, is attributable to differences in the rate of misdiagnosis. The high accuracy of AI-ECG has been validated in multiple prospective interventional studies, with a positive predictive value exceeding 80%.[19,20] This high value is critical for the success of CDSS.[9] The ARISE trial demonstrated a trend of increased STEMI with occluded vessel(s) in the intervention group coupled with a significant decrease in STEMI without coronary angiography, particularly within the inpatient department. The ARISE trial substantiated the potential advantages of AI-ECG in diminishing misdiagnoses, extending cardiology-level bedside care to patients across the hospital, and consequently, enhancing health care quality.

This study has several limitations. First, the sample size of the ARISE trial may have been inadequate to detect

significant differences in secondary end points, particularly in subgroup analyses. Second, this study primarily focused on reducing treatment waiting times, leading to short-term outcome follow-up. The limited sample size made it challenging to obtain sufficient statistical power, even with extended follow-up for STEMI complications. Third, the study was conducted at a single center, which may restrict the applicability of the results to other health care settings with different patient populations and resources. Fourth, the pragmatic data collection process may lead to overestimations of the negative predictive rate and sensitivity of AI-ECG. Fifth, given the nature of the intervention, it was not feasible to blind health care providers and patients, which may have introduced bias into the assessment of outcomes.

Conclusion

The ARISE study evaluated the impact of an AI-ECG intervention on STEMI management. The incorporation of AI-ECG as an affordable CDSS resulted in a significant reduction in door-to-balloon time, underscoring its potential to enhance the timeliness of care delivery. The intervention also demonstrated promising accuracy in identifying potential STEMI cases, enhancing the attention of and proactive management by health care providers. Further research with larger sample sizes and extended follow-up periods is necessary to provide additional validation of the benefits on clinical outcomes.

Disclosures

Author disclosures and other supplementary materials are available at ai.nejm.org.

Supported by the National Science and Technology Council, Taiwan (grant NSTC110-2314-B-016-010-MY3 to Dr. Chin Lin and grant NSTC112-2321-B-016-003 to Dr. Shih-Hua Lin); the Cheng Hsin General Hospital, Taiwan (grant CHNDMC-113-11205 to Dr. Chin Lin and grant CHNDMC-113-01 to Dr. Chin-Sheng Lin); and the Medical Affairs Bureau, Taiwan (grants MND-MAB-110-113, MND-MAB-D-111045, MND-MAB-C13-112050, MND-MAB-C07-113020, and MND-MAB-C07-113021 to Dr. Chin Lin and grants MND-MAB-C07-113022, MND-MAB-C13-112051, MND-MAB-C08-111032, and MND-MAB-C08-11032 to Dr. Chin-Sheng Lin).

We sincerely appreciate the participation of the 20 on-duty cardiologists involved in the Artificial Intelligence–Powered Rapid Identification of ST-Elevation Myocardial Infarction via Electrocardiogram trial.

Author Affiliations

[1] Medical Technology Education Center, School of Medicine, National Defense Medical Center, Taipei, Taiwan, R.O.C.

[2] Department of Artificial Intelligence of Things, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, R.O.C.

[3] School of Public Health, National Defense Medical Center, Taipei, Taiwan, R.O.C.

[4] Graduate Institute of Aerospace and Undersea Medicine, National Defense Medical Center, Taipei, Taiwan, R.O.C.

[5] Division of Cardiology, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, R.O.C.

[6] Department of Family and Community Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, R.O.C.

[7] Department of Statistics and Information Science, Fu Jen Catholic University, New Taipei City, Taiwan, R.O.C.

[8] Graduate Institute of Life Sciences, National Defense Medical Center, Taipei, Taiwan, R.O.C.

[9] Division of Endocrinology and Metabolism, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, R.O.C

[10] Division of Nephrology, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, R.O.C.

[11] Division of Cardiovascular Surgery, Department of Surgery, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, R.O.C.

References

1. Lawton JS, Tamis-Holland JE, Bangalore S, et al. 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines [published correction appears in Circulation 2022;145:e772]. Circulation 2022;145:e18-e114. DOI: 10.1161/CIR.0000000000001038.

2. Rokos IC, French WJ, Mattu A, et al. Appropriate cardiac cath lab activation: optimizing electrocardiogram interpretation and clinical decision-making for acute ST-elevation myocardial infarction. Am Heart J 2010;160:995-1003.e8. DOI: 10.1016/j.ahj.2010.08.011.

3. McCabe JM, Armstrong EJ, Ku I, et al. Physician accuracy in interpreting potential ST-segment elevation myocardial infarction electrocardiograms. J Am Heart Assoc 2013;2:e000268. DOI: 10.1161/JAHA.113.000268.

4. Huitema AA, Zhu T, Alemayehu M, Lavi S. Diagnostic accuracy of ST-segment elevation myocardial infarction by various healthcare providers. Int J Cardiol 2014;177:825-829. DOI: 10.1016/j.ijcard.2014.11.032.

5. Wu J, Gale CP, Hall M, et al. Editor's choice — impact of initial hospital diagnosis on mortality for acute myocardial infarction: a national cohort study. Eur Heart J Acute Cardiovasc Care 2018;7:139-148. DOI: 10.1177/2048872616661693.

6. Terkelsen CJ, Sørensen JT, Maeng M, et al. System delay and mortality among patients with STEMI treated with primary percutaneous coronary intervention. JAMA 2010;304:763-771. DOI: 10.1001/jama.2010.1139.

7. Swaminathan RV, Wang TY, Kaltenbach LA, et al. Nonsystem reasons for delay in door-to-balloon time and associated in-hospital mortality: a report from the National Cardiovascular Data Registry. J Am Coll Cardiol 2013;61:1688-1695. DOI: 10.1016/j.jacc.2012.11.073.

8. Miedema MD, Newell MC, Duval S, et al. Causes of delay and associated mortality in patients transferred with ST-segment-elevation myocardial infarction. Circulation 2011;124:1636-1644. DOI: 10.1161/CIRCULATIONAHA.111.033118.

9. Kawamoto K, Houlihan CA, Balas EA, Lobach DF. Improving clinical practice using clinical decision support systems: a systematic review of trials to identify features critical to success. BMJ 2005;330:765. DOI: 10.1136/bmj.38398.500764.8F.

10. Liu WC, Lin CS, Tsai CS, et al. A deep learning algorithm for detecting acute myocardial infarction. EuroIntervention 2021;17:765-773. DOI: 10.4244/EIJ-D-20-01155.

11. Cvach M, Rothwell KJ, Cullen AM, Nayden MG, Cvach N, Pham JC. Effect of altering alarm settings: a randomized controlled study. Biomed Instrum Technol 2015;49:214-222. DOI: 10.2345/0899-8205-49.3.214.

12. Firoozabadi R, Gregg RE, Babaeizadeh S. Intelligent use of advanced capabilities of diagnostic ECG algorithms in a monitoring environment. J Electrocardiol 2017;50:615-619. DOI: 10.1016/j.jelectrocard.2017.04.013.

13. Siontis KC, Noseworthy PA, Attia ZI, Friedman PA. Artificial intelligence-enhanced electrocardiography in cardiovascular disease management. Nat Rev Cardiol 2021;18:465-478. DOI: 10.1038/s41569-020-00503-2.

14. 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;29:1804-1813. DOI: 10.1038/s41591-023-02396-3.

15. Yao X, Rushlow DR, Inselman JW, et al. Artificial intelligence-enabled electrocardiograms for identification of patients with low ejection fraction: a pragmatic, randomized clinical trial. Nat Med 2021;27:815-819. DOI: 10.1038/s41591-021-01335-4.

16. Lin CS, Liu WT, Tsai DJ, et al. AI-enabled electrocardiography alert intervention and all-cause mortality: a pragmatic randomized clinical trial. Nat Med 2024;30:1461-1470. DOI: 10.1038/s41591-024-02961-4.

17. Zhao Y, Xiong J, Hou Y, et al. Early detection of ST-segment elevated myocardial infarction by artificial intelligence with 12-lead electrocardiogram. Int J Cardiol 2020;317:223-230. DOI: 10.1016/j.ijcard.2020.04.089.

18. Chang K-C, Hsieh P-H, Wu M-Y, et al. Usefulness of multi-labelling artificial intelligence in detecting rhythm disorders and acute ST-elevation myocardial infarction on 12-lead electrocardiogram. Eur Heart J Digit Health 2021;2:299-310. DOI: 10.1093/ehjdh/ztab029.

19. Wang YC, Chen KW, Tsai BY, et al. Implementation of an all-day artificial intelligence-based triage system to accelerate door-to-balloon times. Mayo Clin Proc 2022;97:2291-2303. DOI: 10.1016/j.mayocp.2022.05.014.

20. Liu WC, Lin C, Lin CS, et al. An artificial intelligence-based alarm strategy facilitates management of acute myocardial infarction. J Pers Med 2021;11:1149. DOI: 10.3390/jpm11111149.

21. Menees DS, Peterson ED, Wang Y, et al. Door-to-balloon time and mortality among patients undergoing primary PCI. N Engl J Med 2013;369:901-909. DOI: 10.1056/NEJMoa1208200.

22. Lassen JF, Bøtker HE, Terkelsen CJ. Timely and optimal treatment of patients with STEMI. Nat Rev Cardiol 2013;10:41-48. DOI: 10.1038/nrcardio.2012.156.

23. Kaul P, Federspiel JJ, Dai X, et al. Association of inpatient vs outpatient onset of ST-elevation myocardial infarction with treatment and clinical outcomes. JAMA 2014;312:1999-2007. DOI: 10.1001/jama.2014.15236.

24. Garberich RF, Traverse JH, Claussen MT, et al. ST-elevation myocardial infarction diagnosed after hospital admission. Circulation 2014;129:1225-1232. DOI: 10.1161/CIRCULATIONAHA.113.005568.

25. Dai X, Bumgarner J, Spangler A, Meredith D, Smith SC, Stouffer GA. Acute ST-elevation myocardial infarction in patients hospitalized for noncardiac conditions. J Am Heart Assoc 2013;2:e000004. DOI: 10.1161/JAHA.113.000004.

26. Plana D, Shung DL, Grimshaw AA, Saraf A, Sung JJY, Kann BH. Randomized clinical trials of machine learning interventions in health care: a systematic review. JAMA Netw Open 2022;5:e2233946. DOI: 10.1001/jamanetworkopen.2022.33946.

27. Horwitz LI, Kuznetsova M, Jones SA. Creating a learning health system through rapid-cycle, randomized testing. N Engl J Med 2019;381:1175-1179. DOI: 10.1056/NEJMsb1900856.

28. Liu X, Cruz Rivera S, Moher D, Calvert MJ, Denniston AK. Reporting guidelines for clinical trial reports for interventions involving artificial intelligence: the CONSORT-AI extension. Nat Med 2020;26:1364-1374. DOI: 10.1038/s41591-020-1034-x.

29. Altman DG, Bland JM. Statistics notes. Treatment allocation in controlled trials: why randomise? BMJ 1999;318:1209. DOI: 10.1136/bmj.318.7192.1209.

30. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction (2018) [published correction appears in Circulation 2018;138:e652]. Circulation 2018;138:e618-e651. DOI: 10.1161/CIR.0000000000000617.

31. Byrne RA, Rossello X, Coughlan JJ, et al. 2023 ESC guidelines for the management of acute coronary syndromes. Eur Heart J 2023;44:3720-3826. DOI: 10.1093/eurheartj/ehad191.

32. McCabe JM, Kennedy KF, Eisenhauer AC, et al. Reporting trends and outcomes in ST-segment-elevation myocardial infarction national hospital quality assessment programs. Circulation 2014;129:194-202. DOI: 10.1161/CIRCULATIONAHA.113.006165.

33. Hart A. Mann–Whitney test is not just a test of medians: differences in spread can be important. BMJ 2001;323:391-393. DOI: 10.1136/bmj.323.7309.391.

34. Moscucci M, Eagle KA. Door-to-balloon time in primary percutaneous coronary intervention: is the 90-minute gold standard an unreachable chimera? Circulation 2006;113:1048-1050. DOI: 10.1161/CIRCULATIONAHA.105.606905.

35. Krumholz HM, Bradley EH, Nallamothu BK, et al. A campaign to improve the timeliness of primary percutaneous coronary intervention: door-to-balloon: an alliance for quality. JACC Cardiovasc Interv 2008;1:97-104. DOI: 10.1016/j.jcin.2007.10.006.

36. McCabe JM, Armstrong EJ, Hoffmayer KS, et al. Impact of door-to-activation time on door-to-balloon time in primary percutaneous coronary intervention for ST-segment elevation myocardial infarctions: a report from the Activate-SF registry. Circ Cardiovasc Qual Outcomes 2012;5:672-679. DOI: 10.1161/CIRCOUTCOMES.112.966382.

37. Savage ML, Hay K, Vollbon W, et al. Prehospital activation of the cardiac catheterization laboratory in ST-segment-elevation myocardial infarction for primary percutaneous coronary intervention. J Am Heart Assoc 2023;12:e029346. DOI: 10.1161/JAHA.122.029346.