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Clinical paper

Diagnostic test accuracy of life-threatening electrocardiographic findings (ST-elevation myocardial infarction equivalents) for acute coronary syndrome after out-of-hospital cardiac arrest without ST-segment elevation

Satoshi Yoshimura[a], *Takeyuki Kiguchi*[b], *Taro Irisawa*[c], *Tomoki Yamada*[d], *Kazuhisa Yoshiya*[e], *Changhwi Park*[f], *Tetsuro Nishimura*[g], *Takuya Ishibe*[h], *Hitoshi Kobata*[i], *Masafumi Kishimoto*[j], *Sung-Ho Kim*[k], *Yusuke Ito*[l], *Taku Sogabe*[m], *Takaya Morooka*[n], *Haruko Sakamoto*[o], *Keitaro Suzuki*[p], *Atsunori Onoe*[q], *Tasuku Matsuyama*[r], *Satoshi Matsui*[s], *Norihiro Nishioka*[a], *Yohei Okada*[a,t], *Yuto Makino*[a], *Shunsuke Kimata*[a], *Shunsuke Kawai*[a], *Ling Zha*[s], *Kosuke Kiyohara*[u], *Tetsuhisa Kitamura*[s], *Taku Iwami*[a,*]

Abstract

Aim: Life-threatening electrocardiographic (ECG) findings aid in the diagnosis of acute coronary syndrome (ACS), which has not been well-evaluated in patients with out-of-hospital cardiac arrest (OHCA). This study aimed to evaluate the diagnostic test accuracy (DTA) of ST-elevation myocardial infarction (STEMI) equivalents following the return of spontaneous circulation (ROSC) in patients with OHCA to identify patients with ACS.

Methods: Using the database of the Comprehensive Registry of In-Hospital Intensive Care for OHCA Survival study from 2012 to 2017, patients aged ≥18 years with non-traumatic OHCA and ventricular fibrillation or pulseless ventricular tachycardia on the arrival of emergency medical service personnel or arrival at the emergency department, who achieved ROSC, were included. Patients without ST-segment elevation or complete left bundle branch block on ECG and those who did not undergo ECG or coronary angiography, were excluded from the study. We evaluated the DTA of STEMI equivalents for the diagnosis of ACS: isolated T-wave inversion, ST-segment depression, Wellens' signs, and ST-segment elevation in lead aVR.

Results: Isolated T-wave inversion and Wellens' signs had high specificity for ACS with 0.95 (95% confidence interval [CI], 0.87–0.99) and 0.92 (95% CI, 0.82–0.97), respectively, but their positive likelihood ratios were low, with a wide range of 95% CI: 1.89 (95% CI, 0.51–7.02) and 0.81 (95% CI, 0.25–2.68), respectively.

Conclusion: The DTA of STEMI equivalents for the diagnosis of ACS was low among patients with OHCA. Further investigation considering the measurement timing of the ECG after ROSC is required.

Keywords: STEMI equivalent, Electrocardiogram, Out-of-hospital cardiac arrest, Acute coronary syndrome

* Corresponding author at: Department of Preventive Services, School of Public Health, Kyoto University, Yoshida-Konoe-Cho, Sakyo 606-8501, Kyoto, Japan.

E-mail address: iwami.taku.8w@kyoto-u.ac.jp (T. Iwami).

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Introduction

Approximately 30% of out-of-hospital cardiac arrests (OHCAs) are related to coronary artery disease, including acute coronary syndrome (ACS), which is the most common cause of OHCA.[1] In patients with ACS, early reperfusion therapy effectively improves outcomes after cardiac arrest.[2,3] Patients with ST-segment elevation myocardial infarction (STEMI), identified by 12-lead monitoring, are recommended to undergo coronary angiography (CAG) for possible percutaneous coronary intervention.[2,3] However, several studies have reported that the absence of ST-segment elevation cannot rule out an intervenable coronary lesion.[4,5] International guidelines recommend against routine CAG in patients with OHCA after return of spontaneous circulation (ROSC) without ST-segment elevation and recommend individualised decisions with respect to urgent CAG and percutaneous coronary angioplasty when ACS is suspected.[2,3]

In non-STEMI, electrocardiographic (ECG) findings suggestive of ACS have been reported, including left main coronary artery, proximal left anterior descending coronary artery, and severe three-vessel disease.[6,7]

International guidelines also proposed that STEMI equivalents, such as De Winter ST-T, hyper-acute T-wave, isolated T-wave inversion, ST-segment depression, resting U-wave inversion, low QRS voltage, Wellens' signs, and ST-segment elevation in lead aVR, are risk factors for acute coronary ischaemia or occlusion requiring immediate cardiac catheterisation.[6–9] However, after ROSC, ECG changes may be secondary to cardiac arrest or drugs used during cardiopulmonary resuscitation rather than ischaemic changes due to coronary events.[10] Therefore, it is unknown whether the findings of STEMI equivalents are effective in screening for ACS in patients with OHCA without ST-segment elevation.

To develop treatments and improve outcomes in patients with OHCA, we conducted the CRITICAL study, a multicentre, prospective observational data registry in Osaka, Japan, designed to accumulate both pre- and in-hospital data on OHCA treatments among patients.[11] Using this database, the present study aimed to investigate the diagnostic accuracy of STEMI equivalents following ROSC in patients with OHCA to diagnose ACS and coronary artery stenosis.

Methods

Study design and setting

In this study, we analysed the CRITICAL study database. A complete description of the study methodology has been described previously.[11] This report followed the Standards for Reporting of Diagnostic Accuracy statement.[12]

Population and settings

The target area of the CRITICAL study was Osaka Prefecture in Japan, which has an area of 1,897 km^2 and a residential population of 8,839,469 as of 2015; 48.1% of the population are male, 25.8% of whom are aged ≥65 years.[13] In 2013, Osaka had 535 hospitals (108,569 beds).[11] A total of 280 hospitals accepted emergency patients from ambulances. Of these, 16 hospitals had critical care medical centres (CCMCs) that could accept severely ill emergency patients.[11] Fifteen CCMCs and one non-CCMC with an emergency care department in Osaka participated in this study. In Osaka Prefecture, approximately 7,500 OHCA cases occur annually,[14] and approximately 30% of patients with OHCA are transported to and treated at CCMCs.[11] In this study, nine emergency medical centres in Osaka performed the first 12-lead ECG after ROSC. The CRITICAL study, including this retrospective analysis, was approved by the ethics committee of the Kyoto University (R-1045). The requirement for informed consent was waived.

Study patients

We enrolled consecutive patients with OHCA (aged ≥18 years) for whom resuscitation was attempted and who were then transported to the participating institutions with ventricular fibrillation (VF) or pulseless ventricular tachycardia (pVT) at the scene or upon arrival at the hospital between 1 January 2012 and 31 December 2017. This study excluded patients with OHCA who did not receive cardiopulmonary resuscitation (CPR) from physicians after hospital arrival and those who refused participation in the study (refusal by the patient or the patient's family). Additionally, patients with OHCA of non-medical origin and those who did not have ROSC and did not undergo 12-lead ECG and CAG were excluded. Furthermore, we excluded patients whose ECGs were collected with VF or VT, electrical activity/asystole, ST elevation, or complete left bundle branch block (CLBBB). ROSC was defined as the presence of a palpable pulse for >30 s, regardless of the initiation of ECMO.

Data collection and quality control

Registry data collection and quality control details have been reported previously.[11] Prehospital data on patients with OHCA, obtained from the All-Japan Utstein Registry, were uniformly collected according to the Utstein-style international guidelines for reporting OHCAs. Each emergency medical service (EMS) personnel completed a data form in cooperation with the attending physician in charge of the patient. For in-hospital data collection and quality control, the CRITICAL registry collected substantial data on patients with OHCA after arrival at the hospital, as explained in a previous study.[11] For the current registry, anonymised data were entered into the web sheet by either the physician or medical staff in collaboration with the attending physician in charge of the patient. The pre- and in-hospital data were uploaded to the registry system, logically checked by the computer system, and confirmed by the working group, which consisted of experts in emergency medicine and clinical epidemiology.

ECG evaluation

ECGs obtained at the emergency department after ROSC were retrospectively and independently analysed by two cardiologists who were blinded to the patients' clinical data and outcomes. We evaluated the following ECG findings: STEMI equivalent (De Winter ST-T, hyper-acute T-wave, isolated T-wave inversion, ST-segment depression, resting U-wave inversion, low QRS voltage, Wellens' signs, and ST-segment elevation in lead aVR; Fig. 1),[6–9] heart rate, QRS complex axis, presence of normal p-wave, atrial fibrillation, CLBBB, complete right bundle branch block, VF, ventricular tachycardia, and complete atrioventricular block. All disagreements were resolved through a discussion between the two reviewers, if required. Details of the definitions of the ECG findings are available in Supplementary Table S1.

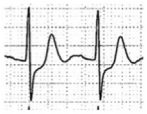
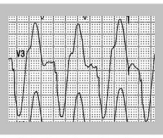
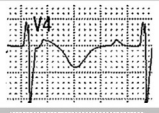
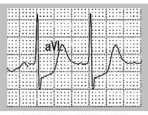
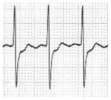
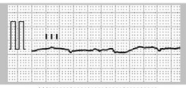
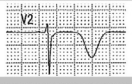
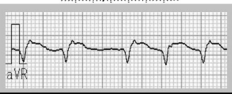
Life-Threatening ST-elevation myocardial infarction (STEMI) Equivalents (6, 8, 9)		
ECG pattern	Criteria	Figure
De Winter ST-T	J-point depression and upsloping ST depression In V1-V6 that continues into tall, positive symmetrical T-waves.	
Hyper Acute T-wave	Hyper acute T wave defined as higher than 1mV anterior T wave.	
Isolated T-wave inversion	T wave inversion >1mm in>=5 leads considering I, II, aVL and V2-6.	
ST-segment depression	J point depressed by >= 0.05mm in leads V2 and V3 or >=1mm in all other leads followed by a horizontal or down sloping ST-segment for >= 0.08s in >=1 leads(except aVR).	
Resting U wave inversion	Discrete negative deflection in the t-p segment (negative in comparison to the following P-R segment) in I, aVL and V4-V6.	
Low QRS voltage	Peak to peak QRS complex voltage <0.5mV in all limb leads and <1.0mV in all precordial leads.	
Wellens signs	Biphasic anterior T wave (Wallen's sign A) and deeply inverted anterior T waves (Wallen's sign B).	
ST-segment elevation in lead aVR	ST elevation in lead aVR (measured >=1.0 mm).	

Fig. 1 – Life threatening ST-elevation myocardial infarction (STEMI) equivalents. ECG, electrocardiogram.

Primary and secondary outcomes

The primary outcome was the diagnosis of ACS, and the secondary outcome was the presence of significant stenosis (defined as >75% stenosis of the coronary arteries on CAG). The diagnosis of ACS and the finding of coronary artery stenosis were made by the cardiologists or emergency physicians at each institution based on the clinical course and CAG findings. The timing of CAG was determined by the physicians in charge of the patients according to the current resuscitation guidelines.

Statistical analysis

Data are presented as median and interquartile range for continuous variables and percentages for categorical variables. In this study, binomial data were compared using the chi-square test. The Kruskal–Wallis test was used to analyse continuous data. We calculated the sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio for the primary and secondary outcomes. A two-tailed P-value < 0.05 was considered statistically significant in all analyses. All statistical analyses were performed using STATA version 16.0 SE software (StataCorp LP, Texas, United States) and R studio (version 1.2.5033).

Results

The patient flowchart based on the Utstein format is shown in Fig. 2. From 8,091 patients with OHCA between 2012 and 2019, 2,491 cases of cardiac arrest of non-medical origin, 3,561 cases without an initial rhythm of VF or pVT, 285 cases without ROSC, and 175 cases in which a 12-lead ECG was not performed were excluded. Consequently, 368 patients were included in the ECG analysis. We evaluated the ECGs of these patients and excluded patients with VF (n = 28), VT (n = 5), pulseless electrical activity/asystole (n = 9), ST elevation, and CLBBB (n = 130). Of 196 patients with non-ST-elevation OHCA, 143 who underwent CAG were included in the analysis. Table 1 presents the baseline patient characteristics. Of 143 patients, 79 were diagnosed with ACS. The proportions of men were 74.7% and 87.5% in the ACS and non-ACS groups, respectively. The ECG results are presented in Table 2. There were no cases of hyper-acute T-waves in either the ACS or non-ACS group and only one case each of De Winter ST-T, resting U-wave inversion, and low QRS voltage. Isolated T-wave inversion was found in 7 (3.2%) patients in the ACS group and 3 (8.8%) patients in the non-ACS group, ST depression in 46 (58.2%) and 38 (59.4%) patients, Wellens' signs in 5 (6.3%) and 5 (7.8%) patients,

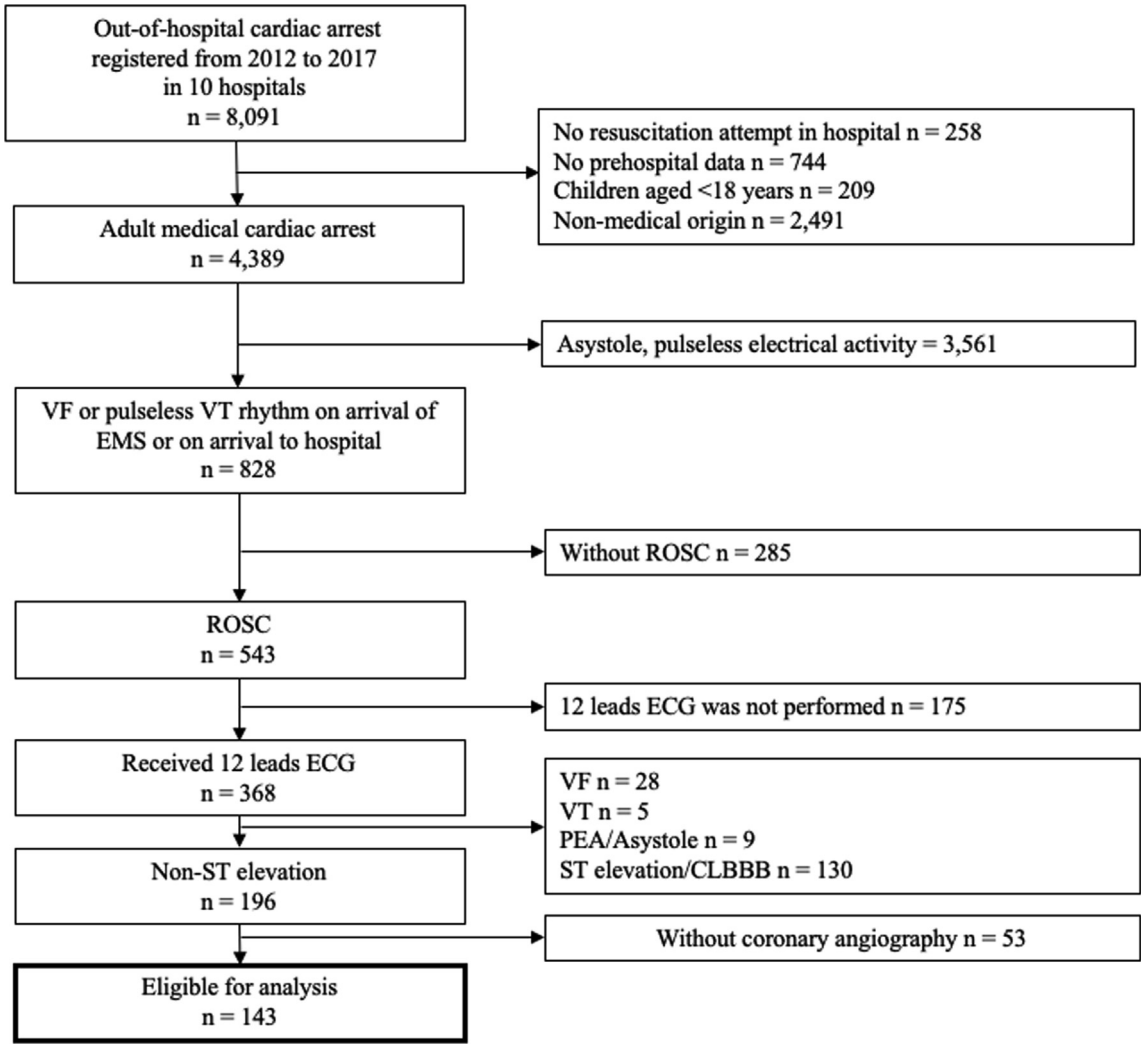


Fig. 2 – Patient flow. CLBBB, complete left bundle branch block; ECG, electrocardiogram; EMS, emergency medical services; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; VF, ventricular fibrillation; VT, ventricular tachycardia.

Table 1 – Baseline characteristics stratified by ACS.

Characteristics	Overall n = 143		ACS n = 79		Non-ACS n = 64		p
Age, year	62	(49.5, 72.5)	59	(42.50, 72.50)	65	(54.75, 72.25)	0.06
Men, n (%)	115	(80.4)	59	(74.7)	56	(87.5)	0.055
Witnessed by bystanders, n (%)	117	(81.8)	67	(84.8)	50	(78.1)	0.303
Bystander-initiated CPR, n (%)	84	(58.7)	47	(59.5)	37	(57.8)	0.839
Shock by public-access AEDs, n (%)	13	(9.1)	5	(6.3)	8	(12.5)	0.202
Defibrillation by EMS, n (%)	140	(97.9)	78	(98.7)	62	(96.9)	
Adrenaline administration, n (%)	59	(41.3)	32	(40.5)	27	(42.2)	0.839
EMS response time (call to contact with the patient by EMS), min	6.0	(5.00, 8.00)	6.0	(5.00, 8.00)	6.0	(4.75, 7.25)	0.328
Call to hospital, min	19.0	(9.00, 26.00)	20.0	(8.50, 28.50)	17.0	(9.75, 25.00)	0.311

Continuous variables are summarized as median and interquartile range, while categorical variables are summarized as frequencies and percentages. AED, automated external defibrillator; ACS, acute coronary syndrome; CPR, cardiopulmonary resuscitation; EMS, emergency medical service; IQR, interquartile range.

Table 2 – ECG findings stratified by ACS.

ECG findings	Overall n = 143		ACS n = 79		Non-ACS n = 64		p
Heart rate, beats per minute	42	(15.00, 61.50)	46	(19.50, 61.00)	31.5	(11.00, 63.00)	0.324
STEMI equivalent (any), n %	103	(72.0)	48	(75.0)	55	(69.6)	0.476
De Winter ST-T	1	(0.7)	0	(0.0)	1	(1.6)	0.265
Hyper-acute T-wave	0	(0.0)	0	(0.0)	0	(0.0)	NA
Isolated T-wave inversion	10	(7.0)	7	(8.9)	3	(4.7)	0.331
ST-segment depression	84	(58.7)	46	(58.2)	38	(59.4)	0.890
Resting U wave inversion	1	(0.7)	1	(1.3)	0	(0.0)	0.366
Low QRS voltage	3	(2.1)	2	(2.5)	1	(1.6)	0.688
Wellen's syndrome	10	(7.0)	5	(6.3)	5	(7.8)	0.729
ST-segment elevation in lead aVR	60	(42.0)	33	(41.8)	27	(42.2)	0.960
Axis deviation, n %							
Normal axis deviation	77	(53.8)	41	(51.9)	36	(56.2)	0.081
Right axis deviation	16	(11.2)	5	(6.3)	11	(17.2)	
Left axis deviation	17	(11.9)	10	(12.7)	7	(10.9)	
Indeterminate axis	33	(23.1)	23	(29.1)	10	(15.6)	
Atrial fibrillation, n %	32	(22.4)	19	(24.1)	13	(20.3)	0.594
Normal P wave, n %	69	(48.3)	35	(44.3)	34	(53.1)	0.294
Right bundle branch block, n %	35	(24.5)	21	(26.6)	14	(21.9)	0.515
Left ventricular hypertrophy, n %	1	(0.7)	0	(0.0)	1	(1.6)	0.265
Complete atrioventricular block, n %	2	(1.4)	2	(2.5)	0	(0.0)	0.200

Continuous variables are summarized as median and interquartile range, while categorical variables are summarized as frequencies and percentages. ACS, acute coronary syndrome; ECG, electrocardiogram; NA, not applicable; STEMI, ST-segment elevation myocardial infarction.

and ST-segment elevation in lead aVR in 33 (41.8%) and 27 (42.2%) patients, respectively.

Isolated T-wave inversion was found in 2 (2.7%) patients in the stenosis group and 8 (11.4%) patients in the non-stenosis group, ST depression in 43 (58.9%) and 41 (58.6%) patients, Wellens' signs in 5 (6.8%) and 5 (7.1%) patients, and ST-segment elevation in lead aVR in 29 (39.7%) and 31 (44.3%) patients, respectively.

The diagnostic performance of STEMI equivalent for ACS is presented in Table 3. As there were few cases of hyper-acute T-wave, De Winter ST-T, or resting U-wave inversion, their diagnostic performance was not evaluated. The diagnostic accuracies of isolated T-wave inversion, ST-segment depression, low QRS voltage, Wellens' signs, and ST-segment elevation in lead aVR for the diagnosis of ACS are presented in Table 3. The isolated T-wave, low QRS voltage, and Wellens' signs had high specificity with 0.95 (95% confidence interval [CI], 0.87–0.99), 0.98 (95% CI, 0.92–1.00), and 0.92 (95% CI, 0.82–0.97), respectively, but their positive likelihood ratios (LR +) were low, with a wide range of 95% CI: 1.89 (95% CI, 0.51–7.02), 1.62 (95% CI, 0.15–17.48), and 0.81 (95% CI, 0.25–2.68), respectively. In the diagnosis of stenosis, the isolated T-wave inversion, low QRS voltage, and Wellens' signs had high specificity with 0.88 (95% CI, 0.77–0.94), 0.97 (95% CI, 0.89–1.00), and 0.92 (95% CI, 0.83–0.97); however, their LR + were low with a wide range of 95% CI: 0.20 (0.05–0.92), 0.41 (0.04–4.37), and 0.81 (0.25–2.68), respectively.

Discussion

Summary

This study aimed to investigate whether STEMI equivalents on ECG obtained after ROSC in patients with OHCA can be used to identify patients with ACS with non-ST-segment elevations using a large, multicentre, prospective OHCA registry in Osaka, Japan. The results showed that STEMI equivalents did not have useful diagnostic performance for the diagnosis of ACS in patients with OHCA without ST-segment elevation.

Comparison with previous studies

To the best of our knowledge, this is the first study to investigate the diagnostic performance of STEMI equivalents in patients with OHCA without ST-segment elevation. In a previous study, among patients with OHCA without ST-segment elevation, ST-segment elevation in aVR after ROSC was demonstrated to be useful in differentiating ACS with a positive predictive value of 55% and negative predictive value of 82%, with an odds ratio of 4.41 (95% CI, 1.12–17.4).[7] However, in our study, ST-segment elevation in aVR was not useful in differentiating ACS, with a positive predictive rate of 55% and negative predictive rate of 45%. Although isolated T-wave inversion, low QRS voltage, and Wellens' signs are also suggested to be associated with the presence of ischaemic heart disease, none of these findings had high specificity, sensitivity, positive predictive value, or positive likelihood ratio and were not helpful in the diagnosis in our study.[15–17]

Possible explanation and implications

The timing of ECG measurements may be a reason for the poor diagnostic performance of STEMI equivalents in patients with OHCA without ST-segment elevation in the current study. In a previous study, the diagnostic accuracy of two different timings of ECGs were evaluated as follows: one was 'initial ECG' defined as ECG within 10 min after admission or within 10 min after ROSC and the other was 'early ECG' (median, 137 min after ROSC). In this study, ST-segment elevation in the aVR lead was observed in 36.5% of the initial ECG and 24.3% of the early ECG; ST-segment elevation in aVR at the initial ECG improved over time in some patients, and the early ECG had good diagnostic accuracy for ACS.[7]

Table 3 – Diagnostic accuracy of STEMI equivalents for ACS.

	sensitivity	95%CI	specificity	95%CI	PPV	95%CI	NPV	95%CI	LR+	95%CI	LR-	95%CI
STEMI equivalent (any)	0.61	0.49–0.72	0.14	0.07–0.25	0.71	0.58–0.87	0.23	0.11–0.39	0.71	0.58–0.87	2.80	1.44–5.43
De Winter ST-T	NA		NA		NA		NA		NA		NA	
Hyper-acute T-wave	NA		NA		NA		NA		NA		NA	
Isolated T-wave inversion	0.09	0.04–0.17	0.95	0.87–0.99	0.70	0.35–0.93	0.46	0.37–0.54	1.89	0.51–7.02	0.96	0.88–1.04
ST-segment depression	0.58	0.47–0.64	0.41	0.29–0.54	0.55	0.44–0.66	0.44	0.31–0.58	0.98	0.74–1.29	1.03	0.69–1.53
Resting U wave inversion	NA		NA		NA		NA		NA		NA	
Low QRS voltage	0.03	0.00–0.09	0.98	0.92–1.00	0.67	0.09–0.99	0.45	0.37–0.54	1.62	0.15–17.48	0.99	0.95–1.04
Wellens syndrome	0.06	0.02–0.14	0.92	0.82–0.97	0.50	0.19–0.81	0.44	0.36–0.53	0.81	0.25–2.68	1.02	0.93–1.11
ST-segment elevation in lead aVR	0.42	0.31–0.53	0.58	0.45–0.70	0.55	0.42–0.68	0.45	0.34–0.56	0.99	0.67–1.46	1.01	0.76–1.33

ACS, acute coronary syndrome; CI, confidence interval; LR+, positive likelihood ratio; LR-, negative likelihood ratio; NA, not applicable; NPV, negative predictive value; PPV, positive predictive value; STEMI, ST-segment elevation myocardial infarction.

Electrophysiologically, ST-segment elevation in aVR suggests subendocardial ischaemia of the entire left ventricle or transmural infarction of the left ventricular base[18,19] and may be influenced not only by coronary artery stenosis or thrombotic occlusion but also by low coronary artery flow due to cardiac arrest. The STEMI equivalents immediately after ROSC may reflect not only ACS but also low flow in the coronary artery due to cardiac arrest itself. Additionally, cardiac contusions due to chest compression, duration or quality of CPR, epinephrine administration, and hypothermia could lead to ECG changes, and the effect of these factors will change temporally. Therefore, continuous ECG measurement, other than immediately after ROSC, may lead to improved diagnostic accuracy of ECG in patients with OHCA. In modern society, artificial-intelligence-based technologies have been evaluated to identify myocardial infarction. These methods, not only with STEMI-equivalent but also any other finding in ECG, such as QRS width, R wave height, ST interval, and PR intervals, may provide some diagnostic clues for suspecting ACS in future studies.

Based on the results of this study, it is necessary to include several ECGs with different measurement timings and temporal changes as well as information on the nature and location of coronary artery lesions.

Limitations

The most important limitation of the present study is that the diagnosis of ACS as a primary outcome is based on the clinical judgement of the physician in the field rather than a clear definition of acute myocardial infarction, such as a universal definition.[20] Coronary artery lesions in ACS that can lead to cardiac arrest are mainly thrombotic occlusions caused by disruption of coronary artery plaques. As mentioned in the discussion, the timing of the ECG was unclear in this study, which is also a key limitation because the duration from ROSC to ECG would affect the ECG accuracy.

Furthermore, in previous studies, clinically relevant outcomes, such as thrombus occlusion, and the location of coronary lesions, such as the left main coronary artery or proximal left anterior descending branch, were measured. [21,22] In contrast, the current study did not measure these outcomes.

Other limitations of this study include the exclusion of cases in which CAG was not performed, ECG was not performed after ROSC, coronary artery spasm was not evaluated, and cases transported to medical institutions other than emergency centres were not evaluated. Furthermore, CLBBB was not included in the analysis because new CLBBB cases were classified as the ST-segment elevation type according to the definition,[20] which was not the focus of our study. Moreover, we did not separate or exclude patients who underwent extracorporeal membrane oxygenation. This is because we believe that, if there is acute thrombotic occlusion, the ECG will reflect the results of severe ischaemia even if the patient is treated with extracorporeal membrane oxygenation. Finally, this study was based on a registry in a limited urban area in Japan; thus, the results may vary in different populations.

Conclusions

We found that the diagnostic accuracy of STEMI equivalents of a single 12-lead ECG alone after ROSC in patients with OHCA without ST-segment elevation to diagnose ACS was insufficient. Further investigation on the diagnostic test accuracy evaluation considering

the measurement timing and temporal changes of the ECG after ROSC is required to determine whether urgent catheterisation is needed.

Ethical approval

This study was conducted in accordance with the principles of the Declaration of Helsinki. The Ethics Committee of Kyoto University and each participating institution approved the study protocol and retrospective analysis, and the need for written informed consent was waived (approval ID: R1045).

Availability of data and materials

The datasets and/or analyses in this study are not publicly available because of the lack of permission from the ethics committee.

CRediT authorship contribution statement

Satoshi Yoshimura: Conceptualization, Methodology, Software, Resources, Formal analysis, Data curation, Writing – original draft, Writing – review & editing, Visualization. **Takeyuki Kiguchi:** Conceptualization, Methodology, Writing – review & editing. **Taro Irisawa:** Investigation, Resources, Project administration. **Tomoki Yamada:** Investigation, Resources. **Kazuhisa Yoshiya:** Investigation, Resources. **Changhwi Park:** Investigation, Resources. **Tetsuro Nishimura:** Investigation, Resources. **Takuya Ishibe:** Investigation, Resources. **Hitoshi Kobata:** Investigation, Resources. **Masafumi Kishimoto:** Investigation, Resources. **Sung-Ho Kim:** Investigation, Resources. **Yusuke Ito:** Investigation, Resources. **Taku Sogabe:** Investigation, Resources. **Takaya Morooka:** Investigation, Resources. **Haruko Sakamoto:** Investigation, Resources. **Keitaro Suzuki:** Investigation, Resources. **Atsunori Onoe:** Investigation, Resources. **Tasuku Matsuyama:** Investigation, Resources. **Satoshi Matsui:** Investigation, Resources. **Norihiro Nishioka:** Investigation, Resources. **Yohei Okada:** Investigation, Resources. **Yuto Makino:** Investigation, Resources. **Shunsuke Kimata:** Investigation, Resources. **Shunsuke Kawai:** Investigation, Resources. **Ling Zha:** Investigation, Resources. **Kosuke Kiyohara:** Investigation, Resources. **Tetsuhisa Kitamura:** Validation, Data curation, Writing – review & editing, Funding acquisition. **Taku Iwami:** Conceptualization, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Conflicts of interest

None.

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Appendix A. Supplementary material

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Author details

[a]*Department of Preventive Services, Kyoto University School of Public Health, Kyoto, Japan* [b]*Critical Care and Trauma Centre, Osaka General Medical Centre, Osaka, Japan* [c]*Department of Traumatology and Acute Critical Medicine, Osaka University Graduate School of Medicine, Suita, Japan* [d]*Emergency and Critical Care Medical Centre, Osaka Police Hospital, Osaka, Japan* [e]*Department of Emergency and Critical Care Medicine, Kansai Medical University, Takii Hospital, Moriguchi, Japan*[f]*Department of Emergency Medicine, Tane General Hospital, Osaka, Japan* [g]*Department of Critical Care Medicine, Osaka City University, Osaka, Japan* [h]*Department of Emergency and Critical Care Medicine, Kindai University School of Medicine, Osaka-Sayama, Japan* [i]*Osaka Mishima Emergency Critical Care Centre, Takatsuki, Japan*[j]*Osaka Prefectural Nakakawachi Medical Centre of Acute Medicine, Higashi-Osaka, Japan*[k]*Senshu Trauma and Critical Care Centre, Osaka, Japan* [l]*Senri Critical Care Medical Centre, Saiseikai Senri Hospital, Suita, Japan* [m]*Traumatology and Critical Care Medical Centre, National Hospital Organization Osaka National Hospital, Osaka, Japan* [n]*Emergency and Critical Care Medical Centre, Osaka City General Hospital, Osaka, Japan*[o]*Department of Pediatrics, Osaka Red Cross Hospital, Osaka, Japan* [p]*Emergency and Critical Care Medical Centre, Kishiwada Tokushukai Hospital, Osaka, Japan* [q]*Department of Emergency and Critical Care Medicine, Kansai Medical University, Hirakata, Osaka, Japan*[r]*Department of Emergency Medicine, Kyoto Prefectural University of Medicine, Kyoto, Japan* [s]*Division of Environmental Medicine and Population Sciences, Department of Social and Environmental Medicine, Graduate School of Medicine, Osaka University, Osaka, Japan*[t]*Health Services and Systems Research, Duke-NUS Medical School, Singapore*[u]*Department of Food Science, Otsuma Women's University, Tokyo, Japan*

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