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Clinical paper

Associations with resolution of ST-segment elevation myocardial infarction criteria on out-of-hospital 12-lead electrocardiograms following resuscitation from cardiac arrest

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Abstract

Introduction: A previous study found that following out-of-hospital cardiac arrest (OHCA), 67% of out-of-hospital 12-lead electrocardiograms (ECGs) diagnostic for ST-segment elevation myocardial infarction (STEMI) changed to non-STEMI on repeat emergency department (ED) ECG. Here we evaluated associations with resolution of STEMI on ED ECG.

Methods: In this secondary analysis of a previous retrospective study, adults (≥18 years) with return of spontaneous circulation (ROSC) following OHCA, at least 1 out-of-hospital and ED ECG and transport to the study hospital were entered. We analyzed variables suspected of influencing ischemic changes on ECG including arrest characteristics, treatment interventions, resuscitation duration, and out-of-hospital and ED ECG acquisition times.

Results: Forty-nine of 176 patients entered had out-of-hospital ECGs diagnostic for STEMI, and 33/49 (67%) had resolved STEMI upon ED evaluation. Shorter resuscitation time (13 [interquartile range 5–18] vs 21 [14–28] minutes), $p = 0.007$), less epinephrine (3 [1–4] vs 5 [2–10] milligrams, $p = 0.018$), lower incidence of norepinephrine (5/33 (15%) vs 11/16 (69%), $p \leq 0.001$), less time from ROSC to out-of-hospital ECG acquisition (5.5 [1–8] vs 8.5 [7–14] minutes, $p = 0.044$), and more time between out-of-hospital and ED ECG acquisition (34 [25–52] vs 21 [14–27] minutes, $p = 0.001$) were associated with resolution of out-of-hospital STEMI on ED evaluation. More defibrillations were associated with increased ischemia on ED ECG for patients with non-STEMI out-of-hospital ECGs.

Conclusion: ROSC patients with STEMI on out-of-hospital ECG commonly resolve in the ED (67%). These identified associations may better inform clinical decision making. Post-ROSC out-of-hospital 12-lead ECGs should be repeated on arrival in the ED.

Keywords: Cardiac arrest, 12-lead electrocardiogram, Out-of-hospital, Acute myocardial infarction, Resuscitation

Introduction

The American and European resuscitation guidelines recommend acquiring an out-of-hospital (OOH) 12-lead electrocardiogram (ECG) in patients resuscitated from cardiac arrest, in part, to inform decision making for emergency medical services (EMS), including mobilization of the receiving hospital's cardiac catheterization laboratory for ST-segment elevation myocardial infarction (STEMI).[1–3] However, established ST-segment elevation criteria on OOH 12-lead ECG have been shown to have poor predictive value for acute coronary occlusion in patients resuscitated from cardiac arrest.[4–6] Further, a recent study demonstrated that 67% of adult patients resuscitated from cardiac arrest with STEMI on OOH 12-lead ECG had non-STEMI on emergency department 12-lead ECG.[7] Factors associated with resolution of OOH STEMI following emergency department evaluation are poorly characterized.

The purpose of this study, then, was to identify treatments, cardiac arrest characteristics, and time factors associated with this high rate of emergency department resolution of OOH 12-lead ECG STEMI classification in adult patients resuscitated from cardiac arrest. Associations with change in OOH ischemic and non-ischemic classified ECGs were also analyzed.

Methods

The methods for the original, retrospective case series have been previously published.[7] Briefly, entry criteria were: (1) adults (≥18 years of age), (2) successfully resuscitated from out-of-hospital cardiac arrest of presumed cardiac origin in the Milwaukee County Emergency Medical Services (EMS) system, (3) had at least 1 out-of-hospital 12-lead ECG and 1 emergency department 12-lead ECG acquired, and (4) were transported to the study hospital in Milwaukee, Wisconsin. This study was approved by the Institutional Review Board of the Medical College of Wisconsin (Number: PRO00037647).

Two emergency medicine physicians and one cardiologist independently classified all OOH and emergency department (ED) ECGs based on the American College of Cardiology/American Heart Association's 2018 Expert Consensus criteria and blinded to all patient information except age and sex.[8] After independent classification, they met and generated a single, final consensus opinion classification for each ECG (at least 2 of 3 opinions were required for consensus). OOH and ED ECGs received a final consensus opinion classification as: (1) STEMI, (2) ischemic, or (3) non-ischemic. The previous inter-rater reliability kappa statistic for classification of the ECGs was 0.63 ± 0.02 indicating substantial classification agreement.[9]

If there were multiple OOH and/or ED ECGs for an individual patient, the most ischemic OOH ECG (considered most likely to influence EMS decision-making) was compared with the last ECG acquired in the ED (considered most likely to influence patient disposition).

Patient demographics, cardiac arrest characteristics, EMS dispatch times, and OOH treatment interventions were obtained from Milwaukee County EMS patient care reports. Times of interventions were acquired preferentially from EMS Zoll X-series cardiac monitors or alternatively obtained from EMS provider documentation if Zoll files were unavailable. ED interventions were obtained from review of the hospital electronic health record.

Patient demographics (age, gender, and race), arrest witnessed status (with witnessed arrests including both EMS- and bystander-witnessed), bystander CPR provision (defined as CPR performed by anyone other than an emergency responder prior to EMS arrival), initial arrest rhythm, number of re-arrests, duration of resuscitation (time from EMS arrival to ROSC), time from ROSC to EMS ECG acquisition, time between OOH and ED 12-lead ECG acquisition, and treatment interventions including number and total of OOH and ED defibrillations, epinephrine, norepinephrine, and dopamine administration were assessed for association with resolved OOH STEMI 12-lead ECG classification. We primarily analyzed associations with resolved OOH STEMI ECG classification but also analyzed ischemic evolution of OOH ischemic and OOH non-ischemic classified ECGs.

Statistical analysis

Arrest characteristics, times, and treatments were analyzed for association with change in ECG classification between the OOH and ED settings with respect to OOH ECG classification. For OOH STEMI, stability was assessed by comparing patients with resolved OOH

STEMI versus those with sustained OOH STEMI on ED ECG. Univariable comparisons of subjects with resolved versus sustained OOH STEMI were conducted using Wilcoxon rank sum test for continuous measures and Pearson's chi-squared test for categorical variables. Fisher's exact test was used instead of the chi-square test when a cell with an expected count below 5 was present.

Odds Ratios (OR) with a 95% confidence interval were calculated for patients with both OOH ischemic and non-ischemic classifications using univariable logistic regression with Firth's penalty. The penalization allows for estimation of meaningful odds ratios and confidence intervals when one group has no events. For prehospital ischemic ECGs (ischemic or STEMI), ORs were calculated to assess associations with sustained ischemia or evolution to STEMI versus resolved ischemia. For prehospital non-ischemic ECGs, ORs were calculated to assess associations with sustained non-ischemia versus evolution to ischemia or STEMI. Previous inter-rater reliability for classification of the ECGs was assessed using Feiss' Kappa reported with a standard error.[9] Statistical analyses were performed with an alpha of 0.05.

Results

Demographics and characteristics

Between the period of July 27th, 2012 and July 18th, 2019, 176 patients met study eligibility criteria. Of these, 49/176 (27.8%) had STEMI, 61/176 (34.7%) had ischemia, and 66/176 (37.5%) non-ischemic classifications on OOH 12-lead ECG. Of the 49 patients with OOH STEMI, 33/49 (67.3%) had resolved STEMI on repeat ED ECG and 16/49 (32.7%) had sustained STEMI on repeat ED ECG (Fig. 1).

Table 1 shows OOH STEMI patient demographics, cardiac arrest characteristics, OHCA treatments, re-arrests, resuscitation duration, and ECG acquisition times. OOH STEMI patients were on average 62.0 ± 15.7 years old, and 35/49 (71%) were male. Based on hospital record-reported race, 38/49 (78%) patients were White, 7/49 (14%) Black, 2/49 (4%) Asian, and 2/49 (4%) were of unknown race. Three of forty-nine (6%) patients were Hispanic, 44/49 (90%) were non-Hispanic, and 2/49 (4%) were of unknown ethnicity.

Twenty-six of 49 (54%) patients presented with an initial rhythm of ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT), 9/49 (19%) with pulseless electrical activity (PEA), and 13/49 (27%) with asystole. Thirty-four of 49 (69%) cardiac arrests occurred in private residences while 15/49 (31%) occurred in a public setting. Twenty-nine of 49 (59%) arrests were witnessed by bystanders or EMS, while 20/49 (41%) were unwitnessed. Median EMS response time from 911 call to first EMS unit on-scene arrival was 4 min (interquartile range [IQR] 3–5). Overall, 17/49 (34.7%) of patients survived to hospital discharge.

The incidence of ED STEMI by OOH ischemic classification is shown in Fig. 2. Of the 49 patients with OOH STEMI, 16/49 (32.7%) had STEMI in the ED. Of the 61 patients with OOH ischemic ECGs, 3/61(4.9%) had ED STEMI. Of the 66 patients with OOH non-ischemic ECGs, 2/66 (3.0%) had ED STEMI. While 49/176 (27.8%) patients had OOH STEMI, only 21/176 (11.9%) patients had STEMI on ED ECG. However, OOH STEMI accounted for 16/21 (76.2%) of all ED STEMIs,

Associations with resolution of out-of-hospital STEMI

Patient demographics, cardiac arrest characteristics, and treatment interventions assessed for associations with resolved OOH STEMI classification are shown in Table 1. Age, gender, bystander CPR, arrest witnessed status, initial cardiac arrest rhythm, number of defibrillations, and administration of dopamine or epinephrine infusions following ROSC were not associated with change in STEMI classification between the OOH and ED settings. Lower OOH ($p = 0.025$), ED ($p = 0.007$), and total ($p = 0.018$) epinephrine dose were significantly associated with resolution of STEMI on ED ECG. Similarly, lower incidence of OOH ($p = 0.009$), ED ($p = 0.002$), and total ($p < 0.001$) norepinephrine drip administration were significantly associated with resolution of OOH STEMI classification. Shorter duration from OOH CPR to ROSC was significantly associated with resolution of OOH STEMI classification ($p = 0.007$). Shorter time from ROSC to OOH ECG acquisition ($p = 0.044$) and greater time

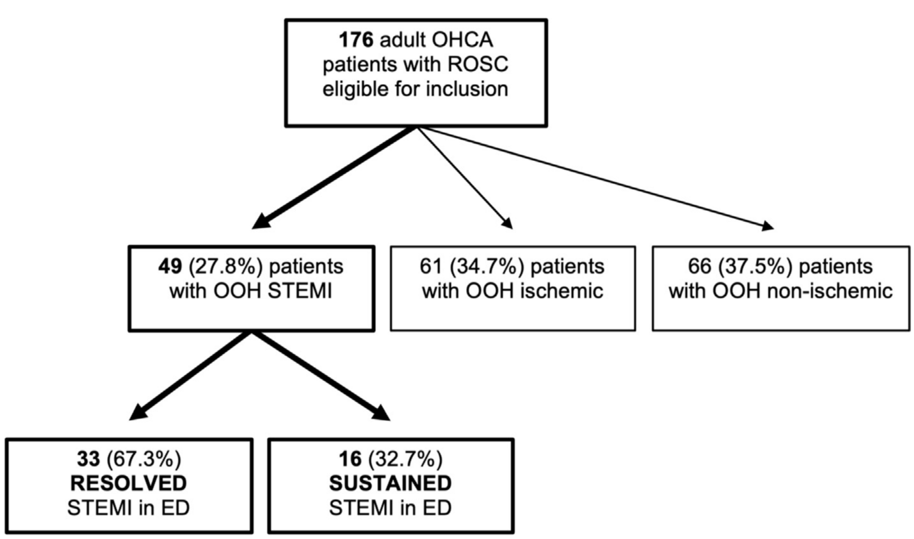

Fig. 1 – Study Consort Diagram. OHCA = out-of-hospital cardiac arrest; ROSC = return of spontaneous circulation; % = percent; OOH = out-of-hospital; STEMI = ST-elevation myocardial infarction; ED = emergency department.

Table 1 – Comparison of patient demographics, cardiac arrest characteristics, and treatment interventions for out-of-hospital STEMI patients with resolved versus sustained STEMI in the emergency department.

Characteristic	All OOH STEMI (N = 49)	**Resolved** STEMI (N = 33)	**Sustained** STEMI (N = 16)	p-value
Age [Median (IQR)]	62.0 (15.7)	57 (47–74)	62 (56, 72)	0.4
Male Sex	35 (71%)	22 (67%)	13 (81%)	0.3
Witnessed Arrest [N (%)][a]	29 (59%)	20 (61%)	9 (56%)	0.8
Bystander CPR [N (%)][b]	19 (39%)	13 (39%)	6 (38%)	0.9
Initial Rhythm [N (%)]				>0.9
VF/VT	26 (54%)	17 (53%)	9 (56%)	
PEA	9 (19%)	6 (19%)	3 (19%)	
Asystole	13 (27%)	9 (28%)	4 (25%)	
Unknown (Excluded)	1	1	0	
Out-of-hospital Defibrillations [Mean (SD)]	1.5 (1.9)	1.5 (2.0)	1.4 (1.8)	>0.9
ED Defibrillations [Mean (SD)]	0.1 (0.2)	0 (0.2)	0.1 (0.3)	0.2
Total Defibrillations [Mean (SD)]	1.6 (1.9)	1.6 (2.0)	1.6 (1.9)	>0.9
Out-of-hospital Epinephrine Dose (mg) [Mean (SD)]	3.0 (2.4)	2.4 (2.1)	4.1 (2.7)	0.025
ED Epinephrine Dose (mg) [Mean (SD)]	0.9 (2.0)	0.6 (1.7)	1.7 (2.5)	0.007
Total Epinephrine Dose (mg) [Mean (SD)]	3.9 (3.7)	3.0 (3.0)	5.8 (4.4)	0.018
Epinephrine Infusion	38 (78%)	7 (21%)	4 (25%)	>0.9
Out-of-hospital Norepinephrine Infusion [N (%)]	4 (8%)	0 (0%)	4 (25%)	0.009
Incidence of ED Norepinephrine Infusion [N (%)]	15 (31%)	5 (15%)	10 (62%)	0.002
Total Incidence of Norepinephrine Infusion [N (%)]	16 (33%)	5 (15%)	11 (69%)	<0.001
Dopamine Infusion [N (%)]	9 (18%)	5 (15%)	4 (25%)	0.4
Total Number of Re-arrests [Mean (SD)]	1.0 (1.4)	0.8 (1.3)	1.4 (1.4)	0.06
Time from ROSC to Out-of-hospital ECG Acquisition (min) [Mean (SD)], N = 44[c]	8.1 (9.1)	5.5 (4.1)	8.5 (4.4)	0.044
Time Between Out-of-hospital and ED ECG Acquisition (min) [Mean (SD)]	42.8 (45.7)	52.5 (52.5)	22.6 (12.1)	0.001
Duration of Out-of-hospital CPR to ROSC (min) [Mean (SD)], N = 48[d]	15.3 (8.9)	13 (8.3)	19.8 (8.3)	0.007

N = number; % = percent; SD = standard deviation; IQR = inter-quartile range; OOH = out-of-hospital; STEMI = ST-elevation myocardial infarction; CPR = cardiopulmonary resuscitation; VF = ventricular fibrillation; VT = ventricular tachycardia; PEA = pulseless electrical activity; mg = milligram; ED = emergency department; ROSC = return of spontaneous circulation; ECG = 12-lead electrocardiogram; min = minutes. IQR values generated using exclusive method.

[a] Includes bystander-witnessed and EMS-witnessed arrests.

[b] Bystander CPR defined as CPR performed by anyone other than an emergency responder prior to EMS arrival.

[c] Five patients were excluded from analysis due to their only out-of-hospital ECG being acquired prior to cardiac arrest.

[d] One patient was excluded from analysis due to achieving ROSC prior to EMS arrival.

between OOH and ED ECG (p = 0.001) were significantly associated with resolution of OOH STEMI classification. The total number of re-arrests was non-significantly less in patients with resolution of OOH STEMI classification (p = 0.06).

Additional associations by out-of-hospital ECG classification

A forest plot of odds ratios for associations of ischemic out-of-hospital 12-lead ECG change in classification during ED evaluation is shown in Fig. 3. Of 61 patients with out-of-hospital Ischemic ECGs, 3 (5%) evolved to STEMI on ED ECG, while 22 (36%) remained ischemic, and 36 (59%) had resolution of ischemia on ED ECG. Greater age was associated with sustained ischemia or evolution to STEMI on ED ECG (OR per 10 years of age = 1.39, 95% CI [1.03–1.93]). Greater ED (OR = 3.35, 95% CI [1.14–20.94]) and total defibrillations (OR = 1.52, 95% CI [1.05–2.45]) were also associated with sustained ischemia or evolution to STEMI on ED ECG.

A forest plot of odds ratios for associations of non-ischemic out-of-hospital 12-lead ECG change in classification during ED evaluation is shown in Fig. 4. Of 66 patients with OOH non-ischemic ECGs, 14/66 (21%) showed increased ischemia on ED ECG, with 2/66 (3%) evolved to STEMI. An initial shockable rhythm (VF, VT, or AED shock advised) was associated with evolution to ischemia or STEMI on ED ECG (OR = 11.32, 95% CI [2.64–61.31]). Greater OOH defibrillations (OR = 1.97, 95% CI [1.33–3.06]) and total defibrillations (OR = 1.72, 95% CI [1.21–2.54]) were also associated with evolution to ischemia or STEMI.

Discussion

This study identified factors and interventions following resuscitation from OHCA associated with resolution in out-of-hospital 12-lead ECG STEMI. OOH ECGs diagnostic for STEMI were more likely to have resolution of STEMI on ED ECG if they received lower cumulative doses of epinephrine, were not given norepinephrine infusion, had shorter duration of resuscitation, less time after ROSC before OOH ECG acquisition, or more time between EMS and ED comparison ECGs. These associations were not noted for any changes in classification of non-STEMI OOH ECGs.

The mechanism(s) underlying the high incidence (67.3%) of resolution of OOH STEMI is unknown. However, several proposed physiological processes may explain or contribute to this phenomenon. Evidence suggests that spontaneous thrombolysis is an innate and effective mechanism protecting against tissue damage following arterial occlusion which may partially or fully restore arterial perfusion.[10] Transient vasospasm has been found in ∼10% of patients with STEMI following out-of-hospital cardiac arrest and

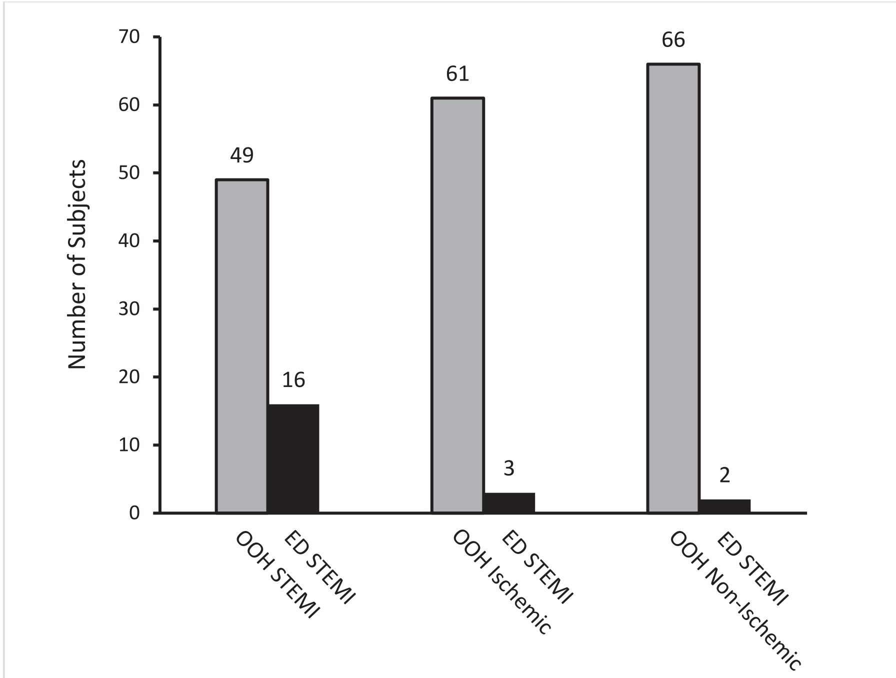

Fig. 2 – Distribution of emergency department STEMIs (n = 21) by initial out-of-hospital 12-lead ECG classification. OOH = out-of-hospital; STEMI = ST-elevation myocardial infarction; ED = emergency department.

may be responsible for transient STEMI in some cases.[11] High-dose vasopressors administered during and after pulselessness may initiate or exacerbate vasospasm, which might resolve as the drug metabolizes. Hypoperfusion and a documented low peripheral perfusion index following prolonged resuscitation and post-ROSC cardiogenic shock have been associated with higher rates of false-positive STEMI on 12-lead ECG, suggesting that hypoperfusion and its attendant metabolic, electrolyte, and electromechanical abnormalities in the immediate post-ROSC period can manifest as transient transmural ischemia in the setting of OHCA.[12,13] Further supporting this mechanism is a significant and inverse relationship between the post-ROSC perfusion index and the total amount of epinephrine administered to the patient, suggesting an additional negative effect on perfusion.

Consistent with previous findings, this study provides further evidence that 12-lead ECGs obtained soon after ROSC may have limited diagnostic utility.[5–7] Time is significantly associated with false positive STEMI post-ROSC, possibly also consistent with the hypoperfusion and low peripheral perfusion index mechanism. Shorter resuscitation time prior to ROSC (less severe metabolic derangement improving more rapidly), shorter time between ROSC and OOH ECG acquisition (little time for improvement in electrolyte, metabolic, and electromechanical abnormalities) and longer time between OOH ECG and ED ECG (more time for improvement in metabolic abnormalities) were all associated with resolution of OOH STEMI during ED evaluation. In our original study,[7] time from ROSC to OOH ECG acquisition (measured as a dichotomous variable) did not reach statistical significance. In this study we analyzed time from ROSC to OOH ECG as a continuous variable, demonstrating statistical significance of shorter time from ROSC to OOH ECG and resolution of OOH STEMI during ED evaluation.[14] It is possible that duration of resuscitation may be a mediating factor when assessing the association between STEMI resolution and epinephrine dosing, as lengthier duration of resuscitation likely results in greater cumulative epinephrine dosing.

This study also provides insight into changes in non-STEMI OOH ECG classification. A greater number of defibrillations was associated with a change to increased ischemia (ischemia or STEMI) for patients with non-STEMI OOH ECGs. Further, an initial arrest rhythm of VF/VT was associated with ischemic evolution for patients with non-ischemic OOH ECGs. Primary VF cardiac arrest requiring treatment with defibrillation has a higher association with coronary occlusion than other cardiac arrest rhythms.[15,16]

Expanded electrocardiographic criteria to detect occlusive myocardial infarction has received recent attention.[17–19] It has been shown that a subset of patients with non-STEMI ECG criteria have complete coronary occlusion on angiography,[17–19] and additional electrocardiographic features beyond AHA/ACC STEMI criteria have been described which are predictive of occlusive myocardial infarction.[8,20–24] A growing body of evidence suggests that STEMI criteria represent an imperfect classification system to accurately identify coronary occlusion, and broader diagnostic criteria to detect occlusive myocardial infarction have been proposed.[25] It is unclear how the findings of our study may differ when applying expanded diagnostic criteria for occlusive myocardial infarction compared to STEMI criteria. Artificial intelligence-enhanced electrocardiography analysis has also shown promise to identify high-risk patients who may benefit from further diagnostic or therapeutic interventions for obstructive coronary artery disease.[26,27] It is possible that future use of these expanded electrocardiographic criteria may provide greater insight into the role of vasoactive medications, resuscitation duration, timing of ECG acquisition, and the diagnostic reliability of the post-ROSC 12-lead ECG.

This study has limitations. First, it is subject to all the limitations of a retrospective case series study including poor control over which patients received out-of-hospital 12-lead ECGs, availability and

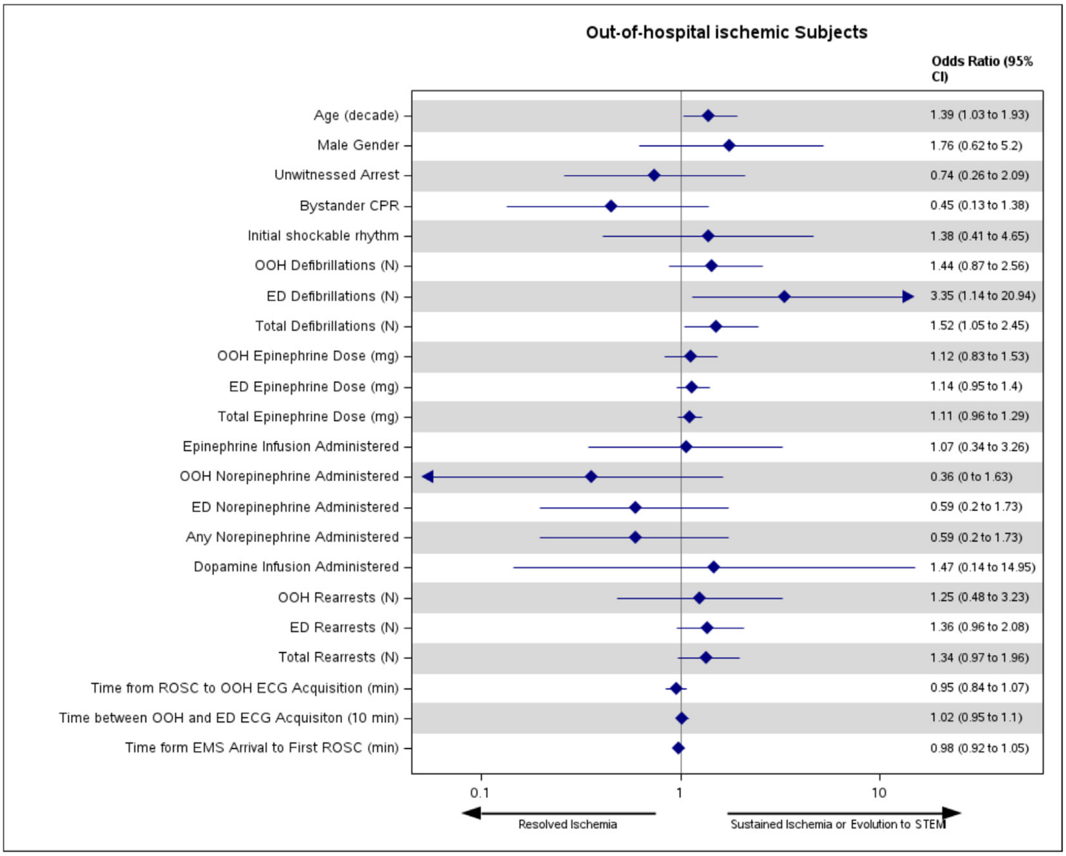

Fig. 3 – Forest plot of odds ratios for associations of ischemic out-of-hospital 12-lead ECG change in classification during ED evaluation. 95% confidence intervals are shown. Bystander CPR was defined as CPR provided by anyone other than an emergency responder prior to EMS arrival. % = percent; CI = confidence interval; CPR = cardiopulmonary resuscitation; OOH = out-of-hospital; ED = emergency department; ROSC = return of spontaneous circulation; ECG = electrocardiogram; STEMI = ST-elevation myocardial infarction; EMS = emergency medical services; N = number; mg = milligrams; min = minutes.

accuracy of the data records, and selection bias. Second, sample size was limited. Third, coronary angiography was not routinely performed on these patients, and correlation of 12-lead ECG findings with coronary artery anatomy was not possible. Finally, the study from this single site may not be generalizable elsewhere.

Conclusion

ROSC patients with STEMI on out-of-hospital ECG commonly resolve in the ED (67%). These identified associations may better inform clinical decision making. Post-ROSC out-of-hospital 12-lead ECGs should be repeated on arrival in the ED.

CRediT authorship contribution statement

Christopher J. Naas: Writing – original draft, Visualization, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Hadi O. Saleh:** Writing – review & editing, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Thomas W. Engel:** Writing – review & editing, Methodology, Formal analysis, Data curation, Conceptualization. **David D. Gutterman:** Writing – review & editing, Methodology, Formal analysis, Data curation, Conceptualization. **Aniko Szabo:** Writing – review & editing, Visualization, Resources, Methodology, Formal analysis. **Thomas Grawey:** Writing – review & editing. **Benjamin W. Weston:** Writing – review & editing, Data curation. **Christopher E. Monti:** Writing – review & editing, Visualization. **John E. Baker:** Writing – review & editing. **Jacob Labinski:** Writing – review & editing, Resources, Project administration, Data curation. **Lujia Tang:** Writing – review & editing. **Jamie Jasti:** Writing – review & editing. **Jason A. Bartos:** Writing – review & editing. **Rajat Kalra:** Writing – review & editing. **Demetris Yannopoulos:** Writing – review & editing. **M. Riccardo Colella:** Writing – review & editing, Data curation. **Tom P. Aufderheide:** Writing – original draft, Visualization, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: “Tom P. Aufderheide is on the editorial board of Resuscitation and reports a relationship with National Heart Lung and Blood Institute that includes: funding grants. Tom P. Aufderheide reports a rela-

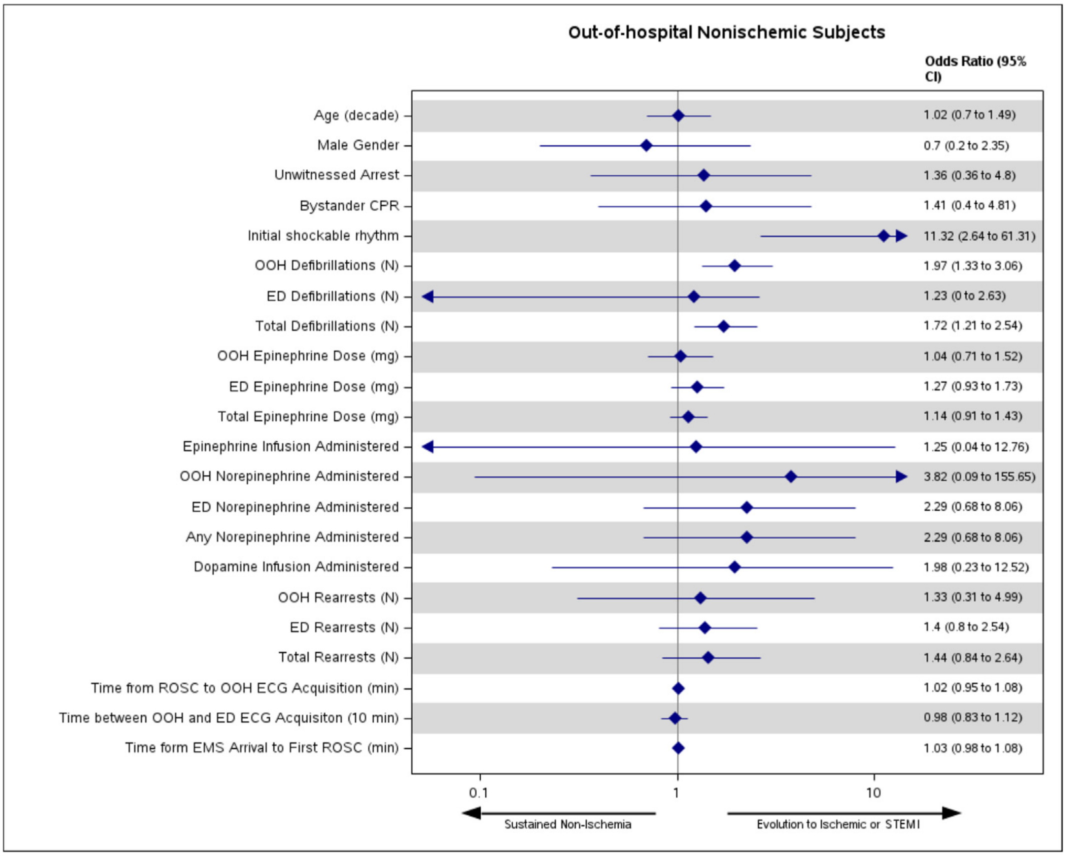

Fig. 4 – Forest plot of odds ratios for associations of non-ischemic out-of-hospital 12-lead ECG change in classification during ED evaluation. 95% confidence intervals are shown. Bystander CPR was defined as CPR provided by anyone other than an emergency responder prior to EMS arrival. % = percent; CI = confidence interval; CPR = cardiopulmonary resuscitation; OOH = out-of-hospital; ED = emergency department; ROSC = return of spontaneous circulation; ECG = electrocardiogram; STEMI = ST-elevation myocardial infarction; EMS = emergency medical services; N = number; mg = milligrams; min = minutes.

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