Clinical paper

Do not disregard the initial 12 lead ECG after out-of-hospital cardiac arrest: It predicts angiographic culprit despite metabolic abnormalities

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Abstract

Objectives: The initial 12 lead electrocardiogram (ECG) following return of spontaneous circulation (ROSC) after out-of-hospital cardiac arrest (OHCA), is often disregarded by clinicians in ability to predict acute thrombotic coronary occlusion (ATCO) due to markedly abnormal metabolic milieu (AMM). We sought to evaluate the accuracy of initial vs. follow-up ECG prior to invasive coronary angiography (ICA) to predict ATCO following resuscitated OHCA.

Methods: We included OHCA patients with initial shockable rhythm who underwent invasive coronary angiography (ICA). AMM was defined as one of: pH < 7.1, lactate >2 mmol/L, serum potassium <2.8 or >6.0 mEq/L. Two ECGs A (initial) and B (follow-up) following ROSC but prior to ICA were adjudicated by 2 experienced readers using expanded ECG criteria to predict angiographic ATCO on ICA.

Results: 152 consecutive patients (mean age 58 years, 75% male) met inclusion criteria, 77% had AMM. Among those with both ECGs (n = 102), overall accuracy, sensitivity, specificity, positive predictive value, negative predictive value for correctly predicting angiographic ATCO for ECG A was 72%, 63%, 81%, 60%, 83% and for ECG B was 71%, 50%, 91%, 73%, 80% respectively. Predictive accuracy for angiographic ATCO was similar between ECG A [odds ratio (OR) 7.31, CI 2.87 –18.62, p < 0.0001] and ECG B [OR 10.67; CI 3.6 –31.61, p < 0.0001], and consistent in AMM.

Conclusions: In OHCA, despite AMM, the initial post ROSC ECG retains a statistically significant, and similar accuracy as the follow-up ECG to predict angiographic ATCO using expanded criteria.

Keywords: Out of hospital cardiac arrest, Electrocardiogram, Coronary angiogram, Metabolic abnormalities

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**Introduction**

Out of hospital cardiac arrest (OHCA) is a devastating clinical occurrence with historically poor long-term outcomes. According to the American Heart Association, there were more than 350,000 cases of OHCA in 2016, and overall survival was low at 12%.

The initial rhythm of patients presenting with OHCA defines the strategy of management after return of spontaneous circulation (ROSC), patients with VF/VT or "shockable rhythm" are more likely to have underlying coronary artery disease (CAD), and specifically, an acute thrombotic coronary occlusion (ATCO), as the precipitating cause of the OHCA. Immediate coronary revascularization is recommended if ATCO is suspected in the context of resuscitated OHCA.

Following ROSC, an immediate 12-lead electrocardiogram (EGC) is a critical test to triage patients for immediate invasive coronary angiography (ICA), usually by identifying a current of injury or ST-segment elevation (STE). However, it is often difficult to accurately predict angiographic ATCO based on the immediate post-arrest ECG due to several potential caveats and pitfalls impacting the accurate interpretation of the ECG tracing. In particular, clinicians may have reduced confidence in the accuracy of the first 12-lead ECG in identifying ATCO when obtained in the context of an abnormal metabolic milieu (AMM) following ROSC. In this setting, metabolic abnormalities (affecting lactate, pH, as well as derangements in potassium levels), could potentially adversely affect the accuracy of the initial 12-lead ECG.

Frontline clinicians may disregard the initial ECG due to these metabolic abnormalities, and instead rely upon a follow-up ECG to predict presence or absence of ATCO, performed after some of the metabolic abnormalities have been corrected. Lack of recognition of findings of ATCO or incorrect attribution of ECG abnormalities to metabolic factors, could result in critical delays in performance of immediate coronary angiography and revascularization.

The goal of our study was to determine the predictive accuracy of the initial vs. follow up 12-lead ECG performed following ROSC but prior to ICA in the context of OHCA, to identify angiographic ATCO, and assess the impact of AMM in accuracy of ECG interpretation.

**Methods**

**Study Design:** This was a retrospective observational study performed at HCMC, a tertiary level 1 trauma center belonging to Hennepin Healthcare System in downtown Minneapolis, Minnesota. All patients presenting with resuscitated OHCA between January 2008 and December 2015 were identified from the electronic health record using ICD-9 diagnostic codes. This database was further linked with the cardiac catheterization laboratory database to identify those who underwent ICA during the index hospital stay. The retrospective study protocol was reviewed and approved by the Institutional Review Board at HCMC (consent waived).

**Study Population:** The inclusion criteria for this study were patients presenting with a resuscitated OHCA (defined as cardiac arrest prior to or en-route to hospital) with an initial rhythm of ventricular tachycardia/fibrillation (VT/VF) or initial shockable rhythm, who underwent ICA during the index hospitalization. Patients with cardiac arrest wherein the initial rhythm was pulseless electrical activity/asystole or "non-shockable," those with in-hospital cardiac arrest, those who died prior to undergoing ICA, and those who did not undergo ICA during the index hospitalization were excluded from this study.

**Study Protocol:** After presenting to the hospital with OHCA due to a VT/VT/shockable rhythm, an initial 12-lead ECG (ECG A) was obtained, typically immediately following ROSC. A second 12-lead ECG (ECG B) was obtained as part of routine care in a majority of patients after varying degrees of inter-medic stabilization. Of note, both 12 lead ECGs A and B were obtained prior to performance of ICA. The time duration between ECGs A and B was measured for all patients. ECGs A and B (when available) were interpreted and coded by 2 experienced readers (each with >20 years of ECG interpretation experience in clinical practice).

**EGC criteria:** The principal coding criteria were whether the 12-lead ECG was diagnostic [ECG (+)] or was not [ECG (−)] diagnostic for ATCO. ECG criteria for the diagnosis of ATCO was made by experienced readers using pattern recognition guided by the following expanded criteria: a) classic criteria for ST elevation AMI, b) left main equivalent (defined as ST elevation in aVR with diffuse ST depression elsewhere), c) modified Sgarbossa criteria in LBBB and ventricular paced rhythms, and d) diffuse ST depression diagnostic for posterior infarction but not meeting classic STEMI criteria. If none of these 4 criteria were met, the ECG was coded as being (−) for ATCO. The guiding principles for these ECG criteria were that they were deemed to be clinically significant to merit urgent activation of the cardiac catheterization laboratory due to suspicion for ATCO (even if not meeting "classic" STEMI criteria). In the event of discrepancy between ECG coding between the 2 readers, a third experienced ECG reader’s interpretation was used as a tiebreaker and the majority vote used for the final ECG coding. ECG readers were blinded to all clinical data including clinical context, patient demographics, computerized ECG interpretation, and results of coronary angiography. Both the initial and follow-up ECGs of each patient were interpreted in a random and unpaired sequence.

**Data Collection:** Initial vital signs on physical examination and laboratory values were obtained for all patients by linking with the electronic health record. Measured initial vitals included blood pressure, heart rate, temperature, respiratory rate, and oxygen saturation on presentation. Laboratory evaluation included metabolic parameters (pH, lactate, basic metabolic panel including electrolytes) as well as first and peak cardiac troponin I; by standard operating procedure laboratory blood draw is obtained within 10 min of the patient presenting to the emergency stabilization bay. Normal values for potassium were defined as 3.5–5 mmol/L, pH 7.35–7.45, lactate <2 mmol/L, and cTnI <0.04 mcg/L. Abnormal metabolic milieu (AMM) was defined as the presence of 1 or more of the following 3 metabolic criteria: pH < 7.1, lactate > 2 mmol/L, and potassium <2.8 or >6.0 mmol/L. If none of these 3 findings were present on initial labs, patients were classified as having a normal metabolic milieu (NMM). Chronic medical conditions such as diabetes mellitus, cerebrovascular disease, chronic kidney disease, hypertension, hyperlipidemia, and prior history of CAD and coronary revascularization with either percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery were also obtained using ICD codes.

**Key Outcome Measures:** All patients identified in the final cohort of this study underwent ICA. The coronary anatomy and results of all coronary angiograms were evaluated and recorded separately on a cardiac catheterization database. Native and graft anatomy was detailed along with the presence of lesion, location of lesion, pre-PCI percent stenosis, post-PCI percent stenosis, pre-PCI intervention Thrombolysis in Myocardial Infarction (TIMI) flow, and post-PCI TIMI flow.
flow. The accuracy of the ECGs in the identification of angiographic acute thrombotic culprit occlusion (ATCO) versus no angiographic ATCO was recorded by using the ICA as the gold standard. The initial interpretation recorded on the cardiac catheterization database, based on assessment by the interventional cardiologist performing the ICA, was used for analysis. If further clarity regarding angiographic details was needed, additional review of select coronary angiogram films was performed. Angiographic ATCO was defined as either thrombotic stenosis ≥70% or designation as thrombotic culprit lesion by the interventional or consulting cardiologist. Not all severe angiographic coronary stenoses were labeled as angiographic ATCO if not determined to be the thrombotic culprit lesion by the interventional or consulting cardiologist (e.g. a chronic total occlusion or chronic coronary stenoses). The abstraction for details of ICA was performed by cardiology fellows. Periodic meetings were held by the entire study team, to ensure uniformity of progress, and reconciliation of any conflicting variables. Patients undergoing coronary revascularization during index hospitalization using PCI vs. emergent or urgent coronary artery bypass grafting were recorded separately.

Data Analysis: Comparisons were made between the 2 populations of interest using SAS Enterprise Guide version 4.3. Chi squared statistics were used to determine significant differences between the 2 populations for categorical variables, and t tests were used to compare means between the 2 populations. Inter-reader reliability statistics and predictive modeling of the ECG readings were calculated using unadjusted logistic regression. Statistical significance was measured at values ≤ 0.05. The correlation of blinded ECG reads between the two readers was calculated using the kappa coefficient.

Results

A total of 1288 patients were identified to have arrests of all etiologies during the study period, of whom 325 patients were identified to have an angiographic ATCO. There were 90 patients who had a blinded adjudication of ECG (+) per majority read in the study cohort. Of these patients, 19/90 (21%) patients had evidence for an angiographic culprit, whereas 71/90 (79%) patients did not. Of all 152 patients in the study cohort, 102 were identified as having both an initial and follow-up ECG with a mean time of 70.7 min (median 33 min, interquartile range 19–96 min) between the first and follow-up ECG; their breakup of the above true and false positive/negative rates was similar to the full cohort, as demonstrated in Table 2. The median time-frame between patient admission and coronary angiogram was 2 h (interquartile range 1–40 h).

For the entire population (n = 152), ECG A had an overall accuracy of 76% for correctly identifying the presence or absence of angiographic ATCO, with sensitivity 71%, specificity 80%, positive predictive value (PPV) 71%, and negative predictive value (NPV) 80%. ECG B had an overall accuracy of 60%, with sensitivity 26%, specificity 93%, PPV 72%, and NPV 65% for correctly identifying the presence or absence of angiographic ATCO. For the subset of the population that had both ECGs (n = 102), ECG A had an overall accuracy of 72% for correctly identifying the presence or absence of angiographic ATCO. For the subset of the population that had both ECGs (n = 102), ECG A had an overall accuracy of 72% for correctly identifying the presence or absence of angiographic ATCO, with sensitivity 63%, specificity 81%, PPV 61%, and NPV 83%. ECG B had an overall accuracy of 71%, with sensitivity 50%, specificity 91%, PPV 73%, and NPV 80% for correctly identifying

| Table 1 – Baseline Features of the Cohort. A description of the demographic, clinical, vital signs, and laboratory variables of the overall cohort. |
|--------------------------|--------------------------|--------------------------|
| ATCO Absent (n = 88)     | ATCO Present (n = 64)    | p-value                  |
| Age (years)              | 57.73 (± 14.98)          | 57.49 (± 10.63)          | NS                       |
| Male                     | 68 (77%)                 | 48 (75%)                 | NS                       |
| Diabetes mellitus        | 25 (28%)                 | 11 (17%)                 | NS                       |
| Chronic Kidney Disease   | 8 (9%)                   | 3 (5%)                   | NS                       |
| Hypertension             | 49 (56%)                 | 30 (47%)                 | NS                       |
| Dyslipidemia             | 36 (41%)                 | 24 (38%)                 | NS                       |
| Prior Coronary Revascularization | 3 (3%)                  | 0                        | NS                       |
| Abnormal Metabolic Milieu | 58 (73%)                 | 41 (84%)                 | NS                       |
| First Potassium (mEq/L)  | 3.73 (± .76)             | 3.69 (± .76)             | 0.7326                   |
| First pH                 | 7.24 (± .15)             | 7.24 (± .15)             | 0.8504                   |
| First Lactate (mmol/L)   | 4.94 (± 3.95)            | 5.70 (± 3.95)            | 0.2933                   |
| First Troponin I (mcg/L) | 0.91 (± 3.90)            | 2.18 (± 6.62)            | 0.1397                   |
| Max Troponin I (mcg/L)   | 10.86 (± 25.06)          | 78.21 (± 136.32)         | <.0001                   |

Abbreviations: mEq-milliequivalents; mmol = millimoles; mcg = micrograms; L = liter; ATCO = Acute Thrombotic Coronary Occlusion.
the presence or absence of angiographic ATCO. Using angiographic ATCO as the gold standard; the c-statistic for ECG A was 0.72, for ECG B was 0.71, thus signifying that the overall accuracy was comparable between the two ECGs. The findings described above in the overall cohort were reproduced in the setting of both abnormal and normal metabolic milieu.

To assess the predictive capability of ECGs A and B to identify angiographic ATCO, only the subset with both ECGs available (n = 102) was utilized. ECG A accurately predicted angiographic ATCO with OR of 7.308 (CI 2.868–18.623, p < 0.0001), whereas ECG B was able to predict angiographic ATCO (OR 10.67; CI 3.6–31.61, p < 0.0001) (Table 3).

Of note, in the full cohort, 129 patients of 152 (85%) had complete data on all the above metabolic parameters, and 99 (77%) were noted to have AMM. For those patients with both ECG A and ECG B available (n = 102), in the setting of AMM (n = 66), ECG A predicted angiographic ATCO (OR 8.26; CI 3.31–20.60, p < 0.0001); whereas ECG B predicted angiographic ATCO (OR 3.89; CI 1.23–12.25, p = 0.0205). In the setting of NMM (n = 23), ECG A predicted angiographic ATCO (OR 13.5; CI 1.94–93.25, p = 0.0083), whereas, again, ECG B did predict angiographic ATCO (OR 12.6; CI 1.07–148.04, p = 0.0439) (Table 3).

The interreader reliability between the two ECG readers in the context of OHCA (blinded to the clinical context) revealed kappa statistic for ECG A of 0.66. In the context of AMM, the kappa statistic was 0.6; whereas in the context of NMM, the kappa statistic was 0.78. The percent agreement between the readers for ECG A was 71% (71 of 99) in AMM and 87% (26 of 30) in NMM.

### Discussion

In our study of OHCA patients presenting with VT/VF as initial rhythm, we found that the overall accuracy of ECG to predict angiographic ATCO was modest, but the initial post ROSC 12-lead ECG had a similar likelihood of correctly predicting an underlying angiographic ATCO as the cause of OHCA compared to follow-up ECG. Of note, ECG A had higher sensitivity, whereas ECG B had higher specificity to detect ATCO, but the overall accuracy of both ECGs was similar, albeit modest. Interestingly, this pattern was consistent despite the milieu of metabolic derangement that is common following ROSC in OHCA. These findings indicate that clinicians must not disregard the first post-ROSC ECG to predict ATCO due to concern for confounding by an abnormal metabolic milieu. These findings have direct implications for first responders and first-line clinicians caring for patients with resuscitated OHCA, who are actively involved in making time-sensitive and critical decisions regarding appropriate triaging for immediate clinical management, including consideration of emergent ICA and revascularization based on the initial 12-lead ECG.

### Table 2

| Categorization per majority read of initial ECG (ECG A) and subset with follow-up ECG (ECG B) available to predict presence/absence of angiographic acute thrombotic coronary occlusion (ATCO) in the context of out of hospital cardiac arrest. |
|--------------------------------------------------|--------------------------------------------------|
| Initial ECG (ECG A) | Follow-up ECG (ECG B) |
| N = 152 | N = 102 |
| Angiographic ATCO | No Angiographic ATCO | Angiographic ATCO | No Angiographic ATCO |
| Present (n = 64) | No Angiographic ATCO (n = 88) | Present (n = 32) | No Angiographic ATCO (n = 70) |
| ECG (+) per majority read (n = 62) | ECG (+) per majority read (n = 22) |
| Row% | Row% |
| 73% | 73% |
| 27% | 27% |
| ECG (-) per majority read (n = 90) | ECG (-) per majority read (n = 80) |
| Row% | Row% |
| 21% | 20% |
| 79% | 80% |

Abbreviations: AMM = abnormal metabolic milieu, ATCO = Acute Thrombotic Coronary Occlusion.

### Table 3

| Population | Parameter | Odds Ratio (95% CI) to predict ATCO | P value |
|------------|-----------|------------------------------------|--------|
| All Patients with both ECGs A and B (n = 102) | ECG A | 7.308 (2.87–18.62) | <.0001 |
| | ECG B | 10.67 (3.6–31.61) | <.0001 |
| AMM (n = 66) | ECG A | 8.26 (3.31–20.60) | <.001 |
| | ECG B | 3.89 (1.23–12.25) | 0.0205 |
| NMM (n = 23) | ECG A | 13.5 (1.94–93.25) | 0.0083 |
| | ECG B | 12.6 (1.07–148.03) | 0.0439 |

Overall accuracy of ECG A (initial 12-lead ECG) and ECG B (follow-up 12 lead ECG) for predicting acute thrombotic coronary occlusion using the invasive coronary angiogram as the gold standard. Of note, 89 of 102 (87%) of patients with A and B ECGs had complete data on metabolic parameters. Abbreviations: AMM = Abnormal Metabolic Milieu, ECG = Electrocardiogram, NMM = Normal Metabolic Milieu.
The 12-lead ECG remains the primary tool used by clinicians to triage patients for emergent ICA/coronary revascularization in the contemporary era, despite several limitations outlined in the literature. Several observational studies have suggested a modest predictive accuracy of ECG in identifying a coronary culprit or correctly identifying STEMI in the context of OHCA. Our study confirms that the overall predictive accuracy of the initial 12-lead ECG was modest in the detection of angiographic ATCO. Yet, the initial 12 lead ECG immediately following resuscitation demonstrates important clues to an angiographic culprit despite metabolic derangements, which are common following resuscitation. Moreover, it is possible that these clues and signs of coronary ischemia/hypoperfusion on the initial ECG could resolve after institution of measures to reduce myocardial oxygen demand (such as intubation, sedation, hemodynamic correction etc.). Therefore, disregarding the initial 12 lead ECG and delaying early clinical decision-making while awaiting improvement of the metabolic milieu may actually decrease the (already modest) sensitivity to detect ATCO.

Given the overall modest level of accuracy of 12 lead ECGs in general, the debate about whether it should serve as a gate-keeper to early ICA, or whether early ICA should be performed in all VT/VT survivors regardless of ECG, has been ongoing in the literature. The more fundamental question of whether early ICA impacts survival if performed in all following resuscitated OHCA is extremely controversial. Several observational studies suggested that early ICA followed by revascularization was associated with survival benefit. However, the non-randomized design of these studies was a significant limitation, with the possibility of significant inherent selection biases and unmeasured confounders. The only randomized controlled trial (RCT) to address this matter in OHCA assigned 552 patients without STE to undergo immediate versus delayed ICA. In this multicenter study, there was no difference in survival at 90 days between these 2 strategies. However, critics have pointed out that the prevalence of coronary occlusion was low (only 5%) in this cohort, suggesting strong selection bias prior to enrollment, with patients judged to have a high probability of coronary occlusion being excluded from randomization. This criticism is strengthened by the fact that, unfortunately, the study did not provide characteristics of the patients who were deemed ineligible for randomization after screening because the treating physician believed the patient required ICA based on clinical judgement. As outlined, our observational study is not intended or designed to discern whether early ICA is indicated or should be pursued in all OHCA survivors, but it bears emphasis that in our cohort of OHCA survivors, the prevalence of ATCO was 42%. Moreover, our study does suggest that while we eagerly await the design of the perfect RCT to help us understand this subject with more clarity, we must not disregard the clues that could be provided by the first post-ROSC ECG in OHCA survivors or attribute them to metabolic factors alone. Moreover, the ECG criteria used in our study (not limited to STE alone) may be more sensitive in the detection of angiographic ATCO, especially in experienced hands, irrespective of the metabolic milieu.

**Limitations and strengths**

Our study has several limitations and strengths. There is a selection bias implicit in our observational study since only patients who were referred for ICA (the “gold standard” for identifying the thrombotic coronary culprit) were included for analysis. However, this is also a strength, since it offers a pragmatic perspective with regards to bedside decisions made by clinicians in the management of this high-risk population. The ECG criteria for identifying an angiographic culprit in our study were guided by but not limited to ST elevation criteria; the expanded ECG criteria included other established criteria commonly used by cardiologists and emergency physicians in the triaging of patients to ICA. The significantly higher maximal cTnI value in the group of patients with angiographic ATCO versus those without angiographic ATCO provides corroborative support regarding the fact that patients were appropriately allocated to having an underlying culprit angiographic lesion and acute MI with ATCO as the proximate cause of the OHCA. The ECG readers in this study were highly experienced, and it is therefore difficult to determine if the findings from this study can be extrapolated to relatively inexperienced ECG readers. Yet, it bears emphasis that the overall accuracy of the first ECG following resuscitated OHCA to detect ATCO on coronary angiography by experienced readers using a wider ECG based definition (not limited to STEMI alone) in this study was modest: sensitivity 71%, specificity 80%. Follow-up studies should evaluate if the results from our study can be reproduced among ECG readers with lesser experience. Based on our study design (readers were blinded to the sequence of the first and second ECG), we are unable to determine if a sequential combination of the first and second ECG would improve the accuracy to detect an angiographic culprit compared to either ECG alone.

**Conclusions**

In summary, to the best of our knowledge, this is the first study to compare the diagnostic utility of the initial compared to the follow-up ECG prior to ICA for prediction of angiographic ATCO in the context of resuscitated OHCA. Our study suggests that the initial 12-lead ECG, despite an abnormal metabolic milieu of resuscitated VT/VT OHCA, provides valuable clinical guidance regarding an underlying angiographic coronary culprit lesion; the accurate interpretation of which is important for downstream clinical management. Disregarding the findings of the initial 12-lead ECG because of concerns about an abnormal metabolic milieu could have the unintended detriment of missing valuable, albeit transient, guidance regarding need to pursue urgent coronary angiography.

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**Author contributions**

Study concept and design (GS/SS/BB).
- Acquisition of the data (DM, AS).
- Analysis and interpretation of the data (HR/GS/SS/BB).
- Drafting of the manuscript (AS/GS).
- Critical revision of the manuscript for important intellectual content (SS/BB).
- Statistical expertise (HR).
- Acquisition of funding (not applicable).
Declaration of competing interest

The authors report no conflict of interest related to this research or manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resplu.2020.100032.

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