Available online at www.sciencedirect.com

ScienceDirect

Journal of Electrocardiology 48 (2015) 921 – 926

JOURNAL OF Electrocardiology

www.jecgonline.com

Rationale, development, and implementation of the Electrocardiographic Methods for the Prehospital Identification of Non-ST Elevation Myocardial Infarction Events (EMPIRE)☆,☆☆,★

Salah S. Al-Zaiti, RN, PhD,[a,*] Christian Martin-Gill, MD, MPH,[b] Ervin Sejdić, PhD,[c] Mohammad Alrawashdeh, BSN, MSN,[a] Clifton Callaway, MD, PhD[b]

[a] *Department of Acute and Tertiary Care Nursing at the University of Pittsburgh, Pittsburgh PA*
[b] *Department of Emergency Medicine at the University of Pittsburgh, Pittsburgh PA*
[c] *Department of Electrical and Computer Engineering at the University of Pittsburgh, Pittsburgh PA*

Abstract

Background: The serum rise of cardiac troponin remains the gold standard for diagnosing non-ST elevation (NSTE) myocardial infarction (MI) despite its delayed response. Novel methods for real-time detection of NSTEMI would result in more immediate initiation of definitive medical therapy and faster transport to facilities that can provide specialized cardiac care.

Methods: EMPIRE is an ongoing prospective, observational cohort study designed to quantify the magnitude of ischemia-induced repolarization dispersion for the early detection of NSTEMI. In this ongoing study, prehospital ECG data is gathered from patients who call 9-1-1 with a chief complaint of non-traumatic chest pain. This data is then analyzed using the principal component analysis (PCA) technique of 12-lead ECGs to fully characterize the spatial and temporal qualities of STT waveforms.

Results: Between May and December of 2013, Pittsburgh EMS obtained and transmitted 351 prehospital ECGs of the 1149 patients with chest pain-related emergency dispatches transported to participating hospitals. After excluding those with poor ECG signal (n = 40, 11%) and those with pacing or LBBB (n = 50, 14%), there were 261 eligible patients (age 57 ± 16 years, 45% female, 45% Black). In this preliminary sample, there were 19 STEMI (7%) and 33 NSTEMI (12%). More than 50% of those with infarction (STEMI or NSTEMI) had initially negative troponin values upon presentation. We present ECG data of such NSTEMI case that was identified correctly using our methods.

Conclusions: Concrete ECG algorithms that can quantify NSTE ischemia and allow differential treatment based on such ECG changes could have an immediate clinical impact on patient outcomes. We describe the rationale, development, design, and potential usefulness of the EMPIRE study. The findings may provide insights that can influence guidelines revisions and improve public health.

Keywords: Ischemia; Repolarization; Non-ST elevation myocardial infarction

Introduction

Current guidelines recommend the use of serum biomarkers of myocardial necrosis (i.e., troponin) as the gold standard to confirm acute myocardial infarction (MI) [1,2]. However, serum cardiac biomarkers are not elevated until a few hours after ischemic injury [3], which limits the clinical utility of using these serum enzymes in the prehospital medical care of acute MI patients. In contrast, findings from the standard, 10-second, 12-lead ECG are readily available during pre-hospital care, which allows immediate intervention to reduce the size of infarction. It is now well-documented that immediate percutaneous intervention (PCI) for those with ST elevation (STE) on the initial ECG (i.e., STEMI) significantly reduces mortality [4], and, as a result, the prehospital ECG is now incorporated in nearly 90% of systems of care in major metropolitan U.S. cities [5]. Unfortunately, the real clinical need remains unmet for the majority (> 70%) of acute MI events that have little, if any, ischemic ECG changes (i.e., NSTEMI or

☆ Funding: This study was funded by grants from (1) the University of Pittsburgh's Center for Medical Innovation, (2) the Emergency Nurses Association (ENA) Foundation and American Nursing Informatics Association (ANIA).

☆☆ Provisional Patent: Application No. 62/146,775, filed April 13, 2015; Country: United States.

★ Conflicts of Interest: None.

* Corresponding author at: Department of Acute and Tertiary Care, University of Pittsburgh, School of Nursing, 336 Victoria Building, 3500 Victoria St, Pittsburgh, PA, 15261.

E-mail address: ssa33@pitt.edu

http://dx.doi.org/10.1016/j.jelectrocard.2015.08.014
0022-0736/

Unstable Angina [UA]) and constitute more diffuse, multi-vessel coronary disease, for which immediate PCI has not been shown to improve outcomes [6]. Furthermore, STE may be transient and lack of diagnostic criteria for STEMI upon hospital arrival does not exclude presence of critical lesions for which immediate PCI is indicated [7]. Recent clinical trial data supports the early use of innovative treatment strategies (e.g., P2Y12 antagonists [8,9] and statins [10–12]) to improve outcomes in NSTEMI [13,14]. To date, we lack the ability to identify NSTEMI very early during care. Concrete ECG algorithms to quantify ischemic burden – and allow us to act on ECG changes – would have an immediate clinical impact by expediting definitive medical care of NSTEMI.

Several ECG patterns associated with particular coronary anatomy and high-risk prognosis in NSTEMI have been identified, including tall positive T waves (with or without ST depression) [15]. However, current guidelines do not consider the configuration of the T wave for urgent PCI, and the significance of such changes – in the absence of STE – is considered more contentious. However, given that ongoing ischemia does not necessarily result in STE, quantitative assessment of the T wave would provide a great opportunity for improving diagnostics. In a recent retrospective analysis, we found that repolarization complexity was significantly correlated with peak troponin level ($r = 0.41$) during acute coronary events; moreover, this complexity could differentiate NSTEMI patients from others with similar symptoms but no ongoing myocardial injury [16]. Our findings – and the findings of others – have led to the development of the EMPIRE (*E*lectrocardiographic *M*ethods for the *P*rehospital *I*dentification of non-ST Elevation of Co*R*onary *E*vents) study. EMPIRE is designed to quantify the magnitude of ischemia-induced repolarization dispersion for the early detection of NSTEMI. The purpose of this report is to describe the rationale, design, methods, and feasibility data of this ongoing, prospective, observational cohort study.

Methods

We are creating a database of patients in the Pittsburgh, PA area who call 9-1-1 to report chest pain. The database includes the digital 12-lead ECGs obtained by onsite Emergency Medical Services (EMS) and data from prehospital and inhospital medical records. Cases are recruited following treatment and transport to the hospital by the City of Pittsburgh Bureau of EMS (Pittsburgh EMS), which staffs 15 ambulances that are distributed in 12 dispatch stations around Pittsburgh. All ambulances are equipped with Philips MRX machines that have 12-lead ECG transmission capacity, and obtaining 12-lead ECGs for non-traumatic chest pain patients is mandated by Pennsylvania statewide protocols. Patients with chest pain are recruited if they are transported by ambulance to one of three main UPMC affiliated hospitals in Pittsburgh (UPMC Presbyterian, Mercy, and Shadyside hospitals). This observational study does not change patient care and possesses minimal risk. There is no direct interaction with study participants – data are collected after 30 days of medical care completion. As such, our preliminary cohort was recruited under waiver of informed consent; this systematic approach is more likely to generate a representative epidemiologic database of all eligible cases because more critically ill patients (i.e., most of those with acute MI) may not be able to be recruited prospectively, or otherwise choose to withdraw from the study, resulting in a biased sample. This study is approved by the Institutional Review Board of the University of Pittsburgh.

Inclusion and exclusion criteria

Consecutively enrolled patients meet the following inclusion criteria: (1) 21 years of age or older; (2) chief complaint of non-traumatic chest pain or other atypical, suspicious symptoms requiring ECG evaluation (i.e. shortness of breath); (3) mode of arrival is by EMS transport; and (4) 12-lead ECG obtained prior to ED arrival. There are no restrictions to sex or race. Children and teens (i.e., ≤ 21 years of age) are less likely to have ischemic etiology of chest pain and are not included. Although acute MI is also not prevalent in patients who are 22 to 40 years old, including a representative sample for which true negative values can be tested is equally necessary for our methods and these patients are included. The following patients are excluded: (1) those with traumatic chest pain (e.g., car accident); (2) those arriving at the ED with no prehospital ECG (i.e. either not performed by EMS or if arrival is by private vehicle); and (3) those with un-interpretable 12-lead ECG due to excessive noise or known interpretation confounders (e.g., pacing or left bundle branch block [LBBB]).

Data collection protocol

After completion of patient care and medical documentation by the EMS providers, the following protocol is followed: (1) Subjects meeting the study criteria are identified using custom reporting software in the prehospital electronic patient care record program (emsCharts, Inc., Warrendale, PA). Data regarding age, sex, date/time of dispatch, and responding EMS agency is documented for each case as a linkage-list to be kept separate from the data. (2) The raw XML files of digital ECGs obtained and transmitted by monitors used on the scene are stored and accessed through a hospital-based server. These XML files are stamped for age/sex, date/time, and EMS agency and, therefore, can be matched with the prehospital records in emsCharts. Linked records are assigned a study ID and stored in a research spreadsheet. (4) Patient identifiers are then used to link prehospital data with inhospital data to abstract necessary medical records for that hospital admission (including the initial ECG in the emergency department). (5) Data are collected in the de-identified spreadsheet with only a linkage number for identification of patient cases.

Outcome data

The primary outcome of the study is the presence of acute MI, documented by elevation of cardiac troponin and (1) subsequent development of labile, ischemic ECG changes (e.g., STE) during hospitalization; (2) coronary angiography demonstrating greater than 70% stenosis, with or without treatment; and/or (3) functional cardiac evaluation (stress testing) that demonstrates ECG, echocardiographic, or