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Use of the HEART Pathway with high sensitivity cardiac troponins: A secondary analysis

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ABSTRACT

Objectives: The HEART Pathway combines a decision aid and serial contemporary cardiac troponin I (cTnI) measures to achieve >99% sensitivity for major adverse cardiac events (MACE) at 30 days and early discharge rates >20%. However, the impact of integrating high-sensitivity troponin (hs-cTn) measures into the HEART Pathway has yet to be determined. In this analysis we compare test characteristics of the HEART Pathway using hs-cTnI, hs-cTnT, or cTnI.

Design & methods: A secondary analysis of participants enrolled in the HEART Pathway RCT was conducted. Each patient was risk stratified by the cTn-HEART Pathway (Siemens TnI-Ultra at 0- and 3-h) and a hs-cTn-HEART Pathway using hs-cTnI (Abbott) or hs-cTnT (Roche) at 3-h. The early discharge rate, sensitivity, specificity, and negative predictive value (NPV) for MACE (death, myocardial infarction, or coronary revascularization) at 30 days were calculated.

Results: hs-cTnI measures were available on 133 patients. MACE occurred in 11/133 (8%) of these patients. Test characteristics for the HEART Pathway using serial cTnI vs 3 hour hs-cTnI were the same: sensitivity (100%, 95%CI: 72–100%), specificity (49%, 95%CI: 40–58%), NPV (100%, 95%CI: 94–100%), and early discharge rate (45%, 95%CI: 37–54%). The HEART Pathway using hs-cTnT missed one MACE event (myocardial infarction): sensitivity (91%, 95%CI: 59–100%), specificity (48%, 95%CI: 39–57%), NPV (98%, 95%CI: 91–100%), and early discharge rate (45%, 95%CI: 37–54%).

Conclusions: There was no difference in the test characteristics of the HEART Pathway whether using cTnI or hs-cTnI, with both achieving 100% sensitivity and NPV. Use of hs-cTnT with the HEART Pathway was associated with one missed MACE.

1. Introduction

Accelerated diagnostic pathways (ADPs), such as the HEART Pathway, objectively combine variables from the patient's history, electrocardiogram findings, and cardiac troponin (cTn) measures to risk stratify patients with acute chest pain. These tools are being increasingly used by Emergency Department (ED) providers and have been incorporated into the guidelines for the early risk stratification of patients with acute chest pain [1].

The HEART Pathway is designed to identify patients who can be safely discharged from the ED without stress testing or coronary angiography. To be considered low-risk and eligible for early discharge the HEART Pathway requires a HEART Score of 0–3 and normal serial contemporary cTn at 0 and 3 h [2–4]. In a recently completed clinical trial, the HEART Pathway significantly increased early discharges and decreased hospital lengths of stay and objective cardiac testing (stress testing and coronary angiography) compared to the usual care group. Reductions in healthcare utilization outcomes were achieved by the HEART Pathway without any low-risk patients experiencing adverse cardiac events at 30 days [4].

Abbreviations: cTn, cardiac troponin; MACE, major adverse cardiac events; hs-cTn, high sensitivity cardiac troponin; RCT, randomized controlled trial; NPV, negative predictive; CI, confidence interval; ADP, accelerated diagnostic pathway; ED, emergency department; ACS, acute coronary syndrome; EMR, electronic medical record; MI, myocardial infarction; URL, upper reference limit; NRI, net reclassification improvement.

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While the HEART Pathway has demonstrated excellent sensitivity for adverse cardiac events using contemporary cTn, many health systems in Europe, Canada, and the Asia-Pacific Region are using high sensitivity troponin (hs-cTn) assays, and approval of hs-cTn assays in the United States is expected soon. Recent studies suggest that hs-cTn measures should be used within the context of an ADP [5,6]. However, the impact of integrating hs-cTn measures into the HEART Pathway has yet to be determined. The objective of this secondary analysis is to determine the test characteristics of the HEART Pathway using hs-cTnI and hs-cTnT assays compared to a contemporary cTnI assays.

2. Materials and methods

2.1. Study design

A pre-planned secondary analysis of participants enrolled in the HEART Pathway Randomized Controlled Trial was conducted. Participants were enrolled from September 2012, through February 2014, and all gave written informed consent at the time of study entry. The HEART Pathway trial was approved by the sponsoring organization's Internal Review Board and was registered with clinicaltrials.gov (clinical trial number NCT01665521).

Methods of the HEART Pathway trial have been previously described [4]. Adults presenting to the ED with symptoms suggestive of acute coronary syndrome (ACS) without ST-elevation on ECG were enrolled. Patients were randomized with equal probability to risk stratification using the HEART Pathway or usual care (based on American College of Cardiology/American Heart Association guidelines). In the HEART Pathway arm, ED providers used a clinical decision aid, the HEART (**H**istory **E**CG **A**ge **R**isk factors **T**roponin) score, paired with serial cTn measures at 0 and 3 h to guide disposition decisions.

2.2. Study setting

Participants were enrolled from the ED of (institution name withheld for review), an academic tertiary care center located in the Piedmont Region of North Carolina. The ED is staffed by board certified/eligible emergency physicians 24 h a day, 7 days a week who directly provide patient care and oversee care delivered by residents, and advanced practice clinicians. During the trial enrollment period ED patient volume consisted of approximately 104,000 encounters per year. The cardiac testing modalities that were routinely available to study participants included exercise stress echocardiogram, dobutamine stress echocardiogram, coronary computed tomography angiography, stress nuclear imaging, stress cardiac magnetic resonance imaging, and invasive coronary angiography.

2.3. Participants

Patients ≥21 years old presenting with symptoms suggestive of ACS were screened for enrollment 6 days per week excluding Saturday (80 h/week). Patients for whom their provider orders an ECG and troponin for the evaluation of ACS were eligible for participation. Patients were excluded for new ST-segment elevation ≥1 mm, hypotension, life expectancy <1 year, a non-cardiac medical, surgical, or psychiatric illness determined by the provider to require admission, prior enrollment, non-English speaking, and incapacity or unwillingness to consent.

2.4. Data collection

2.4.1. Patient data

Data elements were collected prospectively in accordance with Standardized Reporting Guidelines [7], standards of Good Clinical Practice, and Key Data Elements and Definitions [8]. Electronic medical records (EMR) were used as the primary source for variables reliably contained in the medical record. For data elements not reliably present in the EMR, study coordinators used REDCap data collection templates to prospectively collect and store data from the patients and their care providers.

Following the index visit and at 30 days, a structured record review was completed. At 30 days a telephone interview using a validated scripted follow-up dialogue was conducted to identify and clarify events since discharge [9]. Events occurring at out-of-network health care facilities were confirmed using a structured review of medical records requested from the outside facility. Participants with a record of ongoing visits in the EMR were considered to have complete follow-up information and were classified based on available data in the medical record. Participants without ongoing visits were considered lost to follow-up at the point of last contact. The Social Security Death Master File was used to search for patients unable to be reached by phone or without EMR data. When a discrepancy between a participant's self-reported event and the medical record was identified, the medical record was considered accurate.

2.4.2. cTn measurement

All study participants had serum cTn measurements performed using the institutional core-lab contemporary assay: the ADVIA Centaur platform TnI-Ultra™ (Siemens, Munich, Germany). This assay has a 99th percentile of the upper reference limit (URL) and 10% coefficient of variation (CV) at 0.040 μg/L (40 ng/L), which was also the clinical threshold for detection of myocardial injury during the study period. Per study protocol, the contemporary cTnI measures were obtained at 0 and 3 h after the patient was evaluated by the ED clinical team and these results were used for clinical and research purposes.

At 3 h an additional blood specimen for research purposes only was collected in a 10 mL lithium heparin plasma tube on willing participants (n = 259). Following collection, blood was centrifuged at 3000 × *g* Relative Centrifugal Force at 4 degrees Celsius for 15 min. Aliquots (1 mL) of plasma were transferred into cryovials and stored in a − 70 degree Celsius Freezer. Samples were shipped on dry ice to Fred Apple's laboratory for hs-cTnI and hs-cTnT analysis. Blood samples were tested using the Abbott ARCHITECT stat hs-cTnI (Abbott Laboratories, Abbott Park, IL, USA) which has URL of 34 ng/L for males and 16 ng/L for females, a limit of detection of 1.9 ng/L, and a 10% CV at 6 ng/L. Samples were also tested using the Roche Elecsys 2010 hs-cTnT (Roche Diagnostics, Risch-Rotkreuz, Switzerland), which has a URL of 14 ng/L, limit of detection of 5 ng/L, and 10% CV at 13 ng/L. Previously established gender specific URLs of 20 ng/L for males and 13 ng/L for females were used for this analysis [10]. A sensitivity analysis was conducted using different gender specific URLs (15.5 ng/L for males and 9 ng/L for females) established by Saenger, et al. [11]. For this analysis all cTnI values above the URL, or any hs-cTn value above the gender specific URL were considered consistent with myocardial injury and "high risk" when utilized as part of the HEART Pathway. Given that these samples were tested for hs-cTn asynchronously with clinical care, results were not available to the patient's medical care team.

2.4.3. HEAR scores

Participants randomized to the HEART Pathway arm were risk stratified by attending ED providers using the History, Electrocardiogram, Age, and Risk factors (HEAR) components of the HEART score [12–15], and serial cTn measures at 0 and 3 h. To complete a HEAR score, the provider utilized the participant's ECG and a study worksheet at the patient's bedside. Patients were risk stratified (as low-risk or at-risk) based on the HEAR score and cTn results, utilizing the three different assays discussed above (see Fig. 1). Patients were considered low-risk if HEAR scores were 0–3 and cTn results were below the URL. Patients with a HEAR score >4 or a cTn above the URL regardless of HEAR score were considered at-risk. Based on our prior analyses, a HEAR score of 3 or less with two negative cTn measures (a low-risk assessment by the HEART Pathway) is associated with a <1% risk of MACE at 30 days [2–4].

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