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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-hours) and a hs-cTn-HEART Pathway using hs-cTnI (Abbott) or hs-cTnT (Roche) at 3-hours. 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

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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.

Keywords

troponin; chest pain; acute coronary syndrome; HEART Pathway

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 hours [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].

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 hours 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 hours 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 hours/week). Patients for whom their provider order an ECG and troponin for the evaluation of ACS were eligible for participation. Patients were excluded for new ST-segment elevation ≥ 1mm, 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 hours after the patient was evaluated by the ED clinical team and these results were used for clinical and research purposes.

At 3 hours an additional blood specimen for research purposes only was collected in a 10ml 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 minutes. 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 hours. 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 Figure 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].

2.5 Study Measures

MACE was defined as the composite of death, myocardial infarction (MI), or coronary revascularization within 30 days of presentation, based on the standardized reporting guidelines and key data elements and definitions [7, 8]. The Universal Definition of Myocardial Infarction was used to define myocardial infarction; a gradual rise of cTnI above the URL with a CV <10% and gradual fall with at least one of the following: a. ischemic symptoms; b. new pathologic Q waves on the ECG; c. acute ischemic ECG changes (ST segment elevation or depression); d. myocardial imaging demonstrating a new regional wall motion abnormality [16]. Coronary revascularization was defined as coronary artery bypass grafting, stent placement, or other percutaneous coronary intervention. A consensus of two reviewers (CDM, BCH), blinded to HEART Pathway risk assessments, adjudicated elements required to determine the occurrence of MACE. Adjudicators were provided index and discharge records including participant's cTnI measures, follow-up call information, outside records obtained from follow-up, and study definitions. Disagreements were settled by the two reviewers achieving consensus or the involvement of a third reviewer.

2.6 Data Analysis

The percentage of patients identified as safe for early discharge (low-risk) by the three different cTn assays and the HEART Pathway was calculated. The sensitivity, specificity, and positive and negative predictive values for MACE were also determined. Exact 95% binomial confidence intervals were computed. Patients with incomplete follow up were considered to be free of 30-day MACE events. The performance of the HEART Pathway with each assay was compared using McNemar's test and net reclassification improvement (NRI). The HEART Pathway RCT was powered to detect a 15% difference in objective cardiac testing between randomization arms with 80% power at the 5% two-sided level of significance and an expected loss to follow up rate of 10%. Statistical analysis was performed using SAS 9.4 (Cary, North Carolina).

3. Results

From September 2012 to February 2014, 282 patients with symptoms suggestive of ACS were enrolled in the HEART Pathway RCT, of which 259 had blood specimens available for hs-cTn analysis. In the HEART Pathway, arm blood samples were available on 133/141 for hs-cTn measurement (Figure 2). Follow-up for 30 day events was complete for 97.7% (253/259) of participants and 98.4% (131/133) of patients randomized to the HEART Pathway arm. MACE occurred in 20/259 (7.7%) patients in the main cohort: there were no deaths, 14 patients had MI, and 6 patients had coronary revascularization without MI. In the HEART Pathway arm, MACE occurred in 11/133 (8.2%): with no deaths, 7 MIs, and 4 revascularizations without MI. Patient characteristics are summarized in Table 1. When used without a HEAR Score the cTnI, hs-cTnI, and hs-cTnT assays had low sensitivity (60%, 65%, and 60% respectively) for MACE (with most missed events classified as coronary revascularization without MI). Performance of the cTnI, hs-cTnI, and hs-cTnT assays in the entire cohort (n=259) is presented in Table 2. The sensitivity analysis comparing different hs-cTnT gender specific URLs is presented in Appendix 1.

The HEART Pathway had the same test characteristics for MACE using serial cTnI measures or a 3-hour hs-cTnI measure. Both identified 60/133 patients (45.1%, 95% CI 36.5–54.0%) as low-risk. Of these low-risk patients, none had MACE events at 30 days, yielding a sensitivity and NPV of 100% (95% CI 71.5–100% and 95% CI 94.0–100% respectively). Using hs-cTnT, the HEART Pathway identified the same proportion of patients as low-risk (60/133, 45.1%, 95% CI 36.5–54.0%). Of these patients, one patient had an adjudicated index NSTEMI, yielding a sensitivity of 90.9% (95% CI 58.7–99.8%) and NPV of 98.3% (95% CI 91.1–100%). The performance characteristics of the HEART Pathway using the different assays are summarized in Table 3. The use of cTnI or hs-cTnI for the HEART Pathway compared to hs-cTnT, was able to correctly reclassify 1 patient without MACE as low-risk and 1 patient with MACE as high-risk, producing a NRI of 0.099 (95% CI −0.072, 0.270). The test characteristics of the HEART Pathway using the 3 different assays were similar (p=1.0).

4. Discussion

Results of this secondary analysis demonstrate that the HEART Pathway has high sensitivity and NPV for 30-day MACE whether a contemporary or high sensitivity cTn assay using gender specific cut points is utilized. Use of serial cTnI measures at 0 and 3 hours or a single 3-hour hs-cTnI with the HEART Pathway was associated with 100% sensitivity and NPV for 30-day MACE. Use of the HEART Pathway with the hs-cTnT assay resulted in misclassifying one patient with MACE as low-risk. The test characteristics for the HEART Pathway were similar regardless of the assay used. However, it is important to note that this study was not powered to detect small differences, so further evaluation is needed to definitively conclude that the performance of the HEART Pathway which each of these assays is the same.

Numerous studies have demonstrated that hs-cTn assays are more sensitive for the early detection and early rule out of MI than contemporary cTn assays [17–19]. For example, Neumann et al., have confirmed that hs-cTnI measured at baseline and 1 hour after presentation have a very high negative (99.0%) and positive predictive value (87.1%) for AMI; enabling rapid, safe treatment [20]. However, the improved sensitivity of these newer assays comes at the cost of specificity [21]. hs-cTn assays are less specific than contemporary assays for MI, as more patients with non-ACS conditions have hs-cTn elevations that are missed with the contemporary assay [22]. While patients with hs-cTn elevations have increased downstream mortality, regardless of cause [23, 24], the optimal testing and management strategies for non-ACS patients with hs-cTn elevations are unclear. Therefore, some have been concerned about the impact of integrating hs-cTn assays into an ADP, such as the HEART Pathway, which has previously demonstrated a sensitivity >99% for 30-day MACE using serial contemporary cTn measures. They have hypothesized that hs-cTn use could decrease specificity and lead to more patients with diagnostic and therapeutic dilemmas [25, 26].

Our results suggest that the test characteristics of the HEART Pathway were similar regardless of the assay utilized. In fact, use of the cTnI and hs-cTnI assays with the HEART Pathway resulted in identical test characteristics; 100% sensitivity and 49% specificity for

30-day MACE. Based on prior studies of the HEART Pathway, high sensitivity for MACE was expected [2–4]. However, it is particularly interesting that the specificity and proportion of patients identified as low-risk by the HEART Pathway were not decreased by hs-cTnI assay use. All of the patients in our cohort with elevated hs-cTn measurements were identified as high-risk based on their HEAR Score or contemporary cTnI results. These findings are consistent with the results of Aldous et, al. which demonstrated no significant difference in the sensitivity or specificity for MACE of an ADP when using a new generation point of care cTnI versus a hs-cTnI assay [27]. The finding from our study are significant given the current lack of availability of hs-cTn assays in the US and the concern that lack of these assays significantly hampers our ability to perform chest pain risk stratification. Furthermore, this study suggests the HEART Pathway may be utilized without modification in places where hs-cTnI assays are currently available and in the US (when available).

Use of a hs-cTnT assay with the HEART Pathway resulted in a lower sensitivity and specificity for MACE than use of the cTnI and hs-cTnI assays. However, these differences were small, because they resulted from the change in risk classification of just 2 patients. The HEART Pathway using hs-cTnT missed one patient with an adjudicated diagnosis of a Type II non-ST-segment elevation MI. This patient, who is described in Table 4, had a HEAR score of 2 and an undetectable (<3 ng/L) hs-cTnT measure at 3 hours, but had an elevated cTnI and hs-cTnI at the same blood draw. Recent studies have demonstrated the possibility that autoantibodies interfere with the measurement of cTnT by blocking the immunoreactivity of anti-cTnT antibodies to the I-T-C complex released from the myocardium after injury; thus resulting in falsely low concentrations in blood [28]. This one case of missed MACE resulted in a sensitivity of 91% for MACE at 30 days. In addition, one patient with a HEAR Score <3 had an elevated hs-cTnT result despite normal cTnI and hs-cTnI results. This resulted in a slightly lower specificity for MACE (48.4%) for the HEART Pathway using hs-cTnT. The reclassification of one patient without MACE as low-risk and 1 patient with MACE as high-risk resulted in a net reclassification index near zero with a 95% confidence including zero (indicating that no significant reclassification occurred).

Use of hs-cTn assays alone, without the HEART Pathway, yielded poor sensitivity for 30-day MACE underscoring the importance of using these biomarkers within the context of an ADP. This is consistent with several prior studies suggesting that these biomarkers should be combined with an ADP to achieve sufficient sensitivity for 30-day adverse events. For example, in the APACE cohort, a study of 909 patients with serial hs-cTnI measures at 0 and 2 hours resulted in a sensitivity of 82.7% sensitivity for 30-day ACS events [5]. However, when hs-cTnI results used as part of an ADP (in combination with a clinical decision aid and ECG data), the sensitivity for adverse events increased to >99%. Another recent study, by Body et al., reported that hs-cTnT measurements along with a non-ischemic ECG (but without additional clinical data) resulted in an adverse event (death, MI, and all coronary revascularization events) rate of 3.6%, well above the missed event rate that most providers find acceptable [6, 29, 30].

Most of the adverse events missed by the hs-cTn assays in this analysis were revascularization events without MI. While coronary revascularization improves mortality

and re-infarction rates among patients with an acute MI, studies are less clear regarding the role of revascularization in patients without acute MI [31]. Among patients with stable coronary artery disease, the COURAGE trial and recent systematic reviews have failed to show a decreased risk of MI or death among patients receiving revascularization compared to medical management [32–35]. Many have interpreted these results as evidence that ED risk stratification tool, such as ADPs and biomarkers, do not need to detect patients with revascularization events. However, it is important to consider that the COURAGE trial's control group is medical management not early discharge from the ED. Patients who are discharged from the ED based on a low-risk ADP assessment are unlikely to be started on maximal medical management. Therefore, it should not be assumed that an ADP identifying these patients as low-risk will result in equivalent outcomes.

In order to enhance the value of care for patients with acute chest pain it is important that we have tools capable of safely identifying low-risk patients for early discharge from the ED, focusing cardiac testing and hospitalizations on higher-risk patients. The ability of the HEART Pathway to identify patients for early discharge is likely to reduce costs and radiation exposure (from stress testing and angiography), and decrease false positive and non-diagnostic testing. As the US healthcare system switches to value based payment models, tools which can avoid potentially unnecessary testing and hospitalizations will be increasingly implemented. The results of this analysis when viewed in the context of our prior studies suggests that whether high-sensitivity assays or contemporary assays are used, the HEART Pathway can enhance the value of chest pain care. However, the HEART Pathway's ability to identify 44–45% of patients as low-risk leaves substantial room for improvement. New decision aids or modifications of the HEART Pathway should pursue an increase in the proportion of patients identified as low-risk while maintaining a sensitivity >99% for MACE.

A relatively small sample size and enrollment from a single center may limit the generalizability of this analysis. A low occurrence of MACE rate in our cohort results in wide confidence intervals around the point estimate of sensitivity and limits comparisons between the different assays used for the HEART Pathway. Furthermore, the large number of patients screened and excluded from enrollment in the HEART Pathway RCT may have produced a selection bias. In the HEART Pathway RCT, baseline blood samples were not collected for hs-cTn analysis. This prevents us from evaluating the HEART Pathway using a serial (0- and 3-hour) hs-cTn strategy versus serial cTnI measures. In addition, the 3-hour blood sample collected for hs-cTn analysis was not collected in 23 patients enrolled, which may have introduced a selection bias. Another potential limitation of this analysis is incomplete follow-up on 4 patients, which may have caused underestimation of MACE. However, none of these patients were found in the Social Security Death Master File. Furthermore, the likelihood of MACE occurring shortly after discharge among these patients seems low given that all of the known MACE events occurred during the index visit.

5. Conclusions

In conclusion, there were no differences in the test characteristics of the HEART Pathway whether using cTnI or hs-cTnI, with both achieving 100% sensitivity and NPV for 30-day

MACE and a specificity of 49%. While confirmation in a larger cohort is needed, our data suggests that the HEART Pathway may be utilized without modification in places where hs-cTnI assays are already available and when they become available in the U.S. In addition, the performance of the HEART Pathway when using hs-cTnT was very similar to the performance of the HEART Pathway using hs-cTnI or cTnI. When used alone (without the HEART Pathway), hs-cTn measures at 3 hours were insufficiently sensitive for MACE, mostly missing patients with revascularization events. This study provides additional evidence that hs-cTn assays should be used in the context of an ADP.

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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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Appendix 1

Comparison of the test characteristics of the hs-cTnT assay using different gender-specific URLs suggested as by Apple et al. (Male: 20 ng/L, Female: 13 ng/L) and Saenger et al. (Male: 15.5 ng/L, Female: 9 ng/L)

Test characteristics of the hs-cTnT at 3 hours for MACE in the entire cohort using gender specific URLs from Apple et al vs Saenger et al.*

URL	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Apple et al.	60.0% (36.1–80.9%)	93.3% (89.4–96.1%)	42.9% (24.5–62.8%)	96.5% (93.3–98.5%)
Saenger et al.	70.0% (45.7–88.1%)	87.9% (83.0–91.7%)	32.6% (19.1–48.5%)	97.2% (94.1–99.0%)

* Table excludes 2/259 patients without second cTn measure, and 29/259 with second clinical cTn measure at ≥6 hour

Performance characteristics of the HEART Pathway using hs-cTnT gender specific URLs from Apple et al vs Saenger et al.

URL	% Low-Risk (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Apple et al.	45.1% (36.5–54.0%)	90.9% (58.7–99.8%)	48.4% (39.2–57.6%)	13.7% (6.8–23.8%)	98.3% (91.1–100%)
Saenger et al.	45.1% (36.5–54.0%)	90.9% (58.7–99.8%)	48.4% (39.2–57.6%)	13.7% (6.8–23.8%)	98.3% (91.1–100%)

Highlights

- The HEART Pathway using cTnI or hs-cTnI achieved 100% sensitivity and NPV for MACE.
- HEART Pathway test characteristics using hs-cTnT were similar to cTnI and hs-cTnI.
- Use of the HEART Pathway with hs-cTnT did result in one missed MACE.
- Without the HEART Pathway, hs-cTn measures were insufficiently sensitive.

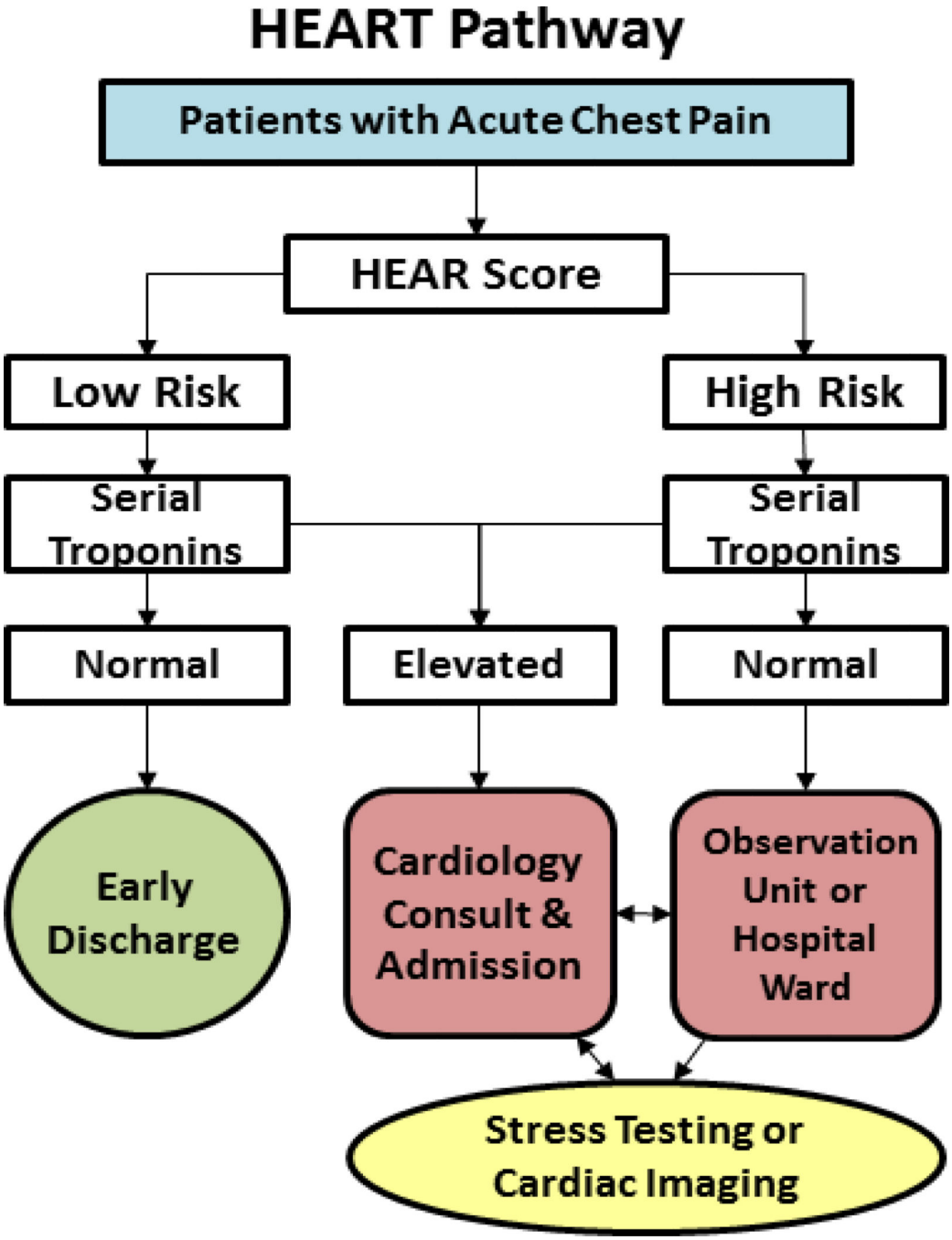

Figure 1.
HEART Pathway algorithm

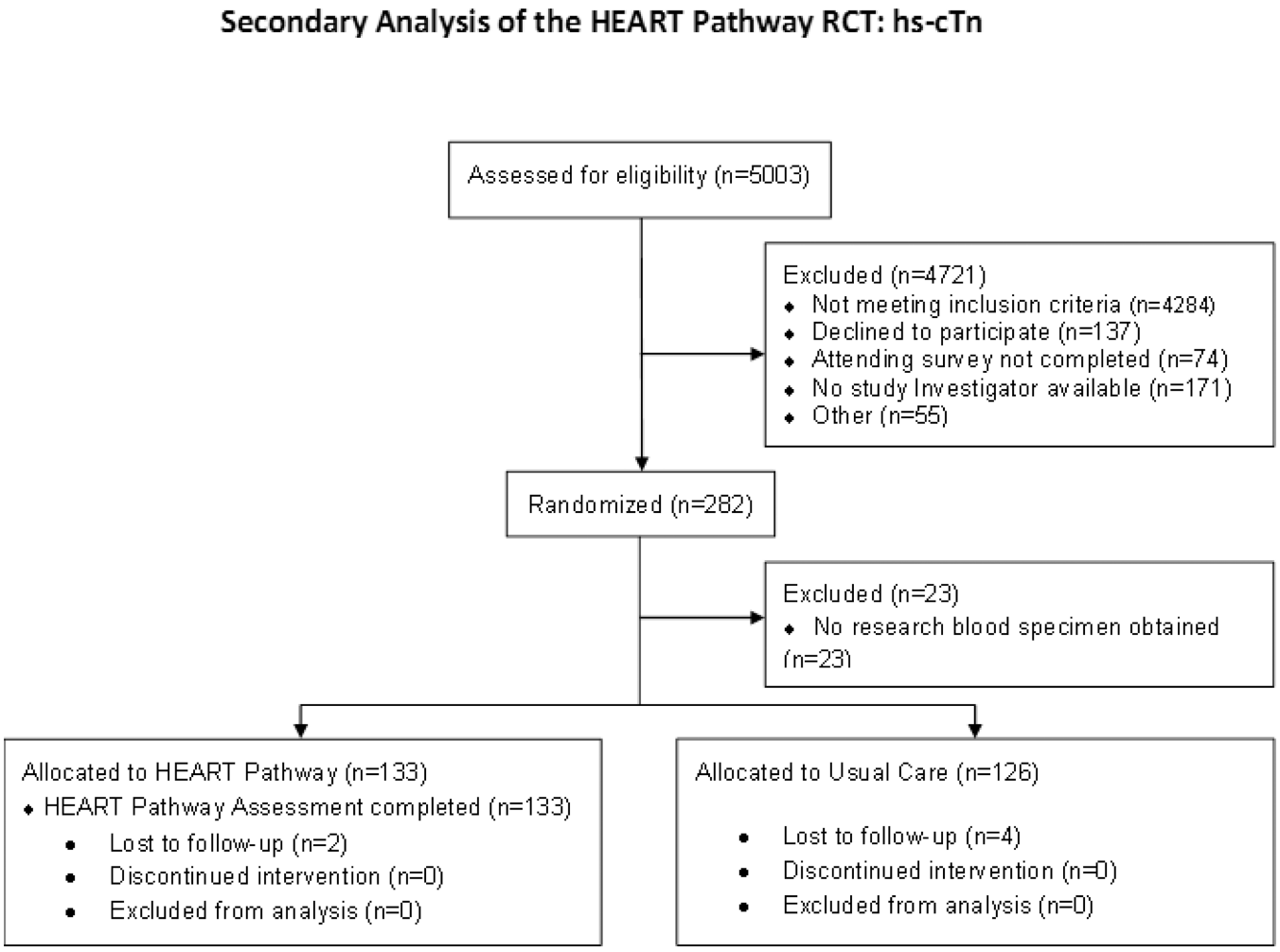

Figure 2.
Enrollment flow diagram

Table 1

Characteristics of the Cohort and HEART Pathway Arm.

Patient Characteristics	Main Cohort N=259	HEART Arm N=133
Age—mean ±SD*	53.6 + 12.0	53.6 + 12.0
Gender		
Female	145 (56.0)	77 (57.9)
Race‡‡		
Caucasian	173 (66.8)	87 (65.4)
African American	81 (31.3)	43 (32.3)
Asian	1 (0.4)	1 (0.8)
Native American	2 (0.8)	1 (0.8)
Other	2 (0.8)	1 (0.8)
Ethnicity		
Hispanic	5 (1.9)	1 (0.8)
Not Hispanic	254 (98.1)	132 (99.2)
Risk Factors		
Current smoking	66 (25.5)	37 (27.8)
Recent Cocaine (last 90 days)	6 (2.3)	3 (2.3)
Hypertension	145 (56.0)	74 (55.6)
Hyperlipidemia	115 (44.4)	60 (45.1)
Diabetes	54 (20.9)	31 (23.3)
Family history of coronary disease	98/257 (38.1)	44/132 (33.3)
BMI >30 (kg/m^2)	137 (52.9)	67 (50.4)
TIMI risk score >1	116 (44.8)	59 (44.4)
Prior Coronary Disease	46 (17.8)	24 (18.1)
Prior MI	41 (15.8)	20 (15.0)
Prior PCI	32 (12.4)	14 (10.5)
Prior CABG	10 (3.9)	7 (5.3)
Prior Cerebral Vascular Disease	11 (4.3)	3 (2.3)
Prior Peripheral Vascular Disease	8 (3.1)	4 (3.0)
Insurance status		
Insured	194/257 (75.5)	100/133 (75.2)
Private	126 (65.0)	64 (64.0)
Medicare	40 (20.6)	21 (21.0)
Medicaid	28 (14.4)	13 (13.0)
Uninsured	63/257 (24.5)	33/133 (24.8)

Table 2

Test characteristics of the cTnI, hs-cTnI and hs-cTnT for MACE in the entire cohort.

cTn Assay	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
cTnI at 0 hrs	50.0% (27.2–72.8%)	96.2% (93.0–98.3%)	52.6% (28.9–75.6%)	95.8% (92.5–98.0%)
cTnI at 3 hrs *	60.0% (32.2–83.7%)	99.1% (96.7–99.9%)	81.8% (48.2–97.7%)	97.2% (94.1–99.0%)
hs-cTnI at 3 hrs	65.0% (40.8–84.6%)	95.4% (91.9–97.7%)	54.2% (32.8–74.5%)	97.0% (94.0–98.8%)
hs-cTnT at 3 hrs	60.0% (36.1–80.9%)	93.3% (89.4–96.1)	42.9% (24.5–62.8%)	96.5% (93.3–98.5%)

* Excludes 2/259 patients without second cTn measure, and 29/259 with second clinical cTn measure at ≥6 hour

Table 3

Performance characteristics of the HEART Pathway using cTnI, hs-cTnI, and hs-cTnT,

Risk Stratification Strategy	% Low-Risk (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
HEART Pathway cTnI	45.1% (36.5–54.0%)	100% (71.5–100%)	49.2% (40.0–58.4%)	15.1% (7.8–25.4%)	100% (94.0–100%)
HEART Pathway hs-cTnI	45.1% (36.5–54.0%)	100% (71.5–100%)	49.2% (40.0–58.4%)	15.1% (7.8–25.4%)	100% (94.0–100%)
HEART Pathway hs-cTnT	45.1% (36.5–54.0%)	90.9% (58.7–99.8%)	48.4% (39.2–57.6%)	13.7% (6.8–23.8%)	98.3% (91.1–100%)

Table 4

Characteristics of the patient with missed MACE using the HEART Pathway with hs-cTnT.

Age	Sex	Race	CAD history	HEAR Score	1st cTnI ng/L (URL)	2nd cTnI ng/L (URL)	hs-cTnI ng/L (URL)	hs-cTnT ng/L (URL)	Event Type	Notes
36	Male	Caucasian	None	2	10 (40)	71 (40)	35.1 (34)	<3 (20)	Type II NSTEMI	MI thought to be secondary to a tachydysrhythmia. No coronary angiography was performed.

CAD= coronary artery disease, MACE= major adverse cardiac events, NSTEMI=Non ST-segment elevation Myocardial Infarction