5-12-2021

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Recommended Citation

Aurora L, McCord J, Nowak R, Giannitsis E, Christenson R, DeFilippi C, Lindahl B, Christ M, Body R, Jacobsen G, and Mueller C. Prognostic Utility of a Modified HEART Score When Different Troponin Cut-points Are Used. Crit Pathw Cardiol 2021.

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Critical Pathways in Cardiology Journal Publish Ahead of Print

DOI: 10.1097/HPC.0000000000000262

Prognostic Utility of a Modified HEART Score When Different Troponin Cut-points Are Used

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Funding: This research was supported by Roche Diagnostics

Conflicts of Interest: L.A.: None J.M.: Research support: Roche, Siemens, Abbott, Beckman. Consulting fees: Roche, Siemens, Beckman R.N.: Research grants: Roche, Abbott, Siemens, Beckman Coulter, Ortho Diagnostics Consulting: Roche, Abbott, Siemens, Beckman Coulter, Ortho Diagnostics G.E.: Honoraria for lectures from Astra Zeneca, Bayer Vital, Roche Diagnostics, Boehringer Ingelheim, Brahms. Consultancy for Roche Diagnostics, Boehringer Ingelheim and Brahms. Research grants from Daiichi Sankyo, Roche Diagnostics, and Deutsche Herzstiftung. R.C.: Consultant fees from Siemens Healthineers, Roche Diagnostics, Quidel Diagnostics, Becton Dickinson, Beckman Coulter, Sphingotec. Research funding from Siemens Healthineers, Roche Diagnostics, Quidel Diagnostics, Becton Dickinson, Beckman Coulter, Spingotec, Abbott Diagnostics, Ortho Diagnostics, Brainbox and Mitsubushi. C.D.: Consulting for Abbott diagnostics, FujiRebio, Ortho clinical diagnostics, Roche diagnostics, Siemens Healthineers, Quidel. Royalties from UpToDate. B.L.: None M.C.: None R.B.: Advisory boards: LumiraDx, Abbott Point of Care, Singulex, Beckman Coulter, Roche, Creavo. Speaker fees: Roche, Ortho, Abbott, Siemens, Beckman, ET Healthcare (joint AACC symposium) Research grants: Abbott Point of Care, Singulex Reagents donated for research: Roche, Singulex, Alere, Siemens. G.J.: None C.M.: Research support/grants from the Swiss National Science Foundation, the Swiss Heart Foundation, the Cardiovascular Research Foundation Basel, the University Hospital Basel, the University of Basel, Abbott, Beckman Coulter, BRAHMS, Ortho Clinical, Quidel, Roche, Siemens, and Sphingotec, as well as speaker/consulting honoraria from Acon, Amgen, Astra Zeneca, Bayer, Boehringer Ingelheim, Osler, Novartis, Roche, and Sanofi.

Running head: Modified HEART Score and Troponin Cut-points

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Abstract

Background: Although the recommended cut-point for cardiac troponin (cTn) is the 99th percentile, many institutions use cut-points that are multiples higher than the 99th percentile for diagnosing acute myocardial infarction (AMI). Prior studies have shown that patients with a HEART score (HS) ≤ 3 and normal serial cTn values (modified HS) are at low risk for adverse events. This study aimed to evaluate the prognostic utility of the HS when various cTn cut-points are used.

Methods: This was a sub-study of TRAPID-AMI, a multicenter, international trial evaluating a rapid rule-out AMI study using high sensitivity cTnT (hs-cTnT). 1,282 patients were evaluated for AMI from 12 centers in Europe, United States of America, and Australia from 2011-2013. Blood samples of hs-cTnT were collected at presentation and 2 hours, and each patient had a HS calculated. The US Food and Drug Administration approved 99th percentile for hs-cTnT (19 ng/L) was used.

Results: There were 213 (17%) AMIs. Within 30 days, there were an additional 2 AMIs and 8 deaths. The adverse event rates at 30 days (death/AMI) for a HS ≤ 3 and non-elevated hs-cTnT over 2 hours using increasing hs-cTnT cut-points ranged from 0.6% to 5.1%.

Conclusions: Using the recommended 99th percentile cut-point for hs-cTnT, the combination of a HS ≤ 3 with non-elevated hs-cTnT values over 2 hours identifies a low-risk cohort who can be considered for discharge from the emergency department without further testing. The prognostic utility of this strategy is greatly lessened as higher hs-cTnT cut-points are used.

Keywords: high sensitivity troponin, hs-cTnT, modified HEART score, HEART score

Introduction

Cardiac disease is the leading cause of death in the United States,[1] and annually there are more than 780,000 acute myocardial infarctions (AMIs) diagnosed.[2] There are approximately 8 to 10 million people that are evaluated each year for possible AMI in the United States.[3] This comprises 5% to 10% of emergency department (ED) visits, out of which the majority are not diagnosed with AMI.[4] Moreover, approximately 2% of AMI cases are missed and discharged from the ED, which subsequently leads to adverse outcomes.[5] There is a substantial amount of cost, time, and resources that are utilized in this evaluation including laboratory tests, stress tests, and cardiac imaging.

Cardiac troponin (cTn) measurements are fundamental in the evaluation of AMI. Over time, cTn has emerged as the preferred cardiac marker in evaluation for AMI due to improved sensitivity and risk stratification.[6] Based on the Fourth Universal Definition of Myocardial Infarction consensus document published in 2018, AMI diagnostic criteria include rising and falling patterns of cTn with at least one value that exceeds the 99th percentile limit of a normal reference population.[7] Guidelines from multiple professional societies recommend using the 99th percentile as the appropriate cTn cut-point for determination of AMI.[7-9] In fact, use of the 99th percentile has been associated with improved outcomes and increase in the frequency of diagnosis of AMI.[10,11] This recommendation was made in hopes of establishing a standard in the diagnosis of AMI; however, it is not commonly utilized worldwide.

Many institutions use cTn cut-points that are much higher than the 99th percentile, which directly affects patient management and resource utilization. In a study of 276 hospitals in 31 countries, there was a large variability across laboratories in the cTn threshold that was used, with more than 25% using cut-points > 5 times the 99th percentile and 15% using cut-points > 10 times the

99th percentile.[12] A study of 824 hospitals in the United States showed that only 49% used the 99th percentile.[13] The CARdiac MArker Guidelines Uptake study demonstrated that only 52% of European laboratories and 45% of United States laboratories utilized the 99th percentile limit for diagnosis of AMI.[14]

Risk scores such as the Emergency Department Assessment of Chest Pain Score, HEART score (HS) and Thrombolysis in Myocardial Infarction (TIMI) score are used to predict the probability of future major adverse cardiac events (MACE) in patients presenting to the ED who are evaluated for possible AMI.[15] The original HS was calculated in such a fashion where a patient could have an elevated high sensitivity cardiac troponin (hs-cTn) greater than the 99th percentile and still be considered low-risk. A modified-HS (m-HS) strategy has been described that identifies a very low-risk population with low hs-cTn measurements and a HS ≤ 3 who could be considered for discharge from the ED without stress testing or cardiac imaging.[16] We specifically studied the HS in combination with hs-cTnT to identify patients at low risk for 30-day MACE. The aim of this study was to describe the prognostic utility of the m-HS when various cut-points of hs-cTnT are used.

Methods

Study Design and Population

The study consisted of a sub-study analysis of the TRAPID-AMI (High Sensitivity Cardiac Troponin T assay for RAPID Rule-out of Acute Myocardial Infarction) study, which was a multicenter, international diagnostic study in the ED evaluating a rapid rule-out AMI protocol over 1 hour using changes in hs-cTnT (Roche Diagnostics, Penzberg, Germany). Details of the study have previously been published.[17] There were 1,282 patients evaluated in the ED for possible AMI from 12 centers in Europe, the United States of America, and Australia studied

from 2011 to 2013. Patients were interviewed by research personnel to determine demographics and presenting symptoms at time of presentation to the ED. Patients were excluded if they had renal failure requiring hemodialysis and all participants provided written informed consent. The study was approved by the Henry Ford Hospital Institutional Review Board. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

Blood samples for determination of hs-cTnT (Roche Diagnostics) and cardiac troponin I-ultra (cTnI-ultra) (Siemens Healthcare, Tarrytown, NY) were collected at presentation and 1, 2, and 4-14 hours. Thereafter, centrifugation samples were frozen at -80°C until assayed using the Elecsys 2010 (Roche Diagnostics) instrument. The limit of detection, 10% coefficient of variation, and 99th percentile of a reference population have been reported at 5 ng/L, 13 ng/L, and 14 ng/L, respectively.[18] The 14 ng/L is the 99th percentile value used outside of the US. The cTnI-ultra assay was performed using the Siemens ADVIA Centaur immunoassay system with a limit of detection, 10% coefficient of variation, and 99th percentile of 6 ng/L, 30 ng/L, and 40 ng/L, respectively.[19,20]

The diagnosis of AMI was centrally adjudicated by 2 independent cardiologists in accordance with the universal definition of AMI, and adjudicated by a third cardiologist in case of disagreement, using all available clinical information and serial measurements of cTnI-ultra.[21] AMI was diagnosed when there was evidence of myocardial necrosis on the basis of a significant rise or fall pattern of the cTnI concentration in a setting consistent with myocardial ischemia (ischemic symptoms, electrocardiogram [ECG] changes, or imaging evidence). The 99th percentile of this assay (40 ng/L) was used as a cutoff for myocardial necrosis. An absolute

change of 20 ng/L or greater with the cTnI-ultra assay during the study was used to define a significant rise and fall.[22]

Modified HS Criteria

Elements of the traditional HS have been described in prior studies.[23,24] The calculation of the HS includes elements of the history, ECG, age, and risk factors. Each of these categories are assigned a 0 (low risk), 1 (moderate risk), or 2 (high risk) and then added into a composite score. The history was categorized retrospectively as either high, moderate, or low suspicion for AMI by using a modified Diamond-Forrester prediction rule[25] including the presence of chest pressure, worsening with physical activity, and radiation to arms or shoulders. Relief of symptoms with rest, used in the original Diamond-Forrester tool, was not used because this information was not collected. For the history component, patients were assigned 2 points if they met 3, 1 point if they met 2, and 0 points if they met 1 or none of the criteria.

For ECG findings, 2 points were given if there was horizontal or down-sloping ST depression ≥ 0.5 mm in 2 contiguous leads or ST elevation ≥ 1 mm in 2 contiguous leads (if V2-V3 was involved, then the following applied: ≥ 2 mm in males ≥ 40 years, ≥ 2.5 mm in males < 40 years, and ≥ 1.5 mm in females); 1 point was given for either right or left bundle branch block, left ventricular hypertrophy, or ventricular paced rhythm; 0 point was given if the ECG did not meet any of the criteria of the other 2 categories. ECGs were categorized by independent cardiologists who were blinded to all clinical information.

Patients ≥ 65 years of age were assigned 2 points, those 45 to 64 years were given 1 point, and patients < 45 years received 0 points. For risk factors, patients were assigned 2 points for ≥ 3 cardiac risk factors or a history of coronary artery disease (prior AMI, percutaneous coronary intervention, or coronary artery bypass grafting surgery), 1 point for 1 to 2 cardiac risk factors,

and 0 point for 0 risk factors. Cardiac risk factors included in this analysis were hypertension, diabetes mellitus, and smoking history. Hyperlipidemia and family history were not included because this information was not collected. Each patient had a HS calculated. The 30-day death/AMI rate was reported using the m-HS at various cut-points multiples higher than the 99th percentile. These calculations were done for the 99th percentile used outside of the US (14 ng/L) and for the US Food and Drug Administration (FDA) approved 99th percentile (19 ng/L).[26]

Statistical Analysis

The baseline demographic and comorbidity variables have been compared between the elevated and non-elevated HS patients using a 2-sample t-test for numerical data and chi-square test for categorical data. Within each troponin setting, the AMI/death status at 30 days has been compared between the elevated and non-elevated HS patients using the chi-square test when there were no expected cell counts < 5, otherwise using Fisher's exact test. Resulting p-values < 0.05 have been considered statistically significant for this descriptive study.

Results

There were 1,282 patients evaluated, of which there were 213/1282 (16.6%) AMIs, consisting of 21 ST-segment elevation myocardial infarctions, and 192 non-ST-segment elevation myocardial infarctions, and 8 deaths. At 30 days, there were 2 additional AMIs diagnosed, yielding 217 (16.9%) patients with a 30-day MACE (6 patients had an AMI and subsequently died). Because of missing HS data, 47 patients were excluded, leaving 1,235 patients to be evaluated with the modified HS.

Baseline demographics are shown by HS status without consideration of hs-cTnT values (Table 1). Patients with higher HS were older and more commonly had cardiac risk factors. The adverse event rates at 30 days (death/AMI) are shown for elevated HS ≥ 4, non-elevated HS ≤ 3, and

non-elevated hs-cTnT over the various time intervals (hours) using various hs-cTnT cut-points (Table 2 and Supplemental Digital Content Table 1 http://links.lww.com/HPC/A233), using both 19 ng/L and 14ng/L as the upper reference limit. As higher hs-cTnT cut-points were used, the 30-day MACE rate increased for those deemed to be low risk by the modified HS. The 30-day death/AMI rate for different hs-cTnT cutoffs alone without taking modified HS in consideration was also calculated (Table 3). These results highlighted the increasing risk with higher hs-cTnT cut-points and were observed to be numerically higher compared to the combined use of the HS. The net reclassification improvement (NRI) comparing performance of lowest cut point of hs-cTnT to different hs-cTnT cut points including 99th percentile (19 ng/L) was generated with Table 3 used as reference (Supplemental Digital Content Table 2 http://links.lww.com/HPC/A233). Specifically, we focused on time interval 0-(4-14) hours for each cut-point.

Discussion

Early diagnosis of AMI is crucial for initiation of appropriate therapies. The evaluation for possible AMI requires prompt clinical assessment along with objective data including cardiac biomarker assays, especially cTn, which has emerged as the gold standard in the diagnosis of AMI.[27] The prognostic significance of a m-HS using various hs-cTnT cutoffs was analyzed. Our findings demonstrate that 30-day MACE rate for the m-HS with serial hs-cTnT measurements ranged from 0.7%-5.7% depending on the cut-point, with the lowest MACE rate using the recommended 99th percentile cut-point. This is clinically relevant as many institutions use the HS to help guide risk stratification and early discharge from the ED, especially for low risk patients.

In fact, American Heart Association guidelines recommend utilization of clinical risk scores for patients presenting with chest pain to aid with clinical decision making.[28] There is an accepted miss rate for 30-day MACE at 1% or less.[29]

Multiple studies have applied a serial testing troponin strategy with HS and demonstrated a MACE rate of 0%-2%. A study by Baugh et al demonstrated 0% MACE using 99th percentile troponin cut-point in patients undergoing standardized clinical assessment and management plan for chest pain based on the HS.[30] The TRAPID-AMI study utilized hs-cTnT and showed a 0.2% 30-day MACE rate using a 0/1-hour protocol.[16] Wang et al compared the performance of risk scores such as HS, Global Registry of Acute Coronary Events, TIMI and showed < 1% MACE rate using serial troponin-I (TnI) measurements at 4-6 hour intervals.[31] The initial study validating the HS showed MACE rate of 0.4% in low HS (0-3) with cTnT (fourth generation) or cTnI using 99th percentile cutoff limit.[32] Similarly, a study looking at the HEART pathway comprised HS with serial cTnI test at 0 and 3 hours and showed 0% MACE rate using 99th percentile reference value.[33] Mahler et al demonstrated MACE rate of 0.6% in patients with low risk HS using TnI 99th percentile cutoff to support decreased utility of cardiac testing in those with low probability of AMI.[34] An analysis comparing HS and North American Chest Pain Rule identified chest pain patients for early discharge and demonstrated < 1% MACE rate using 99th percentile cTnI cut-point.[35]

Despite the Universal Definition of Myocardial Infarction recommendation for use of cTn concentration at the 99th percentile of a normal reference population as the decision level for diagnosis of AMI, there is substantial variation observed across institutions, which can impact patient management.[12] Consequently, there is an important need for standardization of cTn threshold, which affects rapid rule out AMI protocols, testing strategies, costs, and length of

hospitalization. Therefore, studies have looked at the prognostic utility of hs-cTn across different cutoffs. A prospective, multicenter, observational study of patients with suspected AMI utilized measurement of hs-cTnI to identify patients at low and high risk for AMI. Atellica IM TnIH and ADVIA Centaur TNIH (Siemens Healthineers) assays were utilized, measuring cTn ≥ limit of detection at the 99th percentile upper reference limit.[36] This study revealed threshold of < 5 ng/l that identified a low risk cohort at presentation, with sensitivities of 98.6% and negative predictive values of 99.6% for MACE at 30 days across both assays. The European Society of Cardiology Guidelines recommend the use of 0/1-hour algorithm for AMI evaluation which utilizes values less than the 99th percentile with using of hs-cTn.[37]

Using the recommended 99th percentile cut-point for hs-cTnT, the combination of a HS with non-elevated hs-cTnT values identifies a low-risk cohort who can be considered for discharge from the ED without further testing. The prognostic utility of this strategy is greatly lessened as higher hs-cTnT cut-points are used. When comparing the MACE rates of patients with a HS ≤ 3 to those with a HS ≥ 4, the absolute difference between MACE rates was greater as higher hs-cTnT cut-points were used. However, using these higher cut-points led to higher MACE rates which suggests that the lower cut-points are desirable to identify a low-risk cohort who could be directly discharged without further cardiac testing. Santi et al presented a low risk population who could be discharged without any further cardiac risk stratification, revealing 512 (37.2%) patients who met criteria for low HS in combination with hs-cTnT (99th percentile cutoff) with no subsequent MACE (0%).[24] Prevalence of MACE was noted to increase with higher HS, only occurring in patients with a HS > 3. Studies have also shown that very low hs-cTn levels may also obviate the need for risk scores. Neumann et al reported on over 22,000 patients who were evaluated for possible AMI in the ED and found that patients with very low levels of hs-cTnI or

hs-cTnT (well below the 99th%) at presentation, that were not changing significantly within 2 hours, were associated with a low likelihood of AMI and MACE (0.2%) at 30 days.[38]

Study Limitations

Our study does have some limitations to consider. HS was calculated retrospectively, and patients were not managed based on this risk score. In addition, we did not evaluate gender-specific cut-offs which have been advocated.[39] Hyperlipidemia and family history were not collected so could not be used to calculate the HS.

Conclusions

Using the recommended 99th percentile cut-point for hs-cTnT, the combination of a HS with non-elevated hs-cTnT values identifies a low-risk cohort who can be considered for discharge from the ED without further testing. The prognostic utility of this strategy is greatly lessened as higher hs-cTnT cut-points are use.

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Table 1: Baseline characteristics

	All Patients (N=1235)	HEART Score ≥ 4 Patients (N=612)	HEART Score ≤ 3 Patients (N=623)	Comparison P-value
Age, years	61.0 (50.0-74.0)	71.0 (61.0-78.0)	53.0 (45.0-62.0)	<0.001*
Male gender	771 (62.4%)	397 (64.9%)	374 (60.0%)	0.079
Race				
White	1043 (84.5%)	548 (89.5%)	495 (79.5%)	<0.001*
Black	133 (10.8%)	37 (6.0%)	96 (15.4%)	
Other	59 (4.8%)	27 (4.4%)	32 (5.1%)	
Comorbidities				
Hypertension	777 (62.9%)	496 (81.0%)	281 (45.1%)	<0.001*
Diabetes	263 (21.3%)	188 (30.7%)	75 (12.0%)	<0.001*
Hypercholesterolemia	480 (38.9%)	314 (51.3%)	166 (26.6%)	<0.001*
Current smoker	277 (22.4%)	97 (15.8%)	180 (28.9%)	<0.001*
Smoking history	731 (59.2%)	377 (61.6%)	354 (56.8%)	0.088
History of coronary revascularization	375 (30.4%)	323 (52.8%)	52 (8.3%)	<0.001*
History of PCI	275 (22.3%)	231 (37.7%)	44 (7.1%)	<0.001*
History of CABG	100 (8.1%)	92 (15.0%)	8 (1.3%)	<0.001*
History of AMI	305 (24.7%)	255 (41.7%)	50 (8.0%)	<0.001*
History of stable angina pectoris	144 (11.7%)	129 (21.1%)	15 (2.4%)	<0.001*

History of unstable angina pectoris	158 (12.8%)	126 (20.6%)	32 (5.1%)	<0.001*
Cerebrovascular disease	127 (10.3%)	86 (14.1%)	41 (6.6%)	<0.001*
History of congestive heart failure	107 (8.7%)	91 (14.9%)	16 (2.6%)	<0.001*
Presenting data and vital signs				
Hours from onset to presentation	2.8 (1.5-5.3)	2.9 (1.7-5.5)	2.6 (1.4-5.2)	0.037*
Hours from onset to first blood draw	3.4 (2.2-6.0)	3.6 (2.3-6.2)	3.3 (2.0-5.9)	0.072
Creatinine (mg/dL)	0.8 (0.7-1.0)	0.9 (0.7-1.1)	0.8 (0.7-0.9)	<0.001*
Systolic blood pressure (mm Hg)	141.0 (127.0-157.0)	144.0 (128.0-160.0)	140.0 (126.0-153.0)	0.001*
Diastolic blood pressure (mm Hg)	81.0 (72.0-90.0)	80.0 (70.0- 90.0)	83.0 (74.0-93.0)	<0.001*
Heart rate	76.0 (66.0-88.0)	75.0 (64.0-88.0)	77.5 (67.0-88.0)	0.062
ECG findings and HEART score				
Atrial fibrillation	87 (7.0%)	68 (11.1%)	19 (3.0%)	<0.001*
Sinus rhythm	1130 (91.5%)	528 (86.3%)	602 (96.6%)	<0.001*
Other rhythm	18 (1.5%)	16 (2.6%)	2 (0.3%)	<0.001*
Left ventricular hypertrophy	65 (5.3%)	46 (7.5%)	19 (3.0%)	<0.001*
LBBB	36 (2.9%)	29 (4.7%)	7 (1.1%)	<0.001*
RBBB	55 (4.5%)	49 (8.0%)	6 (1.0%)	<0.001*

Paced ventricular complex	23 (1.9%)	23 (3.8%)	0 (0.0%)	<0.001*
Pathologic Q-waves	119 (9.6%)	87 (14.2%)	32 (5.1%)	<0.001*
ST-segment elevation	60 (4.9%)	53 (8.7%)	7 (1.1%)	<0.001*
ST-segment depression	164 (13.3%)	154 (25.2%)	10 (1.6%)	<0.001*
T wave-inversion	183 (14.8%)	133 (21.7%)	50 (8.0%)	<0.001*
Normal ECG	893 (72.3%)	312 (51.0%)	581 (93.3%)	<0.001*
Medication History				
Aspirin	633 (51.3%)	409 (66.8%)	224 (36.0%)	<0.001*
Anticoagulants	187 (15.1%)	131 (21.4%)	56 (9.0%)	<0.001*
Diuretics	304 (24.6%)	222 (36.3%)	82 (13.2%)	<0.001*
ACE inhibitor	369 (29.9%)	257 (42.0%)	112 (18.0%)	<0.001*
Angiotensin receptor blocker	198 (16.0%)	131 (21.4%)	67 (10.8%)	<0.001*
Beta blocker	471 (38.1%)	338 (55.2%)	133 (21.3%)	<0.001*
Calcium antagonist	236 (19.1%)	165 (27.0%)	71 (11.4%)	<0.001*
Nitrates	376 (30.4%)	263 (43.0%)	113 (18.1%)	<0.001*
Platelet inhibitor	170 (13.8%)	125 (20.4%)	45 (7.2%)	<0.001*
Anti-arrhythmic	64 (5.2%)	52 (8.5%)	12 (1.9%)	<0.001*
Other	535 (43.3%)	377 (61.6%)	158 (25.4%)	<0.001*

ACE, angiotensin-converting enzyme; AMI, acute myocardial infarction; CABG, coronary artery bypass graft; ECG, electrocardiogram; LBBB, left bundle branch block; PCI, percutaneous coronary intervention; RBBB right bundle branch block.

Categorical data is given as frequency (percent of column) and numerical data is given as median (interquartile range).

*Statistically significant, $P < 0.05$

Table 2: AMI/Death for modified HEART score ≤ 3 and ≥ 4 using different hs-cTnT cut-points (19 ng/L) over various time intervals

hs-cTnT (ng/L) < various cut-points over different time intervals		Death/AMI n (%) within 30 days		Comparison
		HS ≥ 4	HS ≤ 3	P-value
99th% (19)	0 hour	38 (9.9%)	13 (2.4%)	<0.001
	0-2 hours	15 (4.6%)	3 (0.6%)	<0.001
	0 – (4-14) hours	9 (3.0%)	3 (0.7%)	0.034
2X (38)	0 hour	79 (15.6%)	23 (4.1%)	<0.001
	0-2 hours	49 (11.0%)	13 (2.5%)	<0.001
	0 – (4-14) hours	34 (8.3%)	10 (2.2%)	<0.001
3X (57)	0 hour	96 (17.8%)	32 (5.5%)	<0.001
	0-2 hours	66 (13.8%)	18 (3.4%)	<0.001
	0 – (4-14) hours	57 (12.9%)	14 (3.1%)	<0.001
4X (76)	0 hour	100 (18.3%)	41 (7.0%)	<0.001
	0-2 hours	76 (15.4%)	24 (4.5%)	<0.001
	0 – (4-14) hours	69 (14.9%)	16 (3.5%)	<0.001
5X (95)	0 hour	109 (19.5%)	46 (7.7%)	<0.001
	0-2 hours	84 (16.7%)	27 (5.1%)	<0.001
	0 – (4-14) hours	74 (15.8%)	19 (4.1%)	<0.001
6X (114)	0 hour	116 (20.5%)	46 (7.7%)	<0.001
	0-2 hours	93 (18.2%)	31 (5.8%)	<0.001
	0 – (4-14) hours	79 (16.7%)	22 (4.7%)	<0.001
7X (133)	0 hour	120 (21.1%)	46 (7.7%)	<0.001

	0-2 hours	96 (18.6%)	32 (5.9%)	<0.001
	0 – (4-14) hours	81 (17.0%)	24 (5.1%)	<0.001
8X (152)	0 hour	122 (21.3%)	47 (7.9%)	<0.001
	0-2 hours	100 (19.3%)	33 (6.1%)	<0.001
	0 – (4-14) hours	85 (17.7%)	24 (5.1%)	<0.001
9X (171)	0 hour	126 (21.9%)	48 (8.0%)	<0.001
	0-2 hours	103 (19.7%)	35 (6.5%)	<0.001
	0 – (4-14) hours	91 (18.7%)	27 (5.7%)	<0.001
10X (190)	0 hour	130 (22.4%)	49 (8.2%)	<0.001
	0-2 hours	107 (20.3%)	37 (6.8%)	<0.001
	0 – (4-14) hours	93 (19.0%)	27 (5.7%)	<0.001

99^{th}%, 99^{th} percentile; AMI, acute myocardial infarction; HS, HEART score; hs-cTnT, high-sensitivity cardiac troponin T.

Statistically significant, $P < 0.05$

Table 3: AMI/Death using different hs-cTnT cut-points over various time intervals

hs-cTnT (ng/L) < various cut-points	over different time intervals	Death/AMI n (%) within 30 days
99th% (19)	0 hour	51 (5.5%)
	0-2 hours	18 (2.2%)
	0 – (4-14) hours	12 (1.6%)
2X (38)	0 hour	102 (9.5%)
	0-2 hours	62 (6.5%)
	0 – (4-14) hours	44 (5.1%)
3X (57)	0 hour	128 (11.4%)
	0-2 hours	84 (8.4%)
	0 – (4-14) hours	71 (7.9%)
4X (76)	0 hour	141 (12.4%)
	0-2 hours	100 (9.8%)
	0 – (4-14) hours	85 (9.2%)
5X (95)	0 hour	155 (13.4%)
	-2 hours	111 (10.7%)
	0 – (4-14) hours	93 (10.0%)
6X (114)	0 hour	162 (14.0%)
	0-2 hours	124 (11.8%)
	0 – (4-14) hours	101 (10.8%)
7X (133)	0 hour	166 (14.2%)
	0-2 hours	128 (12.2%)

	0 – (4-14) hours	105 (11.1%)
8X (152)	0 hour	169 (14.5%)
	0-2 hours	133 (12.6%)
	0 – (4-14) hours	109 (11.5%)
9X (171)	0 hour	174 (14.8%)
	0-2 hours	138 (13.0%)
	0 – (4-14) hours	118 (12.3%)
10X (190)	0 hour	179 (15.2%)
	0-2 hours	144 (13.5%)
	0 – (4-14) hours	120 (12.5%)

99^{th}%, 99^{th} percentile; AMI, acute myocardial infarction; hs-cTnT, high-sensitivity cardiac troponin T.