



XI congresso nazionale

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ROMA 24-26 MAGGIO 2018

Dolore toracico e dimissione in sicurezza: Heart Pathway

Dott. Spampinato Michele Domenico

Medico in formazione specialistica in Medicina d'Emergenza-Urgenza

Università degli Studi di Ferrara





AMERICAN
COLLEGE *of*
CARDIOLOGY

Which Emergency Department Chest Pain Patients Do Not Need Further Diagnostic Testing After a Normal Troponin?

Mar 18, 2016 | Jaimi Greenslade, PhD; Louise Cullen, MBBS, PhD

Expert Analysis

European Heart Journal (2002) **23**, 1153–1176

doi:10.1053/euhj.2002.3194, available online at <http://www.idealibrary.com> on **IDEAL**[®]

Task Force Report

Task force on the management of chest pain

**Members: L. Erhardt (Chairman), J. Herlitz (Secretary), L. Bossaert, M. Halinen,
M. Keltai, R. Koster, C. Marcassa, T. Quinn and H. van Weert**

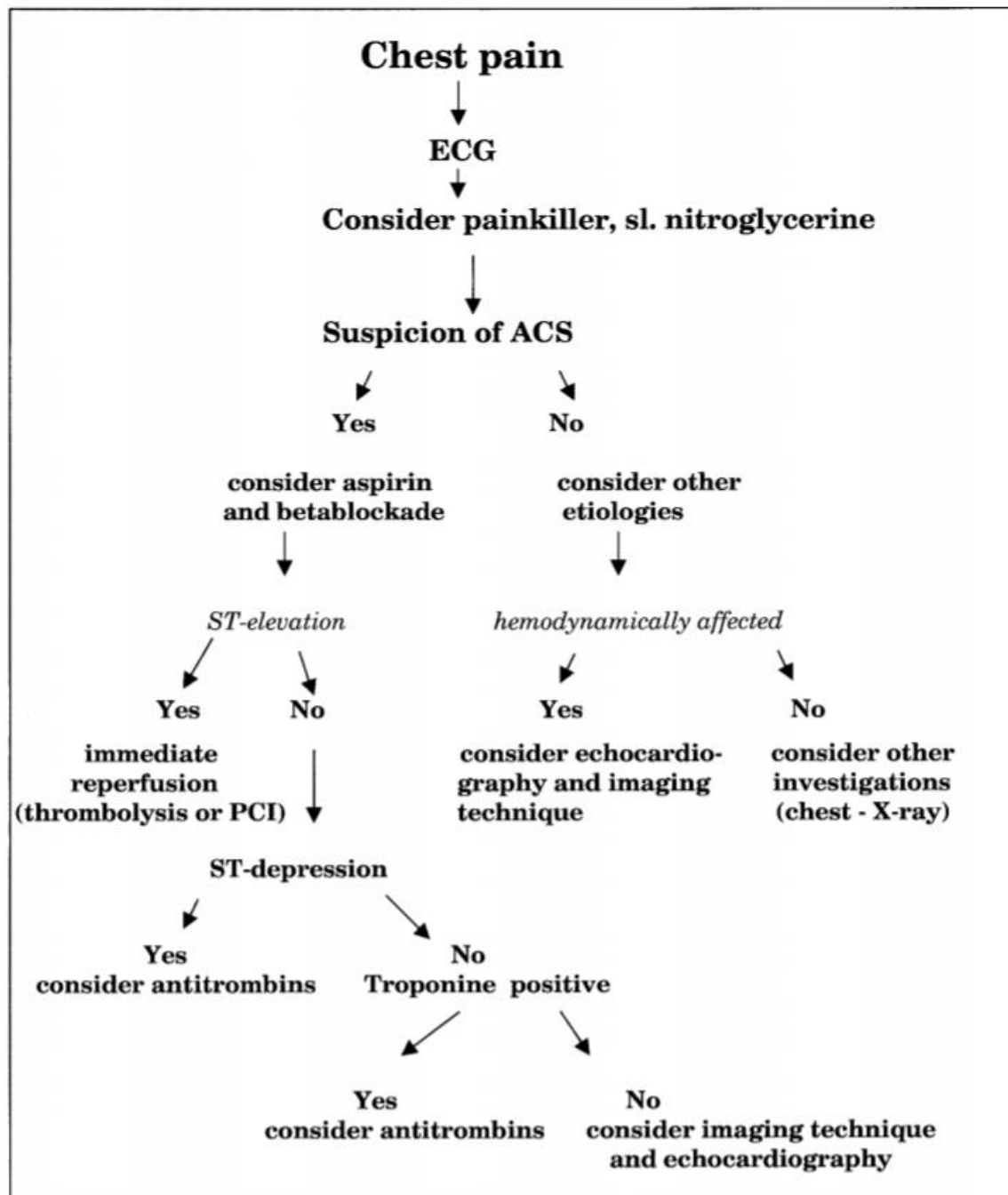


Figure 3 Evaluation and treatment of patients with chest pain in the emergency department.



European Heart Journal (2016) **37**, 267–315
doi:10.1093/eurheartj/ehv320

ESC GUIDELINES

2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC)

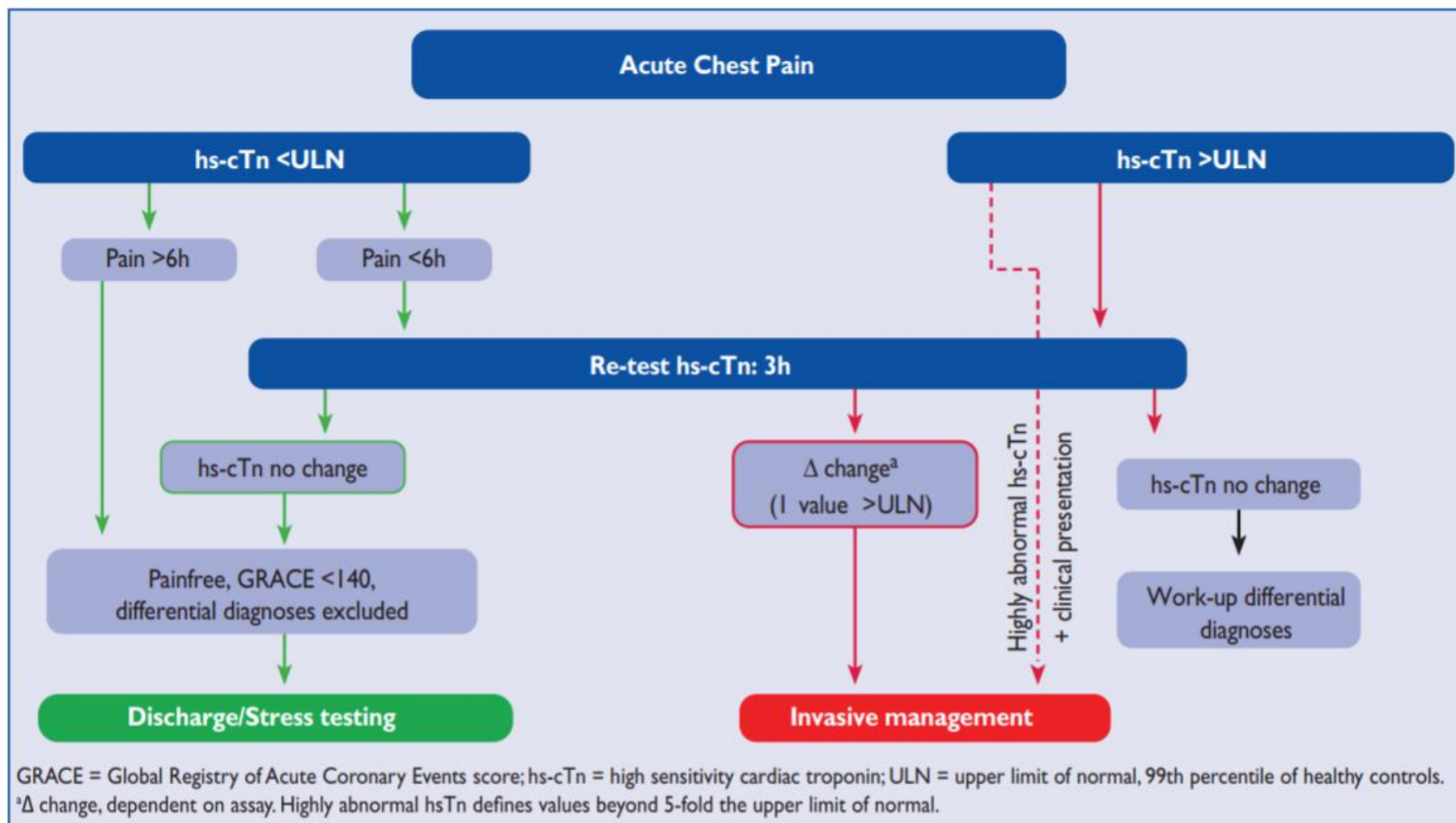


Figure 2 0 h/3 h rule-out algorithm of non-ST-elevation acute coronary syndromes using high-sensitivity cardiac troponin assays.

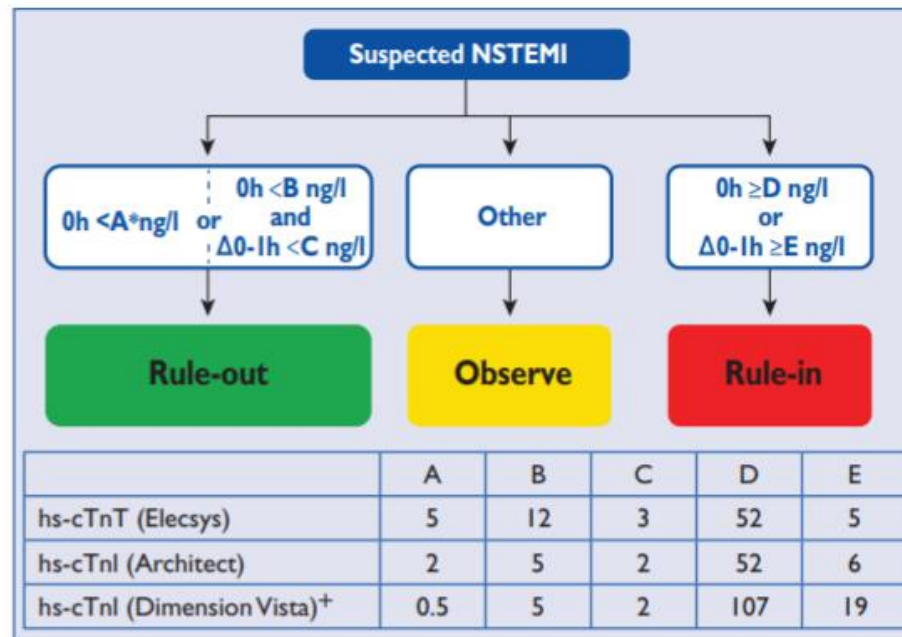


Figure 3 0 h/1 h rule-in and rule-out algorithms using high-sensitivity cardiac troponins (hs-cTn) assays in patients presenting with suspected non-ST-elevation myocardial infarction (NSTEMI) to the emergency department. 0 h and 1 h refer to the time from first blood test. NSTEMI can be ruled-out already at presentation, if the hs-cTn concentration is very low. NSTEMI can also be ruled-out by the combination of low baseline levels and the lack of a relevant increase within 1 h. Patients have a high likelihood for NSTEMI if the hs-cTn concentration at presentation is at least moderately elevated or hs-cTn concentrations show a clear rise within the first hour. Cut-off levels are assay-specific. Cut-off levels for other hs-cTn assays are in development. *Only applicable if chest pain onset >3h, ⁺At the time of the publication of the guideline not yet commercially available.

Table 5 Characteristics of the 0 h/3 h and the 0 h/1 h algorithms

| | 0h/3 h algorithm | 0h/1 h algorithm |
|---|---|--|
| Negative predictive value for acute MI | 98–100% | 98–100% |
| Positive predictive value for acute MI | Unknown, depending on delta change and assay | 75–80% |
| Effectiveness ^a | ++ | +++ |
| Feasibility | ++ requires GRACE score | +++ |
| Challenges | Pain onset cannot be reliably quantified in many patients | Cut-off levels are assay-specific and different from the 99th percentile |
| Validation in large multicentre studies | + | +++ |
| Additional advantages | Already used clinically | Shorter time to decision |

GRACE = Global Registry of Acute Coronary Events; MI = myocardial infarction.

^aEffectiveness is quantified by the percentage of consecutive chest pain patients clearly classified as rule-out or rule-in of acute MI (i.e., approximately 60% for the 0 h/3 h algorithm and approximately 75% for the 0 h/1 h algorithm).

Recommendations for diagnosis, risk stratification, imaging and rhythm monitoring in patients with suspected non-ST-elevation acute coronary syndromes

| Recommendations | Class ^a | Level ^b | Ref. ^c |
|---|--------------------|--------------------|--------------------|
| Diagnosis and risk stratification | | | |
| It is recommended to base diagnosis and initial short-term ischaemic and bleeding risk stratification on a combination of clinical history, symptoms, vital signs, other physical findings, ECG and laboratory results. | I | A | 28, 109– 112 |

ACUTE CORONARY SYNDROMES

Intervention in acute coronary syndromes: do patients undergo intervention on the basis of their risk characteristics?
The Global Registry of Acute Coronary Events (GRACE)

K A A Fox, F A Anderson Jr, O H Dabbous, P G Steg, J López-Sendón, F Van de Werf, A Budaj, E P Gurfinkel, S G Goodman, D Brieger, on behalf of the GRACE investigators

.....

Heart 2007;**93**:177–182. doi: 10.1136/hrt.2005.084830

BMJ Open Should patients with acute coronary disease be stratified for management according to their risk? Derivation, external validation and outcomes using the updated GRACE risk score

Keith A A Fox,¹ Gordon FitzGerald,² Etienne Puymirat,^{3,4,5,6} Wei Huang,² Kathryn Carruthers,¹ Tabassome Simon,^{7,8,9,10,11} Pierre Coste, Jacques Monsegu,¹² Philippe Gabriel Steg,^{13,14,15} Nicolas Danchin,^{3,4,5,6} Fred Anderson²

Does Simplicity Compromise Accuracy in ACS Risk Prediction? A Retrospective Analysis of the TIMI and GRACE Risk Scores

Krishna G. Aragam^{1,3}, Umesh U. Tamhane^{1,3}, Eva Kline-Rogers¹, Jin Li¹, Keith A. A. Fox², Shaun G. Goodman³, Kim A. Eagle¹, Hitinder S. Gurm^{1*}

1 Division of Cardiovascular Medicine, University of Michigan, Ann Arbor, Michigan, United States of America, **2** Cardiovascular Research, Division of Medical and Radiological Sciences, The University of Edinburgh, Edinburgh, Scotland, **3** Canadian Heart Research Centre and Terrence Donnelly Heart Centre, Division of Cardiology, St Michael's Hospital, University of Toronto, Toronto, Ontario, Canada



European Heart Journal (2005) 26, 865–872
doi:10.1093/eurheartj/ehi187



Clinical research

TIMI, PURSUIT, and GRACE risk scores: sustained prognostic value and interaction with revascularization in NSTEMI-ACS

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and Ricardo Seabra-Gomes

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Received 21 November 2004; revised 24 January 2005; accepted 27 January 2005; online publish-ahead-of-print 11 March 2005

Journal of the American College of Cardiology
© 2010 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 55, No. 14, 2010
ISSN 0735-1097/10/\$36.00
doi:10.1016/j.jacc.2009.09.071

STATE-OF-THE-ART PAPER

Acute Coronary Syndrome

Emerging Tools for Diagnosis and Risk Assessment

Benjamin M. Scirica, MD, MPH

Boston, Massachusetts

Chest pain in the emergency room: value of the HEART score

A.J. Six, B.E. Backus, J.C. Kelder

“How often do we miss the diagnosis of nSTE-ACS in patients with nonspecific chest pain, resulting in a seriously adverse outcome?”

Chest pain in the emergency room: value of the HEART score

A.J. Six, B.E. Backus, J.C. Kelder

Table 1. Composition of the HEART score for chest pain patients in the emergency room.

| HEART score for chest pain patients | | Score |
|-------------------------------------|---|-------|
| History | Highly suspicious | 2 |
| | Moderately suspicious | 1 |
| | Slightly suspicious | 0 |
| ECG | Significant ST depression | 2 |
| | Nonspecific repolarisation disturbance | 1 |
| | Normal | 0 |
| Age | ≤65 year | 2 |
| | 45-65 year | 1 |
| | <45 year | 0 |
| Risk factors | ≥3 risk factors or history of atherosclerotic disease | 2 |
| | 1 or 2 risk factors | 1 |
| | No risk factors known | 0 |
| Troponin | >2x normal limit | 2 |
| | 1-2x normal limit | 1 |
| | ≤normal limit | 0 |
| | | Total |

Chest pain in the emergency room: value of the HEART score

A.J. Six, B.E. Backus, J.C. Kelder

Netherlands Heart Journal, Volume 16, Number 6, June 2008

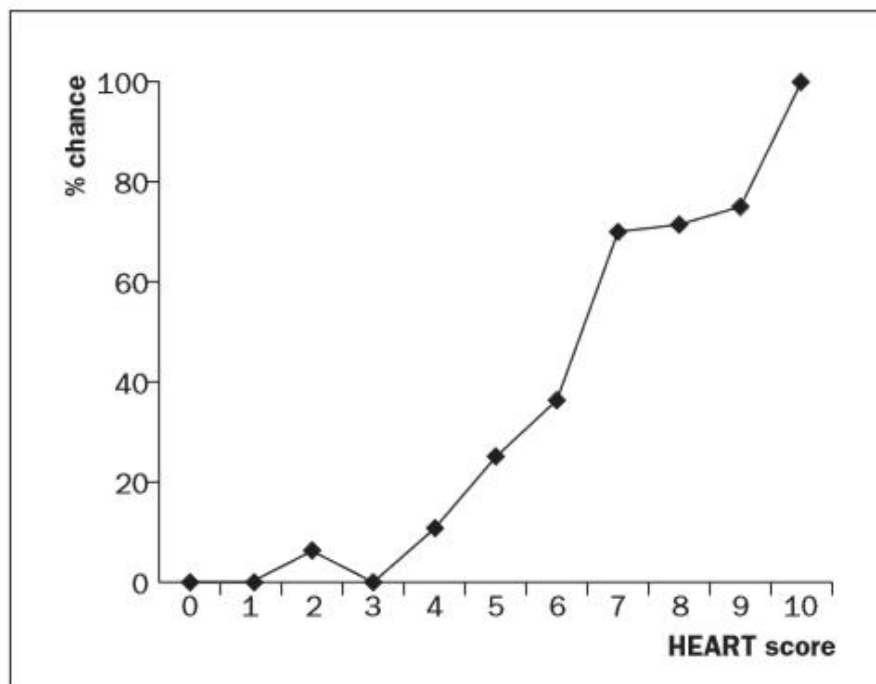







Figure 3. Chances of reaching the combined endpoint in each HEART category.

Endpoints

Endpoints in this study were acute myocardial infarction (AMI), percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG) and death plus a combined endpoint of AMI, PCI, CABG and death.

A score of 0-3 points holds a risk of 2.5% of reaching an endpoint

A retrospective external validation study of the HEART score among patients presenting to the emergency department with chest pain

Matthew Jay Streitz¹  · Joshua James Oliver¹  · Jessica Marie Hyams¹  · Richard Michael Wood¹ · Yevgeniy Mikhaylovich Maksimenko² · Brit Long¹  · Robert Michael Barnwell¹ · Michael David April¹ 

EM - ORIGINAL

The HEART score with high-sensitive troponin T at presentation: ruling out patients with chest pain in the emergency room

Luca Santi¹ · Gabriele Farina² · Annagiulia Gramenzi³ · Franco Trevisani³ · Margherita Baccini⁴ · Mauro Bernardi³ · Mario Cavazza²

Table 3 Performance of the HEART score with high-sensitive troponin

| HEART score | Risk class | Se (95 % CI) | Sp (95 % CI) | PPV (95 % CI) | NPV (95 % CI) |
|------------------|--------------|------------------|------------------|------------------|------------------|
| MACE at 30 days | | | | | |
| ≤3 | Low | 100 (98.2–100) | 43.7 (40.8–46.6) | 23.8 (21.0–26.8) | 100 (99.1–100) |
| 4–6 | Intermediate | 87.4 (82.1–91.6) | 71.4 (68.7–74.0) | 35.0 (28.5–41.5) | 97.0 (96.0–98.0) |
| 7–10 | High | 73.3 (66.7–79.2) | 85.1 (82.9–87.1) | 46.3 (39.4–53.2) | 94.8 (93.5–96.1) |
| MACE at 180 days | | | | | |
| ≤3 | Low | 100 (98.4–100) | 28.5 (25.9–31.2) | 21.9 (16.6–27.2) | 100 (99.8–100) |
| 4–6 | Intermediate | 87.0 (81.9–91.0) | 72.6 (69.9–75.1) | 38.8 (32.5–45.1) | 96.5 (95.4–97.6) |
| 7–10 | High | 70.4 (64.1–76.3) | 85.7 (83.6–87.7) | 49.7 (40.2–56.5) | 93.5 (92.1–94.9) |

SE sensitivity, Sp specificity, PPV positive predictive value, NPV negative predictive value, CI confidence interval

The HEART score for early rule out of acute coronary syndromes in the emergency department: a systematic review and meta-analysis

Van Den Berg and Body

3

European Heart Journal: Acute Cardiovascular Care
1–9

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DOI: 10.1177/2048872617710788

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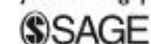


Table 2. Characteristics of included studies.

| Study | Year | Country | Study design | Number of sites | Study period |
|----------------------------------|------|--------------------------|----------------------------|-----------------|--------------------------------------|
| Backus et al. ⁸ | 2010 | Netherlands | Retrospective cohort study | 4 | 1 Jan–31 Mar 2006 |
| Fesmire et al. ¹⁴ | 2012 | USA | Retrospective cohort study | 1 | 13-month period |
| Backus et al. ⁹ | 2013 | Netherlands | Prospective cohort study | 10 | Oct 2008–Nov 2009 |
| Six et al. ¹⁵ | 2013 | 9 Asia-Pacific countries | Retrospective cohort study | 14 | Nov 2007–Dec 2010 |
| Melki and Jernberg ¹⁶ | 2013 | Sweden | Retrospective cohort study | 1 | 1 Jan–12 Feb 2009 |
| Marcoon et al. ¹⁷ | 2013 | USA | Retrospective cohort study | 1 | 1999–2009 |
| Visser et al. ¹⁸ | 2014 | Netherlands | Prospective cohort study | 1 | 1 Dec 2012–31 Jul 2013 |
| Leite et al. ¹⁹ | 2015 | Portugal | Retrospective cohort study | 1 | 23–29 Jan 2012 and 23–29 Jul 2012 |
| Carlton et al. ²⁰ | 2015 | UK | Retrospective cohort study | 1 | Jul 2012–Aug 2013 |
| Bodapati et al. ²¹ | 2016 | Australia | Retrospective cohort study | 1 | 1 Jan 2013–16 May 2013 |
| Sun et al. ²² | 2016 | USA | Retrospective cohort study | 8 | 1 Jun 1999–Aug 2001 |
| Santi et al. ²³ | 2016 | Italy | Retrospective cohort study | 1 | 1 Jan–30 Jun 2014 |

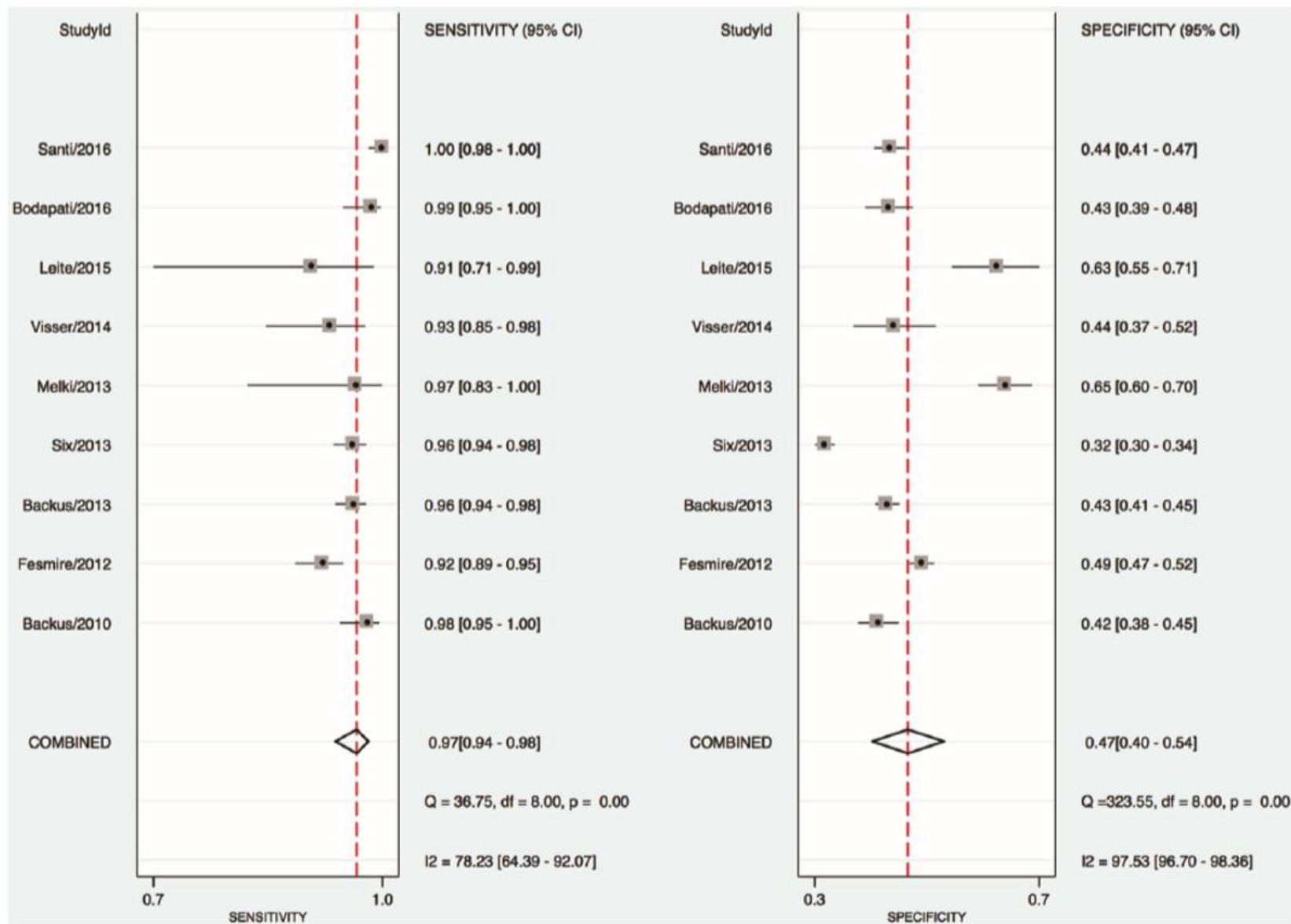


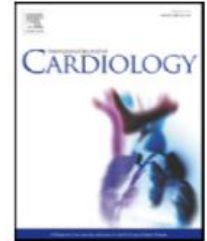
Figure 3. Forest plot of the HEART score sensitivity and specificity for predicting major adverse cardiac events.



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International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard



Comparing HEART, TIMI, and GRACE scores for prediction of 30-day major adverse cardiac events in high acuity chest pain patients in the emergency department☆



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Table 5

Sensitivities, specificities, positive predictive values (PPV), and negative predictive values (NPV) at different cut-off values for the HEART score, TIMI score, and GRACE score.

| | HEART ≤ 3 | HEART ≤ 4 | TIMI = 0 | TIMI ≤ 1 | GRACE ≤ 75 | GRACE ≤ 110 |
|-----------------|----------------|----------------|-----------|---------------|-----------------|------------------|
| Sensitivity (%) | 99.1 | 91.6 | 97.2 | 87.0 | 93.5 | 60.0 |
| Specificity (%) | 24.9 | 42.2 | 15.9 | 37.5 | 20.3 | 54.5 |
| PPV (%) | 42.2 | 46.7 | 39.0 | 43.5 | 39.3 | 42.2 |
| NPV (%) | 98.0 | 90.1 | 91.2 | 83.9 | 85.0 | 71.1 |
| Total, n (%) | 99 (16.4) | 182 (30.1) | 68 (11.3) | 174 (28.8) | 93 (15.5) | 298 (49.3) |

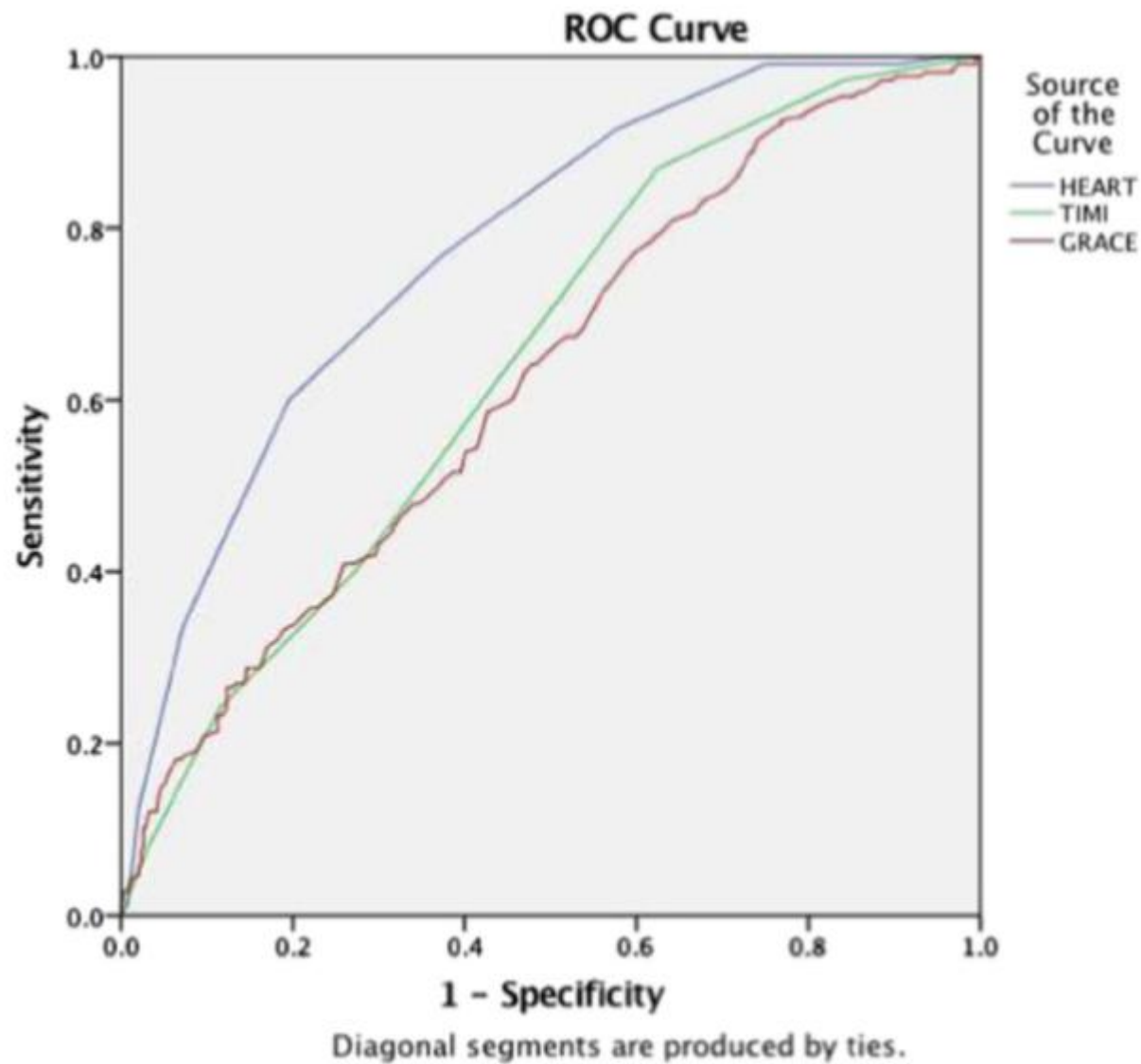


Fig. 2. Receiver operating characteristic (ROC) curve for the HEART score, TIMI score, and GRACE score in predicting 30-day major adverse cardiac events (MACE).

Original Article

The HEART Pathway Randomized Trial Identifying Emergency Department Patients With Acute Chest Pain for Early Discharge

Simon A. Mahler, MD, MS; Robert F. Riley, MD; Brian C. Hiestand, MD, MPH;
Gregory B. Russell, MS; James W. Hoekstra, MD; Cedric W. Lefebvre, MD;
Bret A. Nicks, MD; David M. Cline, MD; Kim L. Askew, MD; Stephanie B. Elliott, BS;
David M. Herrington MD, MHS; Gregory L. Burke, MD; Chadwick D. Miller, MD, MS

Circ Cardiovasc Qual Outcomes is available at <http://circoutcomes.ahajournals.org>

DOI: 10.1161/CIRCOUTCOMES.114.001384

Clinical Trial Registration—URL: <http://www.clinicaltrials.gov>. Unique Identifier: NCT01665521.

(*Circ Cardiovasc Qual Outcomes*. 2015;8:195-203. DOI: 10.1161/CIRCOUTCOMES.114.001384.)



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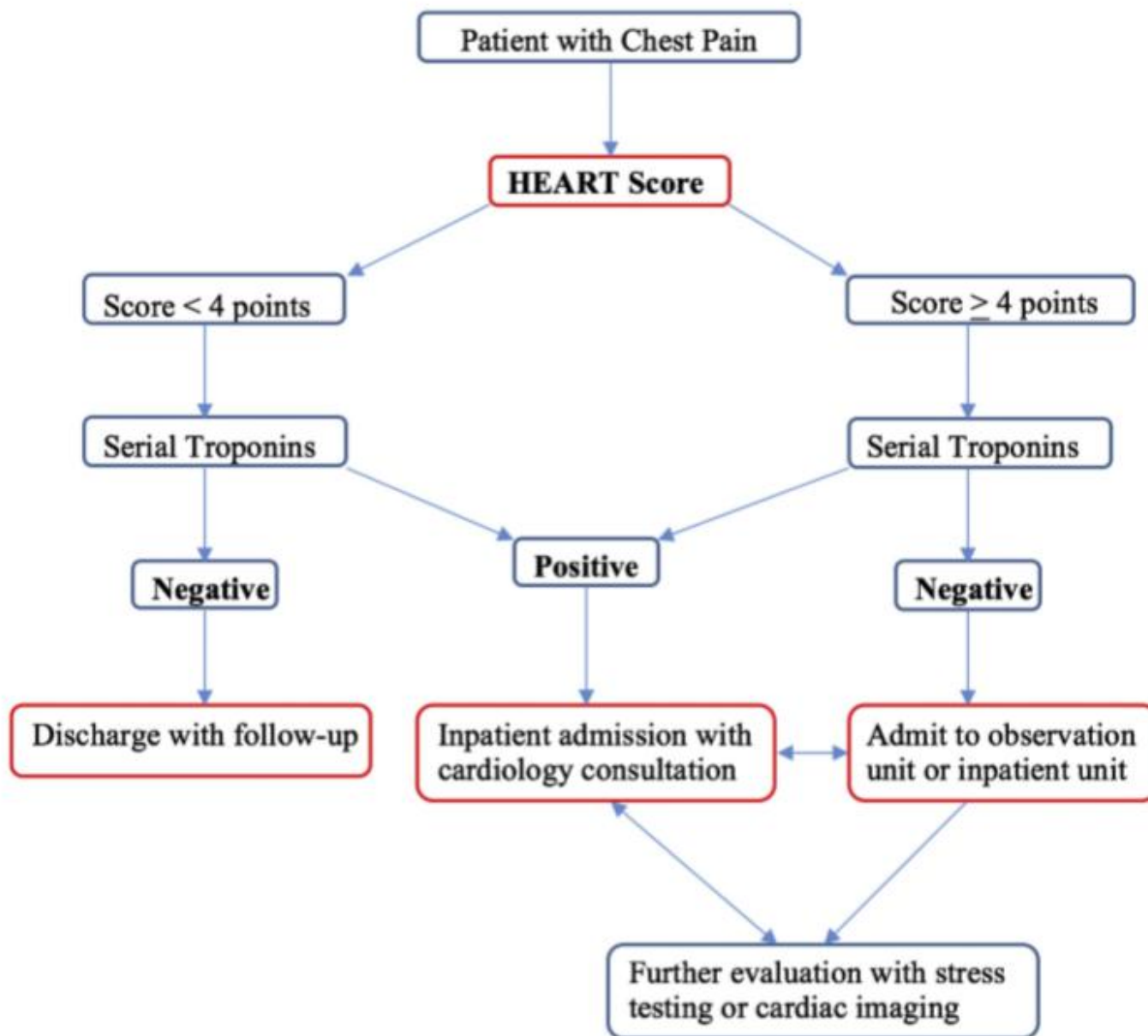


Fig. 1. HEART Pathway [26].

HEART Pathway RCT Flow Diagram

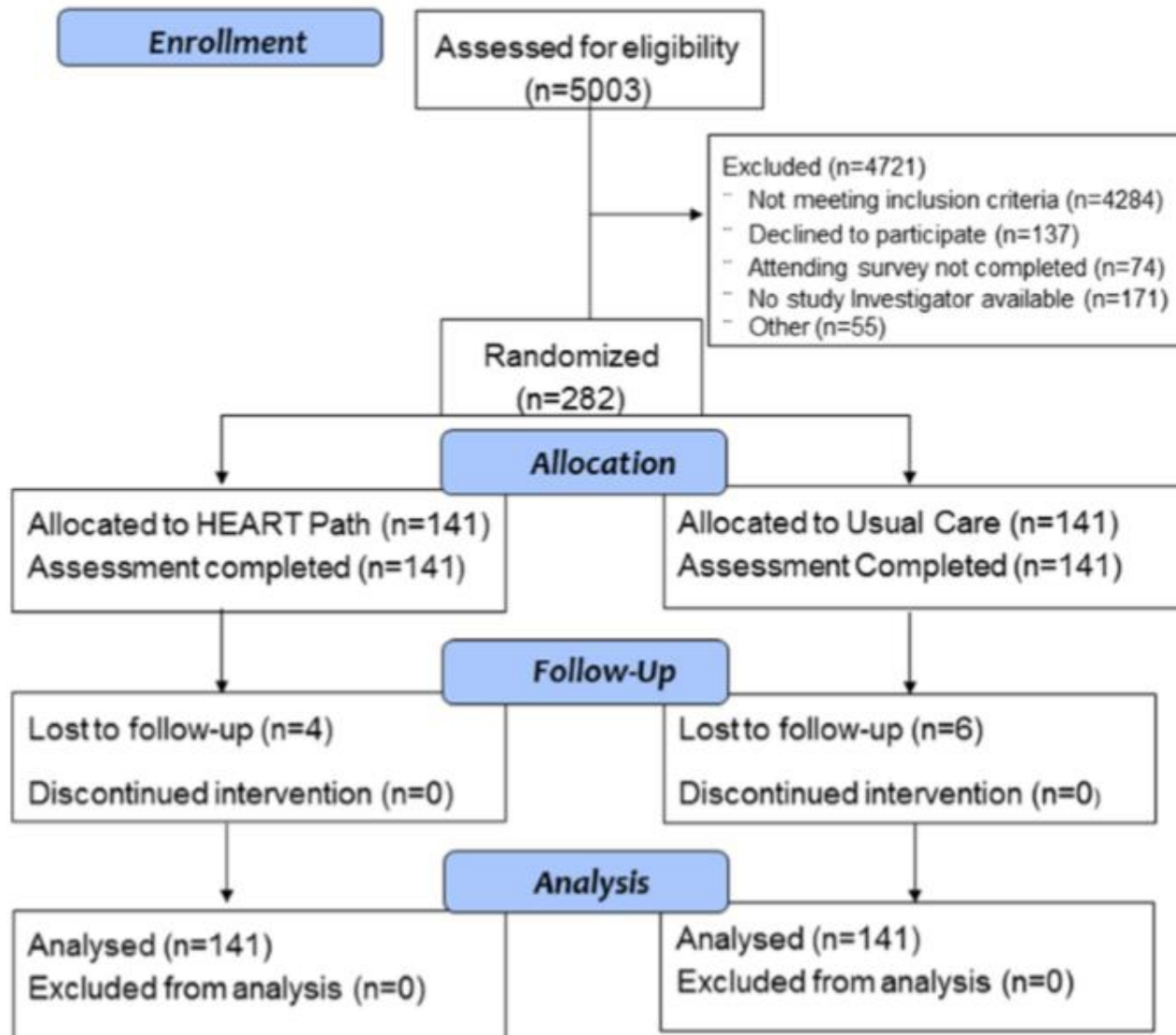


Figure 2. Enrollment flow diagram

Table 4. Safety Events and Healthcare Utilization Outcomes

| Outcomes | HEART Pathway | | | | | | Usual Care | | PValue* |
|---------------------------------------|-------------------|---------|--------------------|---------|----------------|----------|-----------------|---------|---------|
| | Low-Risk Patients | | High-Risk Patients | | Total | | | | |
| | Number, n=66 | Percent | Number n=75 | Percent | Number, n=141 | Percent. | Number, n=141 | Percent | |
| Index length of stay, h; median (IQR) | 6.4 (5.6–8.8) | ... | 25.9 (11.4–46.7) | ... | 9.9 (6.3–26.4) | ... | 21.9 (8.4–28.2) | ... | 0.013 |
| Index visit disposition | | | | | | | | | |
| Hospitalization | 19 | 28.8 | 66 | 88.0 | 85 | 60.3 | 110 | 78.1 | 0.002 |
| Observation unit | 18 | 27.3 | 25 | 33.3 | 43 | 30.5 | 62 | 44.0 | 0.31 |
| Inpatient ward (admission) | 1 | 1.5 | 41 | 54.7 | 42 | 29.8 | 48 | 34.0 | 0.52 |
| Discharge | 47 | 71.2 | 8 | 10.7 | 55 | 39.0 | 31 | 22.0 | 0.003 |
| AMA | 0 | 0 | 1 | 1.3 | 1 | 0.7 | 0 | 0 | >0.999 |
| Early discharge | 47 | 71.2 | 9 | 12.0 | 56 | 39.7 | 26 | 18.4 | 0.0001 |
| Recurrent hospital care at 30 days | | | | | | | | | |
| Repeat ED visit | 2 | 3.0 | 8 | 10.7 | 10 | 7.1 | 18 | 12.8 | 0.16 |
| Cardiac related | 0 | 0 | 4 | 5.3 | 4 | 2.8 | 6 | 4.3 | 0.75 |
| Nonindex hospitalization | 1 | 1.5 | 8 | 10.7 | 9 | 6.4 | 9 | 6.4 | >0.999 |
| Cardiac related | 0 | 0 | 5 | 6.7 | 5 | 3.6 | 4 | 2.8 | >0.999 |
| MACE at 30 days | | | | | | | | | |
| Cardiovascular death | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | ... |
| MI | 0 | 0 | 7 | 9.3 | 7 | 5.0 | 9 | 6.4 | 0.80 |
| With revascularization | 0 | 0 | 1 | 1.3 | 1 | 0.7 | 5 | 3.6 | 0.21 |
| PCI | 0 | 0 | 1 | 1.3 | 1 | 0.7 | 4 | 2.8 | 0.37 |
| CABG | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0.7 | >0.999 |
| Without revascularization | 0 | 0 | 1 | 1.3 | 1 | 0.7 | 0 | 0 | >0.999 |
| PCI | 0 | 0 | 1 | 1.3 | 1 | 0.7 | 0 | 0 | >0.999 |
| CABG | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | ... |

AMA indicates against medical advice; CABG, coronary artery bypass graft; ED, emergency department; IQR, interquartile range; MACE, major adverse cardiac event; MI, myocardial infarction; and PCI, percutaneous coronary intervention.



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Table 5. Test Characteristics of the HEART Pathway and Serial Troponins

| Risk Stratification Strategy | Early Discharge (95% CI) | Sensitivity (95% CI) | Specificity (95% CI) | PPV (95% CI) | NPV (95% CI) |
|------------------------------|--------------------------|----------------------|----------------------|-------------------|------------------|
| Serial troponins | 92.2% (87.8–96.6) | 87.5% (47.4–99.6) | 97.0% (92.5–99.2) | 63.6% (30.8–89.1) | 99.2% (95.8–100) |
| HEART Pathway | 39.7% (31.6–48.3) | 100% (63.1–100) | 49.6% (40.8–58.4) | 10.7% (4.7–19.9) | 100% (94.6–100) |

NPV indicates negative predictive values; and PPV, negative predictive values.



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



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Flow Diagram

Secondary Analysis of the HEART Pathway RCT: hs-cTn

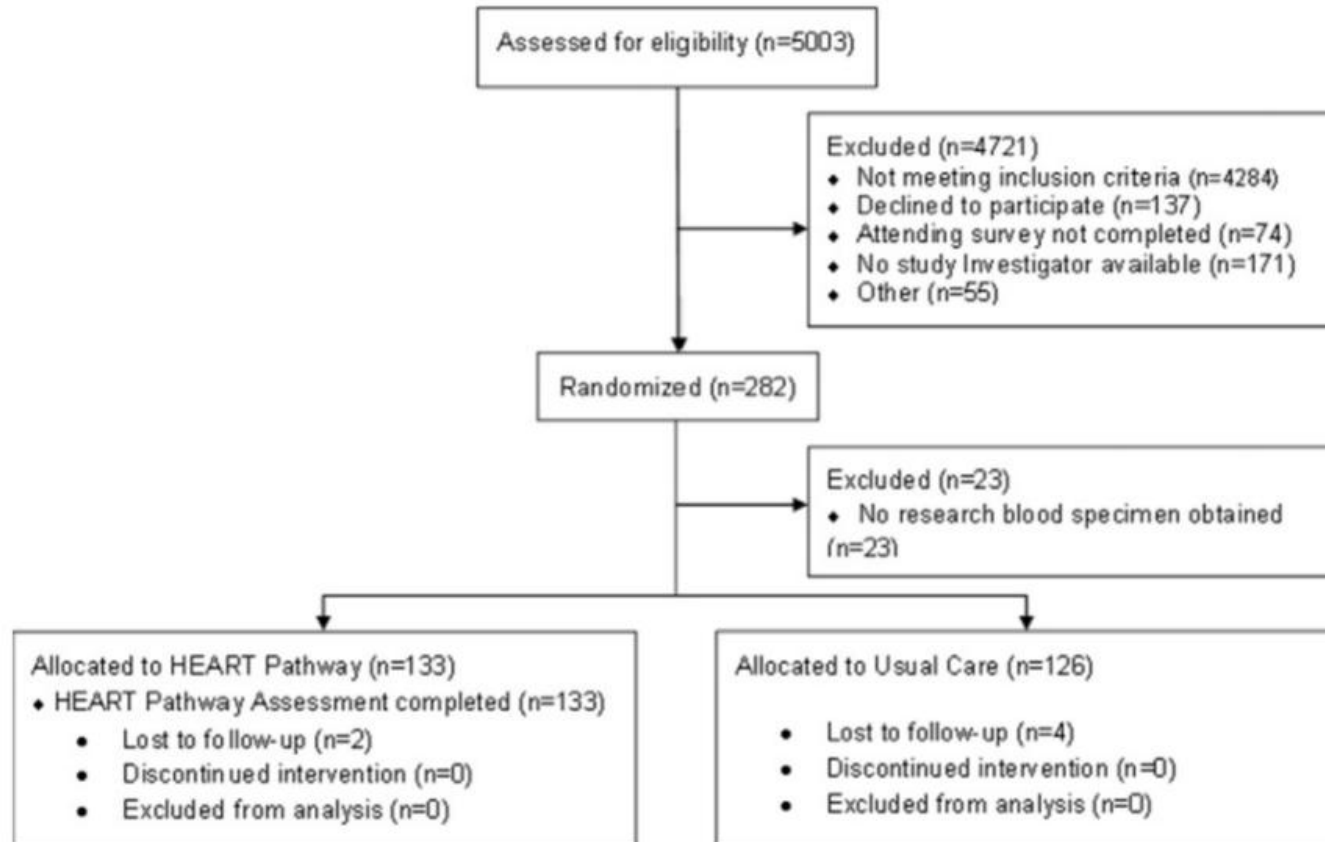


Fig. 2. Enrollment flow diagram.

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%) |



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Author manuscript

Am J Emerg Med. Author manuscript; available in PMC 2018 January 01.

Published in final edited form as:

Am J Emerg Med. 2017 January ; 35(1): 77–81. doi:10.1016/j.ajem.2016.10.005.

Cost Analysis of the HEART Pathway Randomized Control Trial

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Cardiology, University of Washington (RFR), Department of Emergency Medicine, Wake Forest Baptist Health (CDM, ENH, BCH, JWH, CWL, BAN, DMC, KLA, SAM), and Department of Biostatistical Sciences, Wake Forest University (GBR)

Table 3

Cost Comparison Between Usual Care and the HEART Pathway

| <u>Cost</u> | <u>Usual Care (N= 136)</u> | <u>HEART Pathway (N=134)</u> | <u>p-value</u> |
|---|---|---|-----------------------|
| Index visit median cost (Q1, Q3); mean cost (SD) | \$1,412 (\$993, \$2,493), \$3,194 (\$6,064) | \$1,260 (\$692, \$2,348); \$2,512 (\$3,803) | 0.05 |
| 30-day median cost (Q1, Q3); mean cost (SD) | \$1,523 (\$1,065, \$2,693); \$3,323 (\$6,064) | \$1,307 (\$729, \$2,457); \$2,605 (\$3,860) | 0.04 |
| 30-day median cardiac-related cost (Q1, Q3); mean cost (SD) | \$1,550 (\$1,012, \$2,780); \$3,309 (\$6,083) | \$1,375 (\$727, \$2,383); \$2,764 (\$4,166) | 0.10 |



Troponin level I-II

Pathway



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Grazie per l'attenzione



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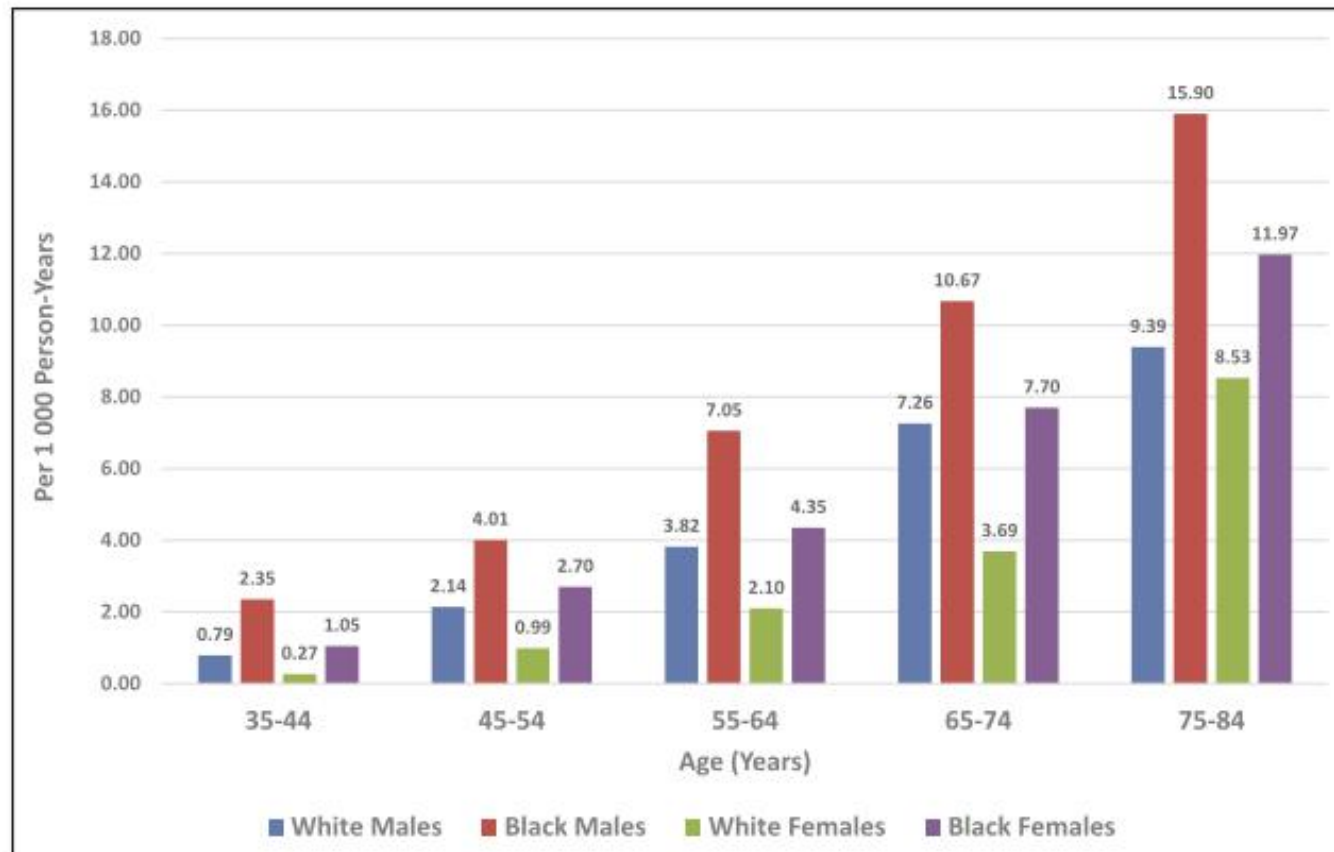


Chart 18-7. Incidence of myocardial infarction by age, sex, and race (ARIC Surveillance: 2005–2014).

ARIC indicates Atherosclerosis Risk in Communities.

Source: Unpublished data from ARIC, National Heart, Lung, and Blood Institute.



Table 2
Baseline characteristics.

| | All patients (n = 1748) | Patients with MACE (n = 326) | Patients without MACE (n = 1422) |
|---|-------------------------|------------------------------|----------------------------------|
| Demographics | | | |
| Male | 937 (54%) | 227 (70%) | 710 (50%) |
| Mean age (SD) | 62 (14) | 67 (11) | 60 (15) |
| Vital signs at presentation | | | |
| Mean systolic blood pressure in mm Hg (SD) | 144 (23) | 147 (23) | 143 (23) |
| Mean diastolic blood pressure in mm Hg (SD) | 81 (13) | 82 (13) | 81 (13) |
| Mean heart frequency per minute (SD) | 73 (15) | 75 (17) | 73 (15) |
| Killip class I | 1723 (99%) | 317 (97%) | 1406 (99%) |
| Cardiac risk factors | | | |
| Diabetes Mellitus | 271 (16%) | 68 (21%) | 203 (14%) |
| Obesity (BMI >30 kg/m ²) | 319 (18%) | 58 (18%) | 261 (18%) |
| Hypercholesterolemia | 559 (32%) | 117 (36%) | 442 (31%) |
| Hypertension | 846 (48%) | 209 (64%) | 637 (48%) |
| Positive family history | 629 (36%) | 117 (36%) | 512 (36%) |
| Current smoking | 441 (25%) | 81 (25%) | 360 (25%) |
| History of cardiovascular disease | 576 (33%) | 154 (47%) | 422 (30%) |
| History of AMI | 277 (16%) | 65 (20%) | 212 (15%) |
| History of PCI | 331 (19%) | 91 (28%) | 240 (17%) |
| History of CABG | 128 (7%) | 36 (11%) | 92 (6%) |
| History of CVA/TIA | 98 (6%) | 27 (8%) | 71 (5%) |
| History of peripheral artery disease | 69 (4%) | 25 (8%) | 44 (3%) |
| Laboratory results at presentation | | | |
| Mean creatinin in µmol/l (SD) | 80 (33) | 85 (22) | 78 (35) |
| Medication at presentation | | | |
| Aspirin | 597 (34%) | 153 (47%) | 444 (31%) |
| P2Y12-inhibitor (clopidogrel) | 107 (6%) | 40 (12%) | 67 (5%) |
| Vitamin K antagonists (coumarin) | 162 (9%) | 33 (10%) | 129 (9%) |
| Other (Dipyridamol, Ticagrelor, DOAC) | 62 (4%) | 14 (4%) | 48 (3%) |

SD: standard deviation, mm Hg: millimetres of mercury, BMI: Body Mass Index, AMI: acute myocardial infarction, PCI: percutaneous coronary intervention, CABG: coronary arterial bypass grafting, CVA: cerebrovascular attack, TIA: transient ischemic attack, DOAC: direct oral anticoagulant.

Titolo del capitolo

CAPITOLO 1

Table 3
Comparison of performance of GRACE score, HEART score and TIMI score in terms of safety and efficiency.

| Scenario 1: at least 95% sensitivity | GRACE score | HEART score | TIMI score |
|---|------------------|------------------|------------------|
| Corresponding cut-off for "low risk" | ≤72 points | ≤3 points | 0 points |
| Number of patients classified "low risk" / total number of patients | 334/1748 (19.1%) | 708/1748 (40.5%) | 439/1748 (25.1%) |
| Percentage of MACE in "low risk" group | 3.6% (12/334) | 2.0% (14/708) | 3.2% (14/439) |
| MACE, of which AMI | 5 | 3 | 0 |
| MACE, of which death | 0 | 1 | 0 |
| Negative predictive value (NPV) | 96% (94–98%) | 98% (97–99%) | 97% (95–98%) |
| Scenario 2: at least 98% sensitivity | GRACE score | HEART score | TIMI score |
| Corresponding cut-off for "low risk" | ≤66 points | ≤2 points | –* |
| Number of patients classified "low risk" / total number of patients | 231/1748 (13.2%) | 381/1748 (21.8%) | – |
| Percentage of MACE in "low risk" group | 2.2% (5/231) | 0.8% (3/381) | – |
| MACE, of which AMI | 1 | 1 | – |
| MACE, of which death | 0 | 0 | – |
| Negative predictive value (NPV) | 98% (95–99%) | 99% (98–100%) | – |

MACE: major adverse cardiac events, AMI: acute myocardial infarction.

* At the lowest TIMI score, this absolute safety level is not reached unless all patients are classified as high risk.

Table 3

Baseline characteristics and cardiac risk factors of patients with and without 30-day major adverse cardiac events (MACE).

| | Total population (n = 604) | No 30-day MACE (n = 389) | 30-day MACE (n = 215) | p-Value |
|------------------------------|----------------------------------|--------------------------------|-----------------------------|---------|
| Age, mean (SD) | 60.8 (13.2) | 60.0 (13.9) | 62.2 (11.8) | 0.05 |
| Male gender, n (%) | 418 (69.2) | 256 (65.8) | 162 (75.3) | 0.02 |
| Diabetes, n (%) | 223 (36.9) | 140 (36.0) | 83 (38.6) | 0.52 |
| Active smoker, n (%) | 89 (14.7) | 51 (13.1) | 38 (17.7) | 0.13 |
| Hypercholesterolemia, n (%) | 369 (61.1) | 237 (60.9) | 132 (61.4) | 0.91 |
| Hypertension, n (%) | 420 (69.5) | 273 (70.2) | 147 (68.4) | 0.64 |
| Family history of CAD, n (%) | 71 (11.8) | 46 (11.8) | 25 (11.6) | 0.94 |
| History of AMI, n (%) | 143 (23.7) | 90 (23.1) | 53 (24.7) | 0.68 |
| History of CABG, n (%) | 64 (10.6) | 37 (9.5) | 27 (12.6) | 0.24 |
| History of PCI, n (%) | 169 (28.0) | 110 (28.3) | 59 (27.4) | 0.83 |
| History of IHD, n (%) | 289 (47.8) | 185 (47.6) | 104 (48.4) | 0.85 |

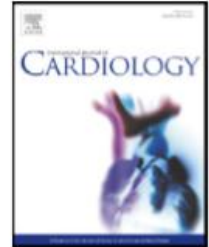
CAD: coronary artery disease; AMI: acute myocardial infarction; CABG: coronary artery bypass graft; PCI: percutaneous coronary intervention; IHD: ischemic heart disease.



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International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard



Comparison of the GRACE, HEART and TIMI score to predict major adverse cardiac events in chest pain patients at the emergency department



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Identifying Patients Suitable for Discharge After a Single-Presentation High-Sensitivity Troponin Result: A Comparison of Five Established Risk Scores and Two High-Sensitivity Assays

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0196-0644/\$-see front matter

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<http://dx.doi.org/10.1016/j.annemergmed.2015.07.006>

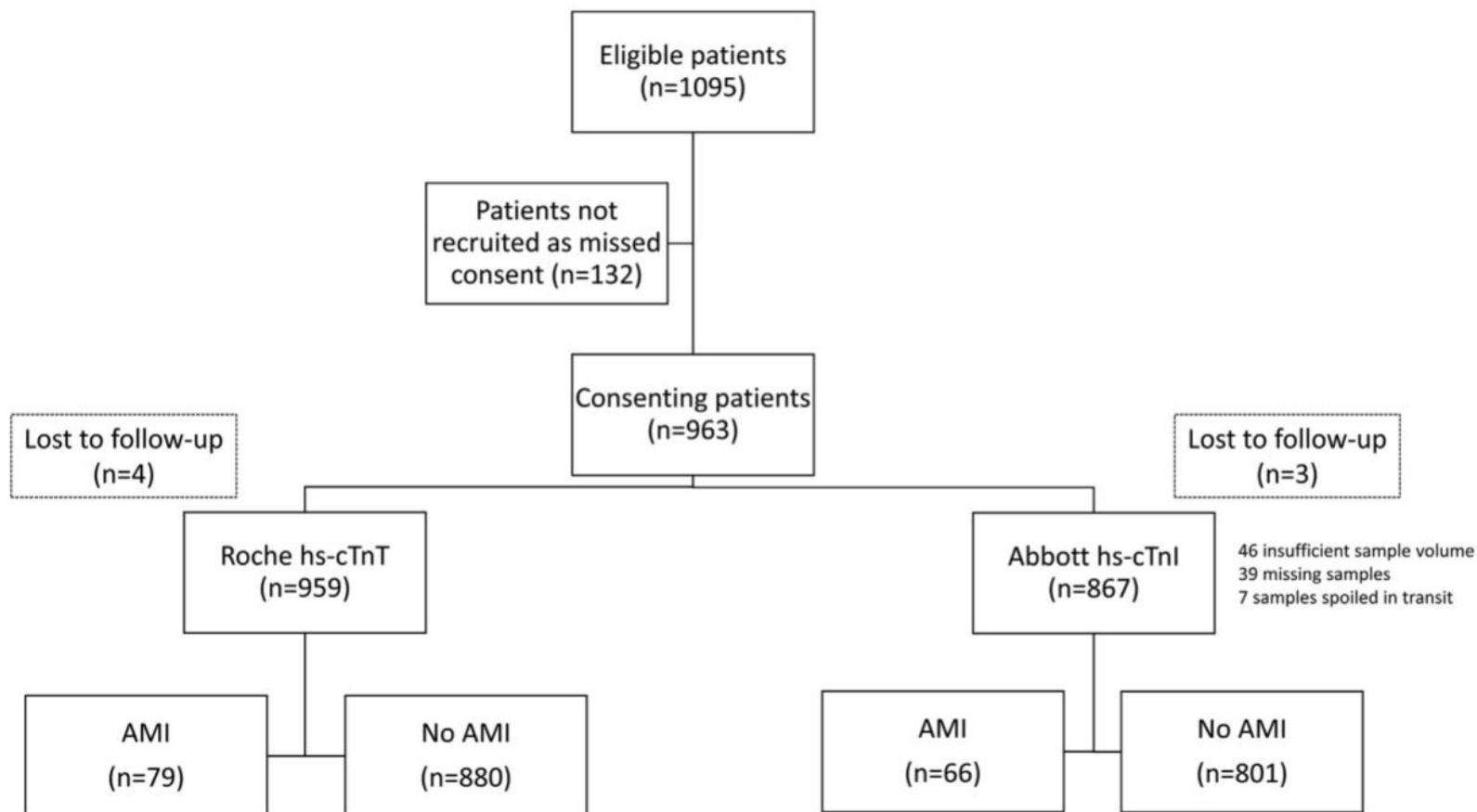


Figure 2. Recruitment flow chart. AMI, Acute myocardial infarction.

Table 2. Test performance of each risk score with high-sensitivity troponin T.

| | hs-cTnT ≤14 ng/L Alone (99th Percentile) | m-Goldman Score 0 and hs-cTnT ≤14 ng/L | m-Goldman Score ≤1 and hs-cTnT ≤14 ng/L | TIMI Score 0 and hs-cTnT ≤14 ng/L | TIMI Score ≤1 and hs-cTnT ≤14 ng/L | GRACE Score <60 (Incorporates hs-cTnT)* | GRACE Score <80 (Incorporates hs-cTnT)* | HEART Score ≤2 (Incorporates hs-cTnT) | HEART Score ≤3 (Incorporates hs-cTnT) | Vancouver Chest Pain Rule (Incorporates hs-cTnT) |
|---|---|---|--|--|---|--|--|--|--|--|
| Sensitivity (95% CI) | 83.5 (73.8–90.5) | 98.7 (92.5–99.9) | 98.7 (92.3–99.9) | 100 (94.3–100) | 94.9 (87.0–98.4) | 100 (94.4–100) | 92.3 (83.7–96.8) | 98.7 (92.4–99.9) | 93.7 (85.5–97.6) | 100 (94.4–100) |
| Negative predictive value (95% CI) | 98.3 (97.3–99.0) | 99.0 (94.2–99.9) | 99.7 (98.4–100) | 100 (98.5–100) | 99.2 (97.8–99.7) | 100 (95.3–100) | 98.0 (95.8–99.2) | 99.2 (95.2–100) | 98.3 (96.2–99.4) | 100 (97.1–100) |
| Specificity (95% CI) | 85.6 (84.7–86.2) | 11.5 (10.9–11.6) | 43.3 (42.7–43.4) | 35.0 (34.5–35.0) | 53.5 (52.8–53.8) | 10.6 (10.1–10.6) | 33.8 (33.0–34.2) | 14.1 (13.5–14.2) | 33.9 (33.1–34.2) | 17.5 (17.0–17.5) |
| Positive predictive value (95% CI) | 34.2 (30.2–37.0) | 9.1 (8.5–9.2) | 13.5 (12.6–13.7) | 12.1 (11.4–12.1) | 15.5 (14.2–16.1) | 9.1 (8.6–9.1) | 11.1 (10.0–11.6) | 9.4 (8.8–9.5) | 11.3 (10.3–11.8) | 9.8 (6.4–9.8) |
| Positive likelihood ratio (95% CI) | 5.789 (4.822–6.549) | 1.115 (1.038–1.130) | 1.741 (1.611–1.766) | 1.538 (1.440–1.538) | 2.043 (1.845–2.130) | 1.119 (1.050–1.119) | 1.393 (1.249–1.470) | 1.149 (1.069–1.165) | 1.416 (1.278–1.484) | 1.212 (1.137–1.212) |
| Negative likelihood ratio (95% CI) | 0.192 (0.111–0.309) | 0.110 (0.006–0.691) | 0.029 (0.002–0.180) | 0 (0–0.165) | 0.095 (0.030–0.245) | 0 (0–0.555) | 0.228 (0.093–0.495) | 0.090 (0.005–0.561) | 0.187 (0.069–0.439) | 0 (0–0.331) |
| % Identified as suitable for discharge (95% CI) | 79.9 (77.2–82.3) | 10.6 (8.8–12.8) | 39.8 (36.7–43.0) | 32.1 (29.2–35.2) | 49.1 (45.9–52.3) | 9.8 (8.0–11.9) | 31.6 (28.7–34.7) | 13.0 (11.0–15.4) | 31.6 (28.7–34.7) | 16.0 (13.8–18.6) |
| Number of AMIs in patients identified as suitable for discharge (%) | 13/766 (1.7) | 1/102 (1.0) | 1/382 (0.3) | 0/308 | 4/471 (0.9) | 0/93 | 6/301 (2.0) | 1/125 (0.8) | 5/303 (1.7) | 0/154 |

*Incomplete GRACE scores in 7 cases because of missing creatinine results.

Table 3. Test performance of each risk score with high-sensitivity troponin I.

| | hs-cTnI ≤26.2 ng/L Alone (99th Percentile) | m-Goldman Score 0 and hs-cTnI ≤26.2 ng/L | m-Goldman Score ≤1 and hs-cTnI ≤26.2 ng/L | TIMI Score 0 and hs-cTnI ≤26.2 ng/L | TIMI Score ≤1 and hs-cTnI ≤26.2 ng/L | GRACE Score <60 (Incorporates hs-cTnI)* | GRACE Score <80 (Incorporates hs-cTnI)* | HEART Score ≤2 (Incorporates hs-cTnI) | HEART Score ≤ 3 (Incorporates hs-cTnI) | Vancouver Chest Pain Rule (Incorporates hs-cTnI) |
|---|---|---|--|--|---|--|--|--|---|--|
| Sensitivity (95% CI) | 62.1 (51.9–70.8) | 98.5 (91.0–99.9) | 92.8 (82.8–97.2) | 95.5 (86.7–98.8) | 87.9 (77.3–94.2) | 98.5 (91.1–99.9) | 89.4 (79.1–95.2) | 98.5 (91.0–99.9) | 97.0 (88.7–99.5) | 100 (93.3–100) |
| Negative predictive value (95% CI) | 96.9 (96.1–97.6) | 99.0 (94.2–99.9) | 98.7 (97.0–99.5) | 99.0 (96.9–99.7) | 98.3 (96.8–99.2) | 98.9 (93.4–99.9) | 97.5 (95.1–98.9) | 99.1 (94.8–100) | 99.3 (97.3–99.9) | 100 (96.7–100) |
| Specificity (95% CI) | 97.2 (96.5–98.1) | 12.6 (12.0–12.7) | 47.4 (46.6–47.8) | 35.6 (34.9–35.9) | 56.7 (55.8–57.2) | 11.1 (10.5–11.2) | 34.3 (33.5–34.8) | 14.1 (13.5–14.2) | 34.7 (34.0–34.9) | 16.7 (16.2–16.7) |
| Positive predictive value (95% CI) | 66.1 (55.2–75.4) | 8.5 (7.9–8.6) | 12.7 (11.3–13.3) | 10.9 (9.9–11.3) | 14.3 (12.6–15.4) | 8.4 (7.8–8.5) | 10.2 (9.0–10.8) | 8.6 (8.0–8.8) | 10.9 (10.0–11.2) | 9.0 (8.4–9.0) |
| Positive likelihood ratio (95% CI) | 23.695 (14.969–37.161) | 1.127 (1.035–1.145) | 1.758 (1.551–1.863) | 1.482 (1.330–1.541) | 2.029 (1.749–2.201) | 1.107 (1.017–1.125) | 1.361 (1.190–1.461) | 1.147 (1.052–1.165) | 1.485 (1.345–1.528) | 1.201 (1.114–1.201) |
| Negative likelihood ratio (95% CI) | 0.389 (0.298–0.498) | 0.120 (0.006–0.746) | 0.160 (0.059–0.370) | 0.128 (0.033–0.383) | 0.214 (0.101–0.407) | 0.137 (0.007–0.852) | 0.309 (0.137–0.624) | 0.107 (0.006–0.665) | 0.087 (0.015–0.332) | 0 (0–0.412) |
| % Identified as suitable for discharge (95% CI) | 92.8 (90.9–94.4) | 11.8 (9.7–14.1) | 44.4 (41.1–47.8) | 33.2 (30.1–36.5) | 52.4 (49.0–55.7) | 10.3 (8.4–12.6) | 32.5 (29.4–35.8) | 13.1 (11.0–15.6) | 32.2 (29.2–35.5) | 15.4 (13.2–18.1) |
| Number of AMIs in patients identified as suitable for discharge (%) | 25/805 (3.1) | 1/102 (1.0) | 5/385 (1.3) | 3/288 (1.0) | 8/454 (1.8) | 1/89 (1.1) | 7/280 (2.5) | 1/114 (0.9) | 2/280 (0.7) | 0/134 |

*Incomplete GRACE scores in 6 cases because of missing creatinine results.

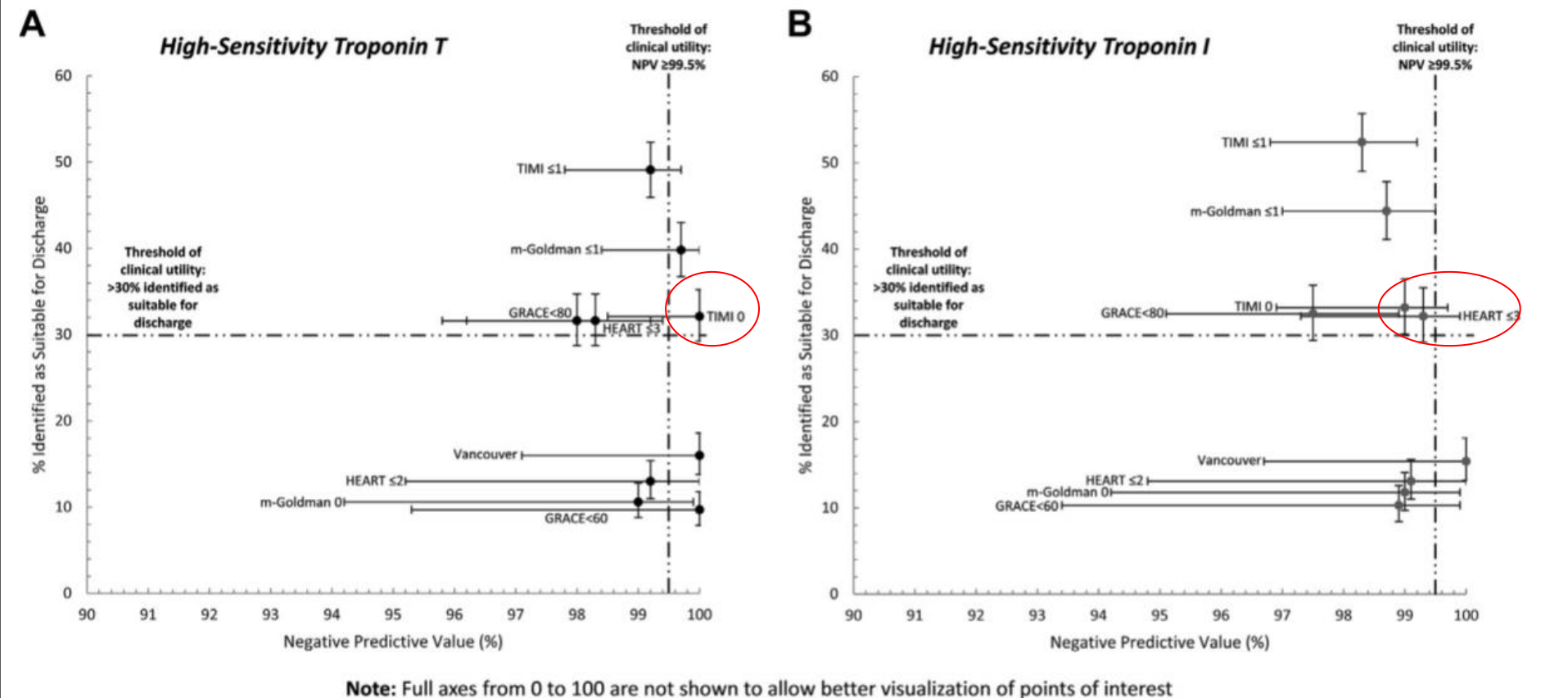


Figure 4. Clinical utility of risk scores in combination with presentation high-sensitivity troponin T (A) and high-sensitivity troponin I (B) results. Error bars: 95% CIs.

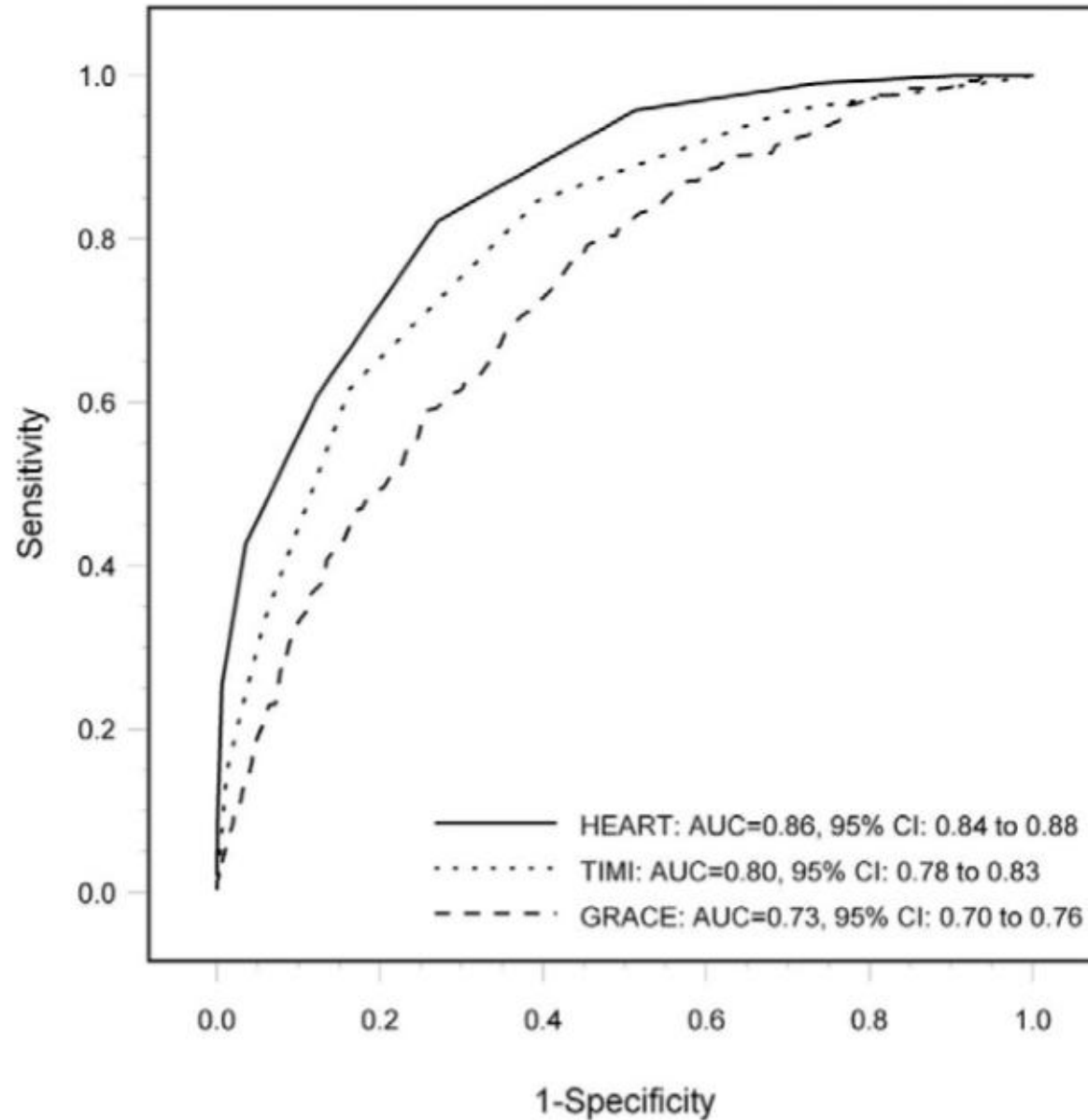


Fig. 2. Receiver-operating-characteristic (ROC) curves and corresponding Areas under the curve (AUCs) of the GRACE, HEART and TIMI score to predict major adverse cardiac events within 6 weeks.