Treatment of ACS – Troponin Protocols

B. Hadley Wilson, MD, FACC
The Sanger Heart & Vascular Institute
Carolinas HealthCare System
Clinical Professor of Medicine
UNC School of Medicine
Governor, North Carolina Chapter
Chair-Elect, Board of Governors
American College of Cardiology

AMERICAN COLLEGE of CARDIOLOGY

Disclosure Statement of Financial Interest

I, B. Hadley Wilson, MD DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

AMERICAN COLLEGE of CARDIOLOGY

2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes

Developed in Collaboration with the Society of Thoracic Surgeons and Society for Cardiovascular Angiography and Interventions

Endorsed by the American Association for Clinical Chemistry

AMERICAN COLLEGE of CARDIOLOGY

Biomarkers: Diagnosis

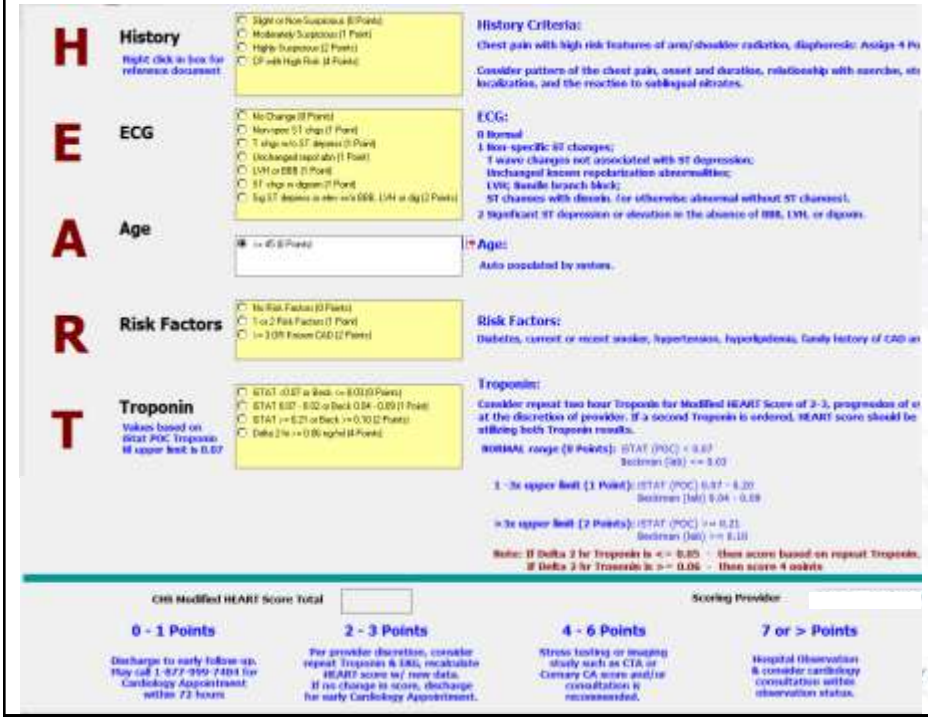
Recommendations	COR	LOE
Cardiac-specific troponin (troponin I or T when a contemporary assay is used) levels should be measured at presentation and 3 to 6 hours after symptom onset in all patients who present with symptoms consistent with ACS to identify a rising and/or falling pattern.	I	A
Additional troponin levels should be obtained beyond 6 hours after symptom onset in patients with normal troponins on serial examination when electrocardiographic changes and/or clinical presentation confer an intermediate or high index of suspicion for ACS.	I	A
If the time of symptom onset is ambiguous, the time of presentation should be considered the time of onset for assessing troponin values.	I	A
With contemporary troponin assays, creatine kinase myocardial isoenzyme (CK-MB) and myoglobin are not useful for diagnosis of ACS.	III: No Benefit	A

AMERICAN COLLEGE of CARDIOLOGY

Biomarkers: Prognosis

Recommendations	COR	LOE
The presence and magnitude of troponin elevations are useful for short- and long-term prognosis.	I	B
It may be reasonable to remeasure troponin once on day 3 or day 4 in patients with MI as an index of infarct size and dynamics of necrosis.	IIb	B
Use of selected newer biomarkers, especially B-type natriuretic peptide, may be reasonable to provide additional prognostic information.	IIb	B

AMERICAN COLLEGE of CARDIOLOGY



MEDPAGE TODAY

Cardiology

Next-Generation Troponin Test Cleared by FDA

— Results with low detection threshold in under 10 minutes

by Crystal Phend
Senior Associate Editor, MedPage Today

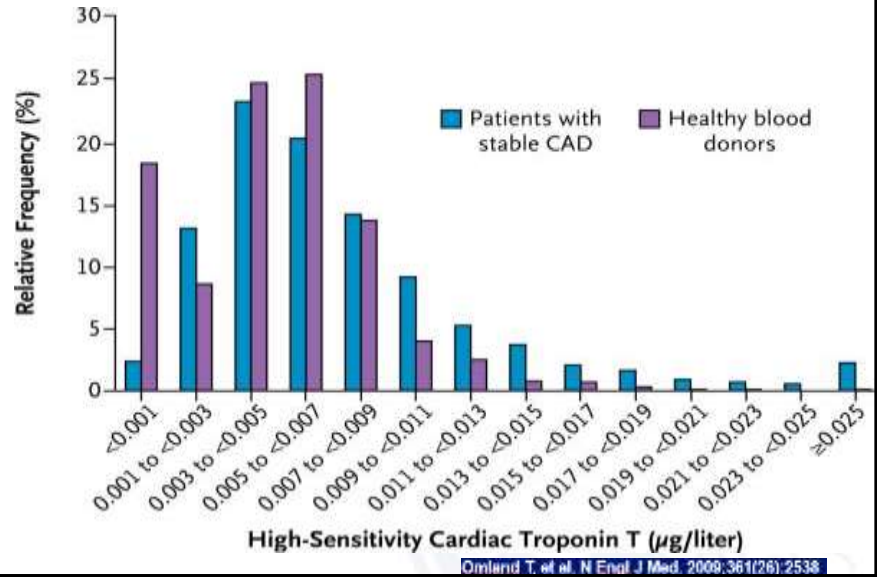
January 19, 2017

American Heart Association.

The FDA cleared the first in a new generation of cardiac troponin T (TnT) blood tests for rapid diagnosis of acute MI, Roche's Elecsys TnT Gen 5 STAT test, the firm said Thursday.

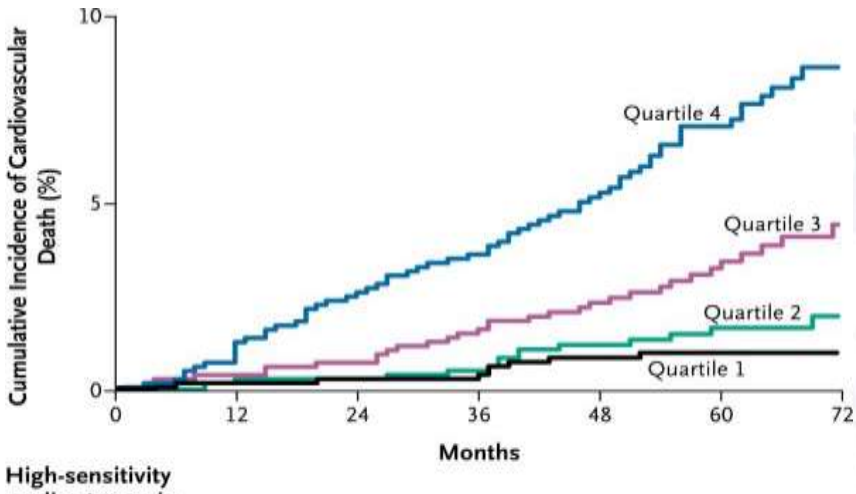
The company's fifth-generation blood test uses two monoclonal antibodies against cardiac troponin T to pick up the marker of myocardial damage with a turn-around time of 9 minutes.

Detectable hsTnT in patients with Stable CAD



Omland T, et al. N Engl J Med. 2009;361(26):2538

Detectable hsTNT and CV Death

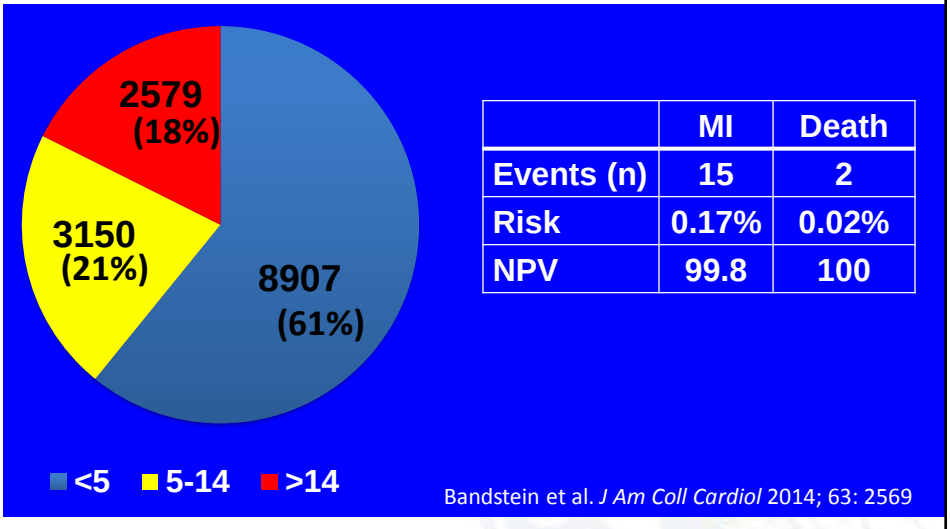


High-sensitivity cardiac troponin T levels (μg/liter)	Q1	Q2	Q3	Q4
Men	≤0.0042	0.0043–0.0062	0.0063–0.0095	≥0.0096
Women	≤0.0027	0.0028–0.0045	0.0046–0.0073	≥0.0074

Omland T, et al. N Engl J Med. 2009;361(26):2538

Low Risk of MI with Undetectable hs-TnT and ECG without Ischemic Changes

n=14,636 pts in ED with Chest Pain



	MI	Death
Events (n)	15	2
Risk	0.17%	0.02%
NPV	99.8	100

Bandstein et al. *J Am Coll Cardiol* 2014; 63: 2569

European Heart Journal Advance Access published August 29, 2015

European Heart Journal
doi:10.1093/eurheartj/ehv320

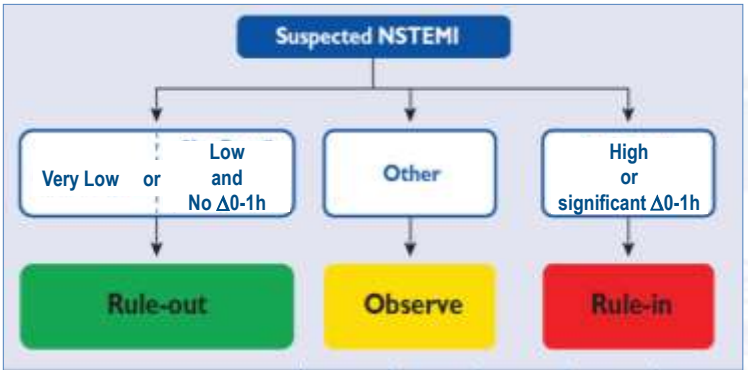
ESC GUIDELINES

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)

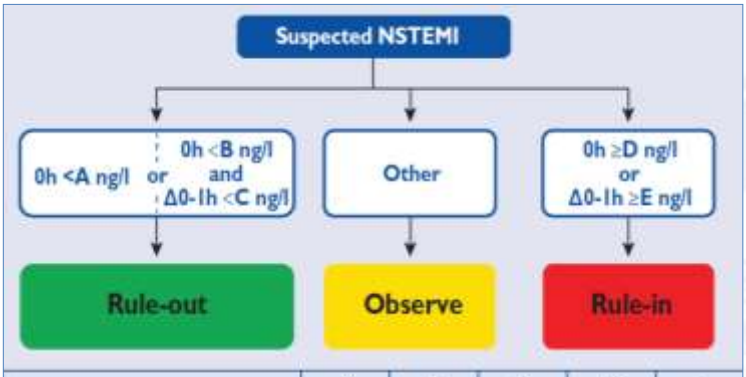
Authors/Task Force Members: Marco Roffi* (Chairperson) (Switzerland), Carlo Patrono* (Co-Chairperson) (Italy), Jean-Philippe Collet† (France), Christian Mueller† (Switzerland), Marco Valgimigli† (The Netherlands), Felicita Andreotti (Italy), Jeroen J. Bax (The Netherlands), Michael A. Borger (Germany), Carlos Brotons (Spain), Derek P. Chew (Australia), Baris Gencer (Switzerland), Gerd Hasenfuss (Germany), Keld Kjeldsen (Denmark), Patrizio Lancellotti (Belgium), Ulf Landmesser (Germany), Julinda Mehilli (Germany), Debabrata Mukherjee (USA), Robert F. Storey (UK), and Stephan Windecker (Switzerland)

0 h/1 h Rule-in & rule-out algorithms using high-sensitivity cardiac troponins (hs-cTn) assays in suspected NSTEMI



- Negative predictive value >98% for acute MI
- Positive predictive value 75-80% for acute MI
- Cut-offs for «rule-in» and «rule-out» assay specific

0 h/1 h Rule-in & rule-out algorithms using high-sensitivity cardiac troponins (hs-cTn) assays in suspected NSTEMI



	A	B	C	D	E
hs-cTnT (Elecsys)	5	12	3	52	5
hs-cTnI (Architect)	2	5	2	52	6
hs-cTnI (Dimension Vista)	0.5	5	2	107	19

Clinical implications of high-sensitivity cardiac troponin assays (1)

Compared with standard cardiac troponin assays, high-sensitivity assays:
• Have higher negative predictive value for acute MI.
• Reduce the "troponin-blind" interval leading to earlier detection of acute MI.
• Result in a ~4% absolute and ~20% relative increase in the detection of type 1 MI and a corresponding decrease in the diagnosis of unstable angina.
• Are associated with a 2-fold increase in the detection of type 2 MI.

Clinical implications of high-sensitivity cardiac troponin assays (2)

Levels of high-sensitivity cardiac troponin should be interpreted as quantitative markers of cardiomyocyte damage (i.e. the higher the level, the greater the likelihood of MI):

- Elevations beyond 5-fold the upper reference limit have high (>90%) positive predictive value for acute type 1 MI.
- Elevations up to 3-fold the upper reference limit have only limited (50–60%) positive predictive value for acute MI and may be associated with a broad spectrum of conditions.
- It is common to detect circulating levels of cardiac troponin in healthy individuals.

Rising and/or falling cardiac troponin levels differentiate acute from chronic cardiomyocyte damage (the more pronounced the change, the higher the likelihood of acute MI).

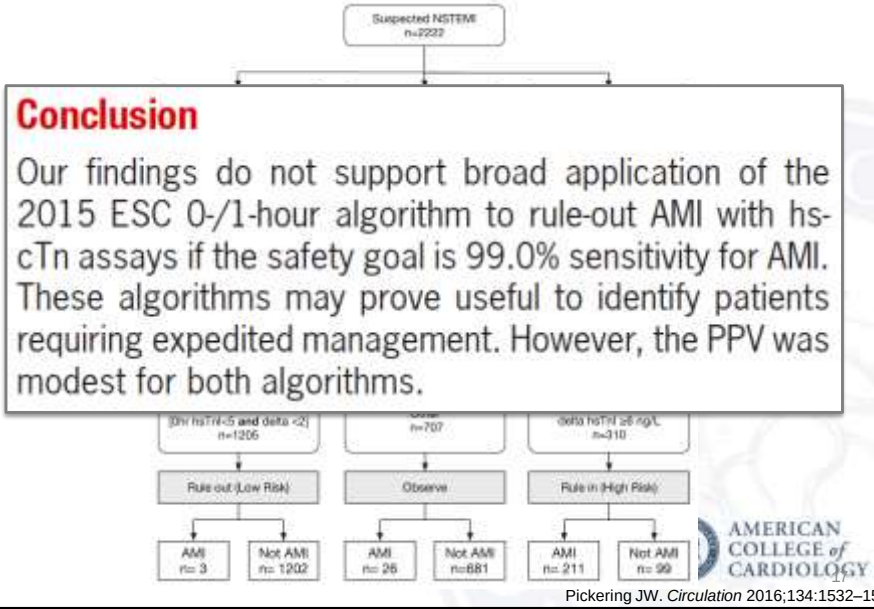
AMERICAN COLLEGE of CARDIOLOGY

Cardiac troponins

Recommendations	Class[a]	Level[b]
It is recommended to measure cardiac troponins with sensitive or high-sensitivity assays and obtain the results within 60 min.	I	A
A rapid rule-out protocol at 0 h and 3 h is recommended if high-sensitivity cardiac troponin tests are available.	I	B
A rapid rule-out and rule-in protocol at 0 h and 1 h is recommended if a high-sensitivity cardiac troponin test with a validated 0 h/1 h algorithm is available. Additional testing after 3–6 h is indicated if the first two troponin measurements are not conclusive and the clinical condition is still suggestive of ACS.	I	B

AMERICAN COLLEGE of CARDIOLOGY

Assessment of the ESC 0-Hour/1-Hour Algorithm to Rule-Out and Rule-In AMI



Pickering JW. *Circulation* 2016;134:1532–1541

Troponin Protocols in ACS:

Conclusions

- Current troponin protocols in use in the US are less sensitive but in accordance with 2014 ACC/AHA Guidelines for diagnosis of NSTE ACS.
- Recently a hs-TnT has been approved for use in the US with a turn-around time of 9 minutes and <10% co-efficient of variation at the 99th percentile upper reference limit (14ng/L).
- hs-Tn protocols have been in use in Europe and elsewhere >7 years with algorithms supporting a broad application for early 0-1 hour rule-out AMI.
- However, exact cutoffs for these assays are unclear and adoption is likely to require coupling with management protocols that guide better interpretation if the benefits for diagnosis are to be realized.