**Critical Appraisal Worksheet – Diagnosis**
**Eastern Virginia Medical School EM Journal Club**

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**Citation:**
Mueller C, et al; TRAPID-AMI Investigators. Multi center Evaluation of a 0-Hour/1-Hour Algorithm in the Diagnosis of Myocardial Infarction With High-Sensitivity Cardiac Troponin T. Ann Emerg Med. 2016 Jul 68(1): 76-87.

**Study Objectives:** Prospectively validate the diagnostic accuracy of the recently developed 0-h/1-h algorithm using high-sensitivity cardiac troponin T (hs-cTnT) for the early rule-out and rule-in of acute myocardial infarction

**Inclusion Criteria**:
Patients age 18 or older, presenting to the ED with symptoms suggestive of acute myocardial infarction (such as acute CP or angina) with an onset or maximum of discomfort or pain within the previous 6 hours.

**Exclusion Criteria**:
Symptoms greater than 6 hours
ESRD
Trauma
Cardioversion
Defibrillation
Thrombolytic therapy
CABG within the last month
Recently hospitalized with AMI within the past 3 weeks
Pregnant and breastfeeding women

**Methodology**:
This was an international, multicenter study conducted at 12 centers in the United States, Europe, and Australia. From August 2011 to June 2013, investigators enrolled 1,282 consecutive patients (mean age 62 years; 63% men) with chest pain suggestive of acute MI. All had symptom onset within the prior 6 hours (median 1.8 hours) and had a median time from chest pain onset to first study blood draw of 3.4 hours. Because definite interpretation of the initial ECG was not required, patients with STEMI were allowed to be enrolled. Hs-cTnT and sensitive cardiac troponin I were measured at presentation and after 1 hour, 2 hours, and 4-14 hours in a central laboratory. Patient triage according the predefined hs-cTnT 0-hour/1-hour algorithm (as below) was compared against a centrally adjudicated final diagnosis by 2 independent cardiologists (of a committee of cardiologists selected for the study). The final diagnosis was based on all available information, including coronary angiography and ECHO results, follow up data, and serial measurements of sensitive cardiac troponin whereas adjudicators remained blind to hs-cTnT.

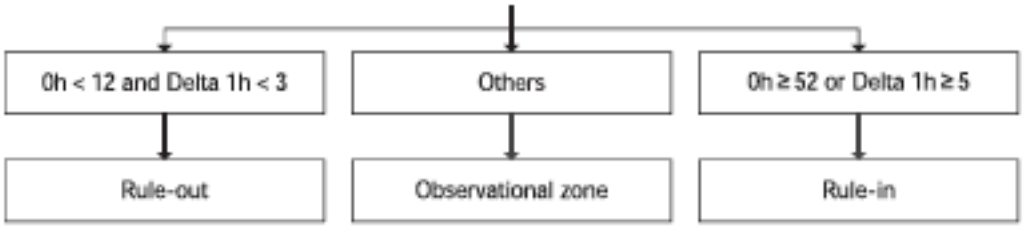


**Figure 1.** Hs-cTnT 0-hour/1-hour algorithm. Values for hs-cTnT are shown in nanograms per liter.

| **Are the Results Valid?*** | |
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| ***Questions*** | ***Comments*** |
| **A. Did clinicians face diagnostic uncertainty?** | Yes, all patients presenting to the ED with CP were enrolled.<br>The adjudicated final diagnosis for the patients was:<br>17% AMI<br>13% Unstable angina<br>9% Cardiac symptoms of origin other than CAD<br>22% Non-cardiac Symptoms<br>**39% Symptoms of unknown origin** |
| **B. Was there a blind comparison with an independent gold standard applied similarly to the treatment group and the control group? (Confirmation bias)** | No. There was no use of a "gold standard" such as angiography in ALL patients. The surrogate "gold standard" was an adjucated diagnosis based upon all clinical data provided to two independent cardiologists. Cardiologists were blinded to hs-cTnT results though not cTnI-ultra results. The authors did not report on the number of patients that underwent stress testing. All patients were given an adjudicated diagnosis based on all diagnostic tests available for each patient. |
| **C. Did the results of the test being evaluated influence the decision to perform the reference standard? (Ascertainment Bias)** | No. It is uncertain whether hs-cTnT results influenced additional diagnostic testing. The hs-cTnT results were not available at the time of patient assessment and therefore did not influence clinical decision making |
| **What are the Results?*** | |
| ***Questions*** | ***Comments*** |
| **A. What reported likelihood ratios were associated with the range of possible test results?** | 1282 patients enrolled<br>813 (63.4 %) → ruled out<br>NPV for AMI 99.1% [98.2% to 99.7%]<br>Sensitivity 96.7% [93.4% to 98.7%]<br><br>*** 7 patients with false negative results (0.9%) miss rate<br>30-day mortality was 0.1% in patients assigned to the ruled-out group.<br><br>184 (14.4%) → ruled in<br>PPV for AMI 77.2 % [70.4% to 83.0%]<br>Specificity 96.1% [94.7% to 97.2%]<br>30-day mortality was 2.7%<br><br>285(22.2 %) → observational zone<br>Prevalence of AMI of 22.5%<br>30-day mortality 0.7%<br><br>*** Sensitivity analysis, in which data for STEMI patients (n=21) were removed, revealed similar findings.<br>NPV 99.14%<br>PPV 74.55 % |

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| **How Can the Results Apply to Patient Care?*** | |
| ***Questions*** | ***Comments*** |
| **A. Will the reproducibility of the test result and its interpretation be satisfactory in my clinical setting?** | When the hs-cTnT tests become available in the US, yes, this algorithm should be applicable in patients meeting the inclusion/exclusion criteria presenting to the ED with symptoms of AMI. |
| **B. Are the results applicable to patients in my clinical setting?** | Maybe. There was a disproportionate number of male patients so applicability in female patients is unclear. Also, the authors stated that they included "Patients presenting to the ED with symptoms suggestive of acute myocardial infarction" This suggests a higher pre-test probability than our patients the majority of whom have a low pre-test probability for AMI. Because of this prevalence of disease is lower increasing likelihood of false positives and potential harms of additional testing. A PPV of 77.2% means that 22.8% of positive hs-cTnTwill be false. |
| **C. Will the results change my management strategy?** | Possibly, this could allow for more rapid identification of patients that can be safely discharged with appropriate outpatient follow up when used in conjunction of full clinical assessment and appropriate risk stratification.<br><br>Additionally, the immediate consequence of being assigned to the rule-in zone would likely be early admission and in general early coronary angiography. This could help to avoid delays in angiography associated with 4-6 hr protocols. |
| **D. Will patients be better off as a result of the test?** | Yes<br>Earlier discharge in rule out patients who are appropriate for discharge, increased satisfaction and reassurance.<br><br>Earlier recognition of AMI, leads to earlier admission and interventions. |

**Limitations:**

Only applicable to ED patients, not validated in patients presenting to a family physician,
No risk stratification of patients with CP
Observational diagnostic study should be compared to usual care:
Compared against a centrally adjudicated final diagnosis and not a true "gold standard"
Now warrants applying it prospectively for clinical decision making and Impact assessment
Additionally, further work can evaluate the cost-effectiveness when implemented in practice

Patient enrollment required the presence of dedicated research personnel in the ED at the patient's presentation → underrepresentation of patients presenting during the night
Can't apply to patients who come in immediately upon developing SSCP. Their median time to sampling was 3.5 hours so utility of hs-cTnT very early on is inconclusive.
There is no universal reference standard so these results apply only to the assays being tested.
Findings might slightly UNDERESTIMATE the true NPV because a threshold of chest pain onset of fewer than 6 hours (vs 12 hours in APACE) was chosen to enrich the study population with the particularly challenging early presenters
Cannot comment on its validity in patients meeting exclusion criteria.

**Your Clinical Bottom Line:**
I predict hs-cTnT will become part of practice in the US, knowing the limitations and appropriate interpretation is essential in fulfilling the high safety standards required in this clinical setting.
Based on the study results, the hs-cTnT 0-hour/1-hour algorithm performs well for early rule-out and less so for rule-in of AMI, but the assessment of patients with acute chest pain in the ED is not limited to the rule-in or rule-out of AMI and the authors do not provide data (beyond mortality) regarding the clinical, economic, ED throughput data from the observation group. .
All patients presenting with acute chest pain require a full clinical assessment to allow for appropriate identification of patients that can be safely discharged, irrespective of the biomarker results.