ACEP Clinical Policy: Critical Issues in the Evaluation and Management of Emergency Department Patients With Suspected Non–ST-Elevation Acute Coronary Syndromes

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PROBLEM

- Miss up to 2% of acute MIs
- Improving miss rates, but increased:
  - False positives
  - LOS in ED
  - Excessive testing

OUTCOME
30 D MACE

- CARDIOVASCULAR DEATH
- MYOCARDIAL INFARCTION
- REVASCULARIZATION

QUESTIONS

- **In adult patients without evidence of ST-elevation ACS, can initial risk stratification be used to predict a low rate of 30-day MACE?**
- **In adult patients with suspected acute NSTE ACS, can troponin testing within 3 hours of ED presentation be used to predict a low rate of 30-day MACE?**
- **In adult patients with suspected NSTE ACS in whom acute MI has been excluded, does further diagnostic testing for ACS prior to discharge reduce 30-day MACE?**
- **Should adult patients with acute NSTEMI receive immediate antiplatelet therapy in addition to aspirin to reduce 30-day MACE?**

In patients with chest pain what is an acceptable miss rate for MACE at 30 days?

- 0% = what we really want
- 1% = what we accept
- 2% ≈ test threshold
- 5% = what some patients accept

BMC Medical Informatics and Decision Making 2005, 5:26

1. In adult patients without evidence of ST-elevation ACS, can initial risk stratification be used to predict a low rate of 30-day MACE?

- ***Level B recommendations.*** In adult patients without evidence of ST-elevation ACS, the History, ECG, Age, Risk factors, Troponin (HEART) score can be used as a clinical prediction instrument for risk stratification. A low score (≤3) predicts 30-day MACE miss rate within a range of 0% to 2%.
- ***Level C recommendations.*** In adult patients without evidence of ST-elevation ACS, other risk-stratification tools, such as Thrombolysis in Myocardial Infarction (TIMI), can be used to predict rate of 30-day MACE.

TIMI = 0

- Sensitivity overall
  - 67 to 100%
- High Sensitivity Troponin
  - 98.4 % [95.9 to 99.4]
  - 100 % [94.3 to 100]
  - 100 % [91.6 to 100]

COMPARISON: Conventional Troponins

- TIMI = 0 (n = 434)
  - Sensitivity 100% [95% C.I. 94.3 – 100]
  - Specificity 8.5% [95% C.I. 5.9 – 12.0]
- HEART ≤ 2 (n=374)
  - Sensitivity 92.8% [95% C.I. 83.2 – 97.3]
  - Specificity 43.6% [95% C.I. 38.0 – 49.4]

Singer AJ et al: Am J EM 2017;35:704-709

High Sensitivity Troponin (hs-Tn)

- Detect troponin at levels 10- to 100-fold lower than contemporary troponin assays
- Coefficient of variance < 10% at 99th percentile value of reference healthy population
- Concentrations above assay's limit of detection are measurable in > 50% of healthy individuals

PERFORMANCE HEART SCORE: 30 d MACE

Source	Score	Class of Evidence	Troponin	Sensitivity (%)	95% CI
Backus et al[47]	0 to 3	III	Conventional	98.3	97.2 to 100
Six et al[33]	0 to 2	III	Conventional	98.9	97.3 to 99.6
Sun et al[60]	0 to 3	III	Conventional	98.2	97.8 to 98.6
Chen et al[41]	0 to 5	III	Conventional	48.9	38.2 to 59.7
Poldevaart et al[56]	0 to 3	III	Conventional and high sensitivity	98.0	96.7 to 98.8
Van Den Berg and Body[57]	0 to 2	III	Conventional and high sensitivity	99.4	96.8 to 99.9
Carlton et al[40]	0 to 2	III	High sensitivity	98.7	92.4 to 99.9
Leung et al[42]	0 to 2 (modified)	III	High sensitivity	100.0	91.6 to 100.0

2. In adult patients with suspected acute NSTE ACS, can troponin testing within 3 hours of ED presentation be used to predict a low rate of 30-day MACE?

- ***Level C recommendations.*** In adult patients with suspected acute NSTE ACS, conventional troponin testing at 0 & 3 hours among low-risk ACS patients (defined by HEART score 0 to 3) can predict an acceptable low rate of 30-day MACE.
- ***Level C recommendations.*** A single high-sensitivity troponin result below the level of detection on arrival to the ED, or negative serial high-sensitivity troponin result at 0 and 2 hours is predictive of a low rate of MACE.
- ***Level C recommendations.*** In adult patients with suspected acute NSTE ACS who are determined to be low risk based on validated ADPs that include a nonischemic ECG result and negative serial high-sensitivity troponin testing results both at presentation and at 2 hours can predict a low rate of 30-day MACE allowing for an accelerated discharge pathway from the ED.

HEART SCORE ≤ 3 PLUS NEG TROP 0 & 3 h: Conventional Troponin

- Mahler (Circ Cardiovasc Qual Outcomes. 2015;8:195-203)
  - 282 patients randomized
  - Zero MACE missed
- MIDAS Study (Int J Cardiol. 2013;168:795-802)
  - Prospective observation cohort
  - 18 US sites
  - 1% MACE missed

CONVENTIONAL TROPONINS: 0 AND 2 HR

- Stopyra et al *Crit Pathw Cardiol*. 2015;14:134-138)
  - 2 hour ADP
  - sensitivity 88.2% (95% CI 63.6% to 98.5%)
- Mahler et al (*Acad Emerg Med*. 2015;22:452-460).
  - sensitivity 83.9% (95% CI 66.3% to 94.5%)

TIMI = 0 PLUS NEG TROP 0 & 2 h: High Sensitivity Troponin

- ADAPT TRAIL (Class I) n=392
  - sensitivity of 99.7% (95% CI 98.1% to 99.9%)
  - specificity of 23.4% (95% CI 21.4% to 25.4%)
- ASPECT (Class II) n=3582
  - sensitivity of 99.3% (95% CI 97.9% to 99.8%)
  - specificity of 11.0% (95% CI 10.0% to 12.2%)

WHAT ABOUT A SINGLE HS TROPONIN < LOD?

- Mokhtari (Ann EM 2016;68:649-658)
  - 1,138 patients
  - 1/3 with troponin < 5 ng/L (LOD)
  - Sensitivity was 99% (0.3% risk of MACE)
- Pickering et al (Ann Intern Med. 2017;166:715-724)
  - 11 studies with 2,825 patients
  - Pooled sensitivity of MACE was 98%

3. In adult patients with suspected NSTE ACS in whom acute MI has been excluded, does further diagnostic testing (eg, provocative, stress test, computed tomography [CT] angiography) for ACS prior to discharge reduce 30-day MACE?

- ***Level B recommendations.*** Do not routinely use further diagnostic testing (coronary CT angiography, stress testing, myocardial perfusion imaging) prior to discharge in low-risk patients in whom acute MI has been ruled out to reduce 30-day MACE.
- ***Level C recommendations.*** Arrange follow-up in 1 to 2 weeks for low-risk patients in whom MI has been ruled out. If no follow-up is available, consider further testing or observation prior to discharge (Consensus recommendation).

RCTs FURTHER TESTING: NO IMPACT

- **Class II (one study)**
  - **Lim et al (J Nucl Cardiol. 2013;20:1002-1012) RCT on effect of stress myocardial perfusion imaging on 30-day outcomes**
  - **Both groups had low 30-day MACE rates: stress myocardial perfusion imaging group 0.4% vs standard management group 0.8% (RR =0.50; 95% CI 0.13 to 2.00)**
- **Class III (two studies)**
  - **Frisoli et al (*Circ Cardiovasc Qual Outcomes*. 2017;10: e003617) randomized 105 patients with HEART ≤ 3 and reassuring 0- and 3-h troponin I to either immediate discharge or stress testing in the ED: NO MACE**
  - **Poon et al (*J Am Coll Cardiol*. 2013;62:543-552) followed patients after coronary CT for 30-day MACE rates after NSTEMI was ruled out with ECG and serial troponins: NO MACE**

4. Should adult patients with acute NSTEMI receive immediate antiplatelet therapy in addition to aspirin to reduce 30-day MACE?

- ***Level C recommendations.*** P2Y12 inhibitors and glycoprotein IIb/IIIa inhibitors may be given in the ED or delayed until cardiac catheterization.

Adenosine Diphosphate–Induced Platelet Aggregation Inhibitors ($P2Y_{12}$ inhibitors).

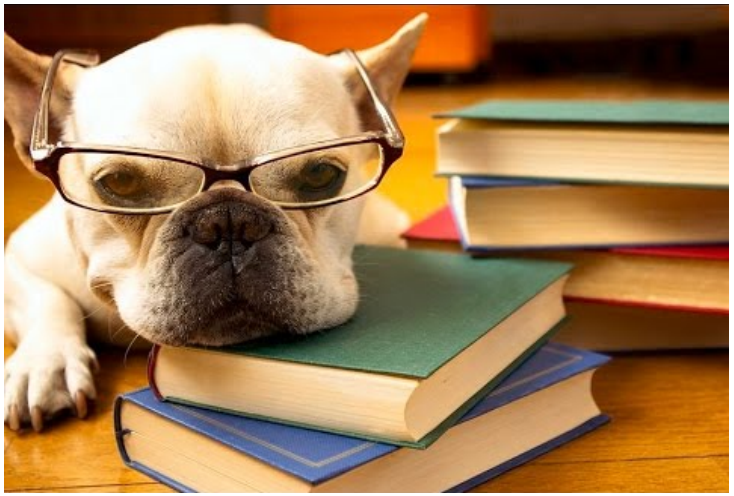
- **Class I RCT (Montalescot et al: *N Engl J Med*. 2013;369:999-1010): PRASUGREL in patients with NSTE ACS who were to undergo catheterization**
  - **prasugrel before angiography did not reduce 30-day MACE**
  - **major bleeding episodes increased in prasugrel group at 30 days (2.8% vs 1.5%, hazard ratio 2.0; 95% CI 1.3 to 3.1)**
- **Class I RCT (Yusuf et al:*N Engl J Med*. 2001;345:494-502): CLOPIDOGREL in patients with NSTE ACS (~14 hrs)**
  - **reduction in MI during 12-mo study (5.2% vs 6.7%; relative risk 0.8; 95% CI 0.7 to 0.9)**
  - **risk of bleeding increased in clopidogrel group (8.5% vs 5.0%; relative risk 1.7; 95% CI 1.5 to 1.9)**

Antiplatelet Glycoprotein IIb/IIIa Inhibitors

- **ABCIXIMAB**
  GUSTO IV-ACS Trial (Lancet. 2001;357:1915-1924)
  - **no difference in 30-day death/MI (odds ratio 1.0; 95% CI 0.83 to 1.24) for placebo vs 24-hr abciximab**
  - **increased mortality (<1%) at 48 hr for patients receiving a 24- or 48-hr of abciximab**
- **EPTIFIBATIDE or TIROFIBAN**
  ACUITY Timing Trial (JAMA 2007;297:591-602)
  - **early administration (0.6 h) vs deferral until time (4.5 h) of PCI (< 72 hr) did not confer benefit**
  - **increased bleeding (6.1 vs 4.9% RR 1.12 [0/67-0.95])**

WHAT WE DID NOT STUDY…

- Delta
- Duration of pain
- Shared decision making



CONCLUSIONS

- **Patients with chest pain & low risk for ACS (eg, HEART score ≤ 3) and normal troponin at 0 and 3 hours post presentation may be discharged safely, with ≤ 2% risk of 30-day MACE**
- **High-sensitivity troponins accelerate rule-out protocol (0 and 2 h)**
- **In low risk cases who rule out, no data to support subsequent noninvasive testing**
- **It is acceptable to delay further antiplatelet therapy, beyond heparin, especially if concern for bleeding**