EM CASES SUMMARY

Episode 128 Low Risk Chest Pain & High Sensitivity Troponin

With Eddy Lang and Andrew McRae
Prepared by Anton Helman, July 2019

Defining low risk chest pain

Patients at low risk for ACS are those who are hemodynamically stable, are without concerning features on history or examination, and do not have immediate objective evidence of myocardial ischemia on initial ECGs and biomarker testing. Consensus guidelines further define the low risk patient as having a < 1% risk of a Major Adverse Cardiac Event (MACE) or death at ≥ 30-days follow up [1], a threshold below which harm caused by further testing may outweigh any clinical benefit [2].

Predictive value of clinical features for ACS

There is no combination of historical features that can accurately rule in or rule out ACS [3].
The rule for ACS presentations is: *Atypical is typical [4].*

- Up to 1/3 of pts with ACS have no CP at all [5].
- **Populations most at risk for atypical presentations** are women and patients with comorbidities that alter their ability to communicate (e.g. stroke, dementia) or alter their sensory perception of chest pain (e.g. diabetes, neuropathies)
- **The most frequent anginal equivalents** in order of prevalence: SOB>weakness>unusual fatigue>sweating>dizziness
- **Risk factors for ACS presenting without chest pain** include older patients (especially >85 years of age), women, diabetes, stroke and heart failure [6].
- Patients with comorbidities might be at an increased risk of ACS related to diagnostic error as a result of us anchoring on their usual complications

Based on the TRAPID-AMI [7] and JAMA clinical exam series [8] the most predictive features of ACS include:

- Radiation to both arms or right arm
- Pain described as pressure
- Associated with nausea or vomiting
- Associated with sweating (especially sweating observed in the ED)
- Pain came on with physical activity

Chest pain that significantly *decreases* the likelihood of ACS include:

- Pleuritic in nature
- Positional pain
- Pain described as sharp
- Pain that is fully reproducible with palpation
- Inframammary location
- Non-exertional

Note that pleuritic chest pain and pain that is reproducible with palpation have been found to be present in up to 7% of patients with ACS.

Response to nitroglycerin has no predictive value for ACS [9].

Severity of pain is not related to the likelihood of ACS at presentation or 30-day MACE [10].

Take Home: *Missed ACS is more often a result of a failure to consider the diagnosis in patients with atypical symptoms rather than a failure to interpret troponin or use a clinical decision tool properly.*

Predictive value of risk factors for ACS

In the ED, traditional cardiac risk factors are poor predictors of ACS in patients >40 year of age. The only traditional risk factors that have predictive value enough to alter pretest probability for ACS in the ED patient with chest pain are diabetes and family history of premature MI in male patients (*not* obesity, smoking, hypertension, hyperlipidemia) [11,12,].

Patients < 40 years of age without any of the traditional risk factors makes the pre-test probability of ACS very low (negative LR of 0.17) and the presence of >4 risk factors, does help predict ACS (positive LR of 7.39)[13].

Important non-traditional risk factors, especially in young patients include: Pregnancy, chronic renal disease, HIV (especially if taking protease inhibitors), cocaine/amphetamine use, chronic steroid use and lupus.

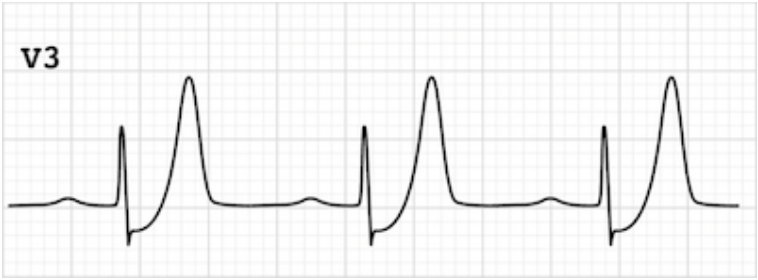
Take Home: C*lassic cardiac risk factors may be more useful in shifting pretest probability for ACS in younger patients; ask about non-traditional risk factors in young patients.*

Some key ACS ECG patterns and their significance

Nonspecific T-wave changes should not be ignored
In a recent retrospective study of over 2300 patients, nonspecific T-wave changes such as isolated T-wave inversion in lead III or V1 confer an increased likelihood of MACE at 30 days [14]. Nonspecific T-wave changes are a feature of the HEART score and should not be ignored in risk stratification of chest pain patients.

De Winter's T Waves pattern is an anterior STEMI equivalent [15]

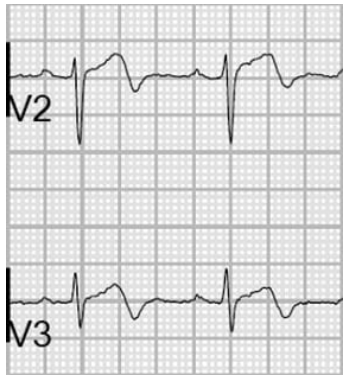
- A De Winter's Waves pattern is an anterior STEMI equivalent found in 2% of patients with acute proximal LAD occlusions
- Upsloping ST-Depression at J Point in leads V1 – V4 without STE
- Tall, symmetric T-Wave in leads V1 – V4
- STE in lead aVR +/- aVL



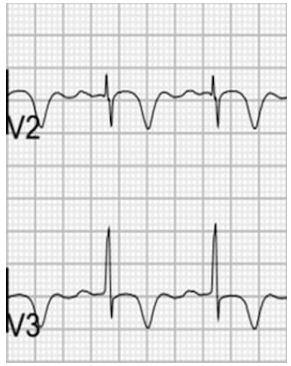
de Winter Waves. Note upsloping ST-depression and tall symmetric T-waves

Wellen's Syndrome signifies a high grade LAD or Left Main coronary lesion that may present with pseudo-normalization [16]

- Type A: While chest pain free, biphasic T waves seen in V1-V4
- During chest pain, paradoxical *pseudo-normalisation* of ST segments may occur
- Type B: Deeply inverted T-waves in leads V1 – V4 OR
- Places patients at high 7-day risk for anterior STEMI



Wellen's Type A. Note biphasic T waves.

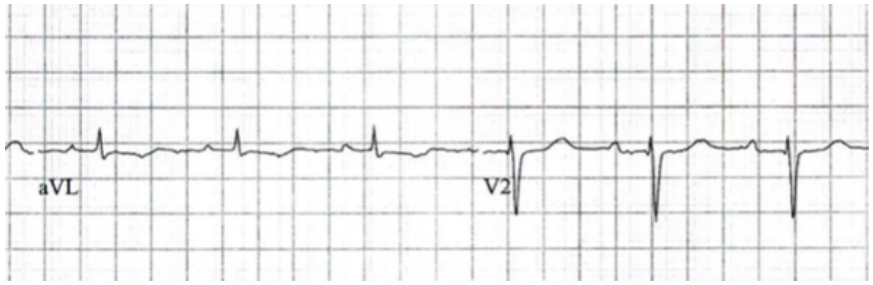


Wellen's Type B. Note deep inverted T-waves.

Flipped T and/or ST depression in aVL: An early sign of inferior STEMI [17]

An isolated flipped T-wave and/or ST depression in aVL may be an early sign of inferior STEMI, as it can represent reciprocal changes that occur prior to ST elevation, and helps to differentiate cardiac ischemia from pericarditis. However, there is a differential diagnosis of flipped T in aVL that you need to consider before you assume an impending STEMI that includes LVH with strain (T waves in same direction 1 *and* avL) and LBBB.

- ST depression in aVL had a sensitivity 99% and specificity of 100% for inferior STEMI
- 84% of patients with inferior MI have reciprocal changes in aVL



Isolated T-wave inversion or ST depression in aVL may be a sign of impending inferior STEMI

Troponin facts, myths and misconceptions for low risk chest pain

Elevated troponin is not specific for myocardial infarction. One observational study of 615 patients with elevated troponin found that the overall positive predictive value for ACS was only 56% [18]. However, troponin is an indicator of myocardial injury independent of cause. An elevated troponin increases the risk of short-term MACE and death regardless of cause [19], whether from sepsis, pulmonary embolism, chronic kidney failure or heart failure [20].

Take Home: *Avoid the terms "troponitis" or "troponemia" as they are trivializing and do not recognize this prognostic value of an elevated troponin.*

Conventional vs high sensitivity troponin: Hs-troponin is not a binary test

Conventional troponin is used primarily as a binary test. Levels below the cut-off for MI require serial testing over 6-12 hours to ensure that myocardial injury is detected with adequate sensitivity. In contrast, hs-troponin assays are not used as binary tests. By definition, 50% of healthy individuals will have detectable hs-troponin concentrations. Hs-troponin assays detect much lower concentrations of serum troponin with much greater precision so that hs-troponin assays can detect clinically significant elevations and changes in troponin concentrations much sooner in an ED evaluation. The accuracy of the diagnosis of myocardial infarction is increased by analyzing the rising and falling pattern of hs-troponin, rather than a binary cut-off.

High sensitivity troponin algorithms to rule out MI and safely discharge patients from the ED

1. A normal ECG and a single *undetectable* hs-troponin drawn 3 hours or more after the onset of symptoms rules out MI at ED arrival in 1/3 of patients and portends a MACE <2% [21].
2. Two-hour serial testing rules-out MI in 60% of patients, rules-in MI in 15% of patients, leaving only 25% of patients undifferentiated after a 2-hour ED evaluation. Delta 2-hour hs-troponin <4 nanograms/liter hs-troponin T portends a MACE <2% [22].
3. Hs-troponins in combination with a 0-3 score in the **HEART pathway** lowers the number of low risk patients from 40% to 10% and portends a MACE <1% [23,24,30].

An absolute change in hs-troponin is recommended rather than relative percentage change to rule in acute MI

The National Academy of Clinical Biochemistry recommends using a dynamic change of 20% or more to define myocardial infarction in patients with baseline elevations in troponin [23]. This change can be an increase or a decrease, in which increasing troponin suggests an evolving myocardial infarction, while decreasing troponin suggests a resolving myocardial infarction. The bulk of the literature suggests that an absolute delta (e.g. 10ng/L troponin T) rather than a relative change (e.g. 20%) generally performs better.

The concern that the higher sensitivity of hs-troponin assays compared to conventional troponins are expected to result in lower specificity and over-diagnosis of ACS with increased admission rates, is unfounded in practice. Based on Canadian experience, where hs-troponins have been widely adapted, the use of high sensitivity troponins compared to conventional assays have decreased length of stay and admissions without missing any additional MIs [25].

Which delta hs-troponin is best – 1hr, 2hr or 3hr?

1-hour [26], 2-hour [22] and 3-hour [27] delta troponin algorithms have all performed well for ruling out MI and predicting >30-day MACE. Our experts recommend using the 2-hour algorithm because the 3-hour algorithm has never been shown to be superior and the 1-hour algorithm has rule-out delta and rule-in deltas that are different by only a few nanograms per liter, which may be within the variation of the assay itself, resulting in misclassification of patients. With 2-hour delta troponins there is less risk of misclassification from assay variation.

Take Home: *A single undetectable hs-troponin after 3 hours of symptom onset* ***or*** *a delta 2-hr hs-troponin T <4ng/L plus normal serial ECGs and a HEART score of 0-3 rules out acute MI and lowers 30-day MACE to well below 1%, a threshold below which ancillary testing may cause more harm than benefit.*

HEART Pathway is the recommended clinical decision tool for low risk chest pain

HEART pathway performs better than the TIMI score [28], and specifically outperforms TIMI at low risk thresholds [29].
HEART score with hs-troponins lowers the number of low risk patients from 40% to 10% and 30-day MACE rate lowers from 1.5% to 0.9%. If you add a second troponin at 2 or 3 hours, the MACE rate falls to 0.3% [31].

HEART pathway is most useful for low-medium risk patients. Patients with ECG changes or high-risk troponin findings don't need a risk score—they need an angiogram. Patients with a normal ECG and low-risk troponin results probably don't need a risk score, or any subsequent testing. So the real value of a risk score is for the patients with low-moderate pre-test probabilities who aren't clearly ruled-in or ruled-out by an accelerated diagnostic pathway.

HEART pathway allows early discharge in 40% of patients compared to 18% with usual care with an NNT = 5 [24].
Limitations of HEART pathway:

- There is variability in how people score the HEART score
- HEART score has not been compared to clinical gestalt alone adequately in the literature
- If HEART score were applied blindly, it would miss about 4% of MACE!
- Pretest probability and gestalt are made up of components of HEART score
- It is possible to have an elevated troponin level and still be considered low risk on the HEART Score
- It is possible to have dynamic ECG changes and score low risk on HEART score
- Patients with normal ECG and two normal hs-troponins have a very low-risk of short-term MACE, and the HEART score may overestimate their risk

Is ancillary testing after the initial ED visit necessary for low risk chest pain?

"Our job in the ED is to identify ACS and not necessarily uncover anyone with coronary artery disease"
-Dr. Eddy Lang

With such a highly sensitive pathway using hs-troponins and HEART score, ancillary testing after the initial ED workup is rarely necessary. Exercise treadmill stress tests have a false positive rate as high as 80% leading to unnecessary angiograms, cardiac stents and CABG [32]. They are poor at identifying coronary artery disease and stress test studies in low risk chest pain patients suffer from inclusion bias. Stress echo and nuclear stress testing have slightly better accuracy than treadmill

exercise stress testing in identifying coronary artery disease, but have never been shown to improve patient oriented outcomes after a negative workup in the ED.

Is there a role for Cardiac Computed Tomography Angiography (CCTA) after ED visits for chest pain?

CCTA shows the presence and extent of coronary disease with reasonable accuracy. However, the use of CCTA in settings that routinely use noninvasive testing for low-to-moderate risk patients results in longer ED stays, greater resource utilization, increased invasive angiography and revascularization without substantial benefits in terms of prevention of MI or mortality [32, 33, 34, 35].

The 2018 ACEP clinical policy paper on suspected non ST elevation ACS does *not* recommend routine use of ancillary testing prior to discharge in low risk patients in whom MI has been ruled out [37]. They argue that limiting complex, expensive, and time-consuming testing can reduce patient cost, ED and hospital length of stay, and patient anxiety caused by unnecessary stress testing and potentially false-positive results, once adequate risk stratification and cardiac rule-out have occurred.

Take home points for low risk chest pain and high sensitivity troponins

- Missed ACS is more often a result of a failure to consider the diagnosis in patients with atypical symptoms rather than a failure to interpret troponin or use a clinical decision tool properly.
- Classic cardiac risk factors may be more useful in shifting pretest probability for ACS in younger patients; ask about non-traditional risk factors in young patients.
- A single undetectable hs-troponin after 3 hours of symptom onset **or** a delta 2-hr hs-troponin T <4ng/L plus normal serial ECGs and a HEART score of 0-3 rules out acute MI and lowers 30-day MACE to well below 1%, a threshold below which admission and/or ancillary testing may cause more harm than benefit.
- An absolute change in hs-troponin is recommended rather than relative percentage change to rule in acute MI
- The HEART pathway is the best clinical decision tool for ED low risk chest pain patients but has several limitations that are important to understand when applying the tool
- Ancillary testing including stress testing and CCTA in low risk chest pain patients should *not* be done routinely during/after an ED visit

REFERENCES

1. Amsterdam EA, Kirk JD, Bluemke DA, et al. Testing of low- risk patients presenting to the emergency department with chest pain: a scientific statement from the American Heart Association. Circulation. 2010;122(17):1756-1776.
2. Pauker SG, Kassirer JP. The threshold approach to clinical decision making. N Engl J Med. 1980;302(20):1109-17.
3. Goodacre S et al. How Useful are Clinical Features in the Diagnosis of Acute, Undifferentiated Chest Pain? Acad Emerg Med 2002. PMID: 11874776.
4. Lusiani L, et al. Prevalence, clinical features, and acute course of atypical myocardial infarction. *Angiology* 1994;45:49-55.
5. Brieger D, Eagle KA, Goodman SG, et al. Acute coronary syndromes without chest pain, an underdiagnosed and undertreated high-risk group: insights from the Global Registry of Acute Coronary Events. Chest. 2004;126(2):461-9.
6. Devon HA, Penckofer S, Larimer K. The association of diabetes and older age with the absence of chest pain during acute coronary syndromes. West J Nurs Res. 2008;30(1):130-44.
7. McCord J et al. Symptoms Predictive of Acute Myocardial Infarction in the Troponin Era: Analysis From the TRAPID-AMI Study. Crit Pathw Cardiol 2019.
8. Fanaroff AC, Rymer JA, Goldstein SA, et al. Does this patient with chest pain have acute coronary syndrome? the rational clinical examination systematic review. JAMA. 2015;314:1955-1965.
9. Chandra, A. et al. Prospective evaluation of the response to nitroglycerin as a predictor of ACS in patients presenting to the ED with undifferentiated chest pain. Annals of Emergency Medicine, Volume 46, Issue 3, 61.

10. Edwards M et al. Relationship Between Pain Severity and Outcomes in Patients Presenting with Potential Acute coronary Syndromes. Ann Emerg Med 2011.
11. Jayes R, Beshansky J, Dagostino R, et al. Do patients' coronary risk factor reports predict acute cardiac ischemia in the emergency department? A multicenter study. J Clin Epidemiol. 1992;45(6):621-626.
12. Body R, McDowell G, Carley S, et al. Do risk factors for chronic coronary heart disease help diagnose acute myocardial infarction in the emergency department? Resuscitation. 2008;79(1):41-45.
13. Han JH, Lindsell CJ, Storrow AB, et al. The role of cardiac risk factor burden in diagnosing acute coronary syndromes in the emergency department setting. Ann Emerg Med. 2007;49(2):145-152.e1.
14. Knowlman T, Greenslade JH, Parsonage W, et al. The association of electrocardiographic abnormalities and acute coronary syndrome in emergency patients with chest pain. Acad Emerg Med. 2017;24(3):344-352.
15. de Winter RJ, Verouden NJ, Wellens HJ, Wilde AA A new ECG sign of proximal LAD occlusion. N Engl J Med. 2008 Nov 6;359(19):2071-3.
16. Macias M et al. The Electrocardiogram in the ACS Patient: High-Risk Electrocardiographic Presentations Lacking Anatomically Oriented ST-Segment Elevation. Am J Emerg Med 2015.
17. Bischof J, Smith SW. ST depression in lead aVL differentiates inferior ST elevation myocardial infarction from pericarditis. Am J Emerg Med. 2016;34(7):1310.
18. Alcalai R, Planer D, Culhaoglu A, et al. Acute coronary syndrome vs nonspecific troponin elevation: clinical predictors and survival analysis. Arch Intern Med. 2007;167(3):276-281.
19. Eggers KM, Jernberg T, Lindahl B. Cardiac Troponin Elevation in Patients Without a Specific Diagnosis. J Am Coll Cardiol. 2019;73(1):1-9.
20. Stacy SR, Suarez-cuervo C, Berger Z, et al. Role of troponin in patients with chronic kidney disease and suspected acute coronary syndrome: a systematic review. Ann Intern Med. 2014;161(7):502-12.
21. Pickering JW, Than MP, Cullen L, et al. Rapid Rule-out of Acute Myocardial Infarction With a Single High-Sensitivity Cardiac Troponin T Measurement Below the Limit of Detection: A Collaborative Meta-analysis. Ann Intern Med 2017;166:715-24.
22. Reichlin T, Cullen L, Parsonage WA, et al. Two-hour algorithm for triage toward rule-out and rule-in of acute myocardial infarction using high-sensitivity cardiac troponin T. Am J Med. 2015;128(4):369-79.e4.
23. Mahler SA, Stopyra JP, Apple FS, et al. Use of the HEART Pathway with high sensitivity cardiac troponins: A secondary analysis. Clin Biochem. 2017;50(7-8):401-407.
24. Mahler SA, Riley RF, Hiestand BC, et al. The HEART Pathway randomized trial: identifying emergency department patients with acute chest pain for early discharge. Circ Cardiovasc Qual Outcomes. 2015;8(2):195-203.
25. Andruchow JE, Kavsak PA, Mcrae AD. Contemporary Emergency Department Management of Patients with Chest Pain: A Concise Review and Guide for the High-Sensitivity Troponin Era. Can J Cardiol. 2018;34(2):98-108.
26. Reichlin T, Twerenbold R, Wildi K, et al. Prospective validation of a 1-hour algorithm to rule-out and rule-in acute myocardial infarction using a high-sensitivity cardiac troponin T assay. CMAJ. 2015;187(8):E243-52.
27. Peacock WF, Baumann BM, Bruton D, et al. Efficacy of High-Sensitivity Troponin T in Identifying Very-Low-Risk Patients With Possible Acute Coronary Syndrome. JAMA Cardiol. 2018;3(2):104-111.
28. Sun B et al. Assessment of Chest Pain in the Emergency Department. Circulation 2015; 132: A13647.
29. Backus BE et al. Risk Scores for Patients with Chest Pain: Evaluation in the Emergency Department. Curr Cardiol Reviews 2011; 7(1): 2-8.
30. Laureano-phillips J, Robinson RD, Aryal S, et al. HEART Score Risk Stratification of Low-Risk Chest Pain Patients in the Emergency Department: A Systematic Review and Meta-Analysis. Ann Emerg Med. 2019.
31. Salim Rezaie, "Management and Disposition of Low Risk Chest Pain", REBEL EM blog, February 18, 2016. Available at: https://rebelem.com/management-and-disposition-of-low-risk-chest-pain/.
32. Natsui S, Sun BC, Shen E, et al. Evaluation of Outpatient Cardiac Stress Testing After Emergency Department Encounters for Suspected Acute Coronary Syndrome. Ann Emerg Med. 2019; in press.
33. Gongora CA et al. Acute Chest Pain Evaluation using Coronary computed tomography Angiography Compared with Standard of Care: A Meta-Analysis of Randomised Clinical Trials. HEART 2018.
34. Hulten EA, Carbonaro S, Petrillo SP, et al. Prognostic value of cardiac computed tomography angiography: a systematic review and meta-analysis. J Am Coll Cardiol. 2011;57(10):1237- 1247.
35. Morris JR, Bellolio MF, Sangaralingham LR, et al. Comparative trends and downstream outcomes of coronary CT angiography and cardiac stress testing in emergency department patients with chest pain: an administrative claims analysis. Acad Emerg Med. 2016;23(9):1022-1030.
36. Hulten E, Pickett C, Bittencourt MS, et al. Outcomes after coronary computed tomography angiography in the emergency department: a systematic review and meta- analysis of randomized, controlled trials. J Am Coll Cardiol. 2013;61(8):880-892.
37. Tomaszewski CA, Nestler D, Shah KH, Sudhir A, Brown MD. Clinical Policy: Critical Issues in the Evaluation and Management of Emergency Department Patients With Suspected Non-ST-Elevation Acute Coronary Syndromes. Ann Emerg Med. 2018;72(5):e65-e106.
38. Amsterdam E, Wenger N, Brindis R, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;130(25):e344-426.