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Washington University Emergency Medicine Journal Club
Clinical Prediction Rules in Low Risk Chest Pain in the Emergency Department

Vignette

You are working a standard Monday afternoon shift in EM1 and have just come out of room 7 where the patient has informed you that he is King of the Gremlins when you see a new patient with chief complaint of chest pain pop up on the board. You go to see the patient, Mr. X, who is a 39 year old nonsmoking male with no prior medical history. He complains of substernal chest pain starting two hours ago while working in his yard. He states the pain was left sided, no radiation, some mild shortness of breath. Symptoms have now resolved. Workup shows a normal EKG and troponin negative x1.

You think about further workup for this patient who has been given aspirin and is now pain-free. The Observation Unit is unfortunately double-booked since Dr. Seltzer is working in EM2 so you consider your other options. Are there any clinical prediction rules that can help risk-stratify this patient and help you decide on a disposition? You "borrow" Dr. Gilmore's iPad from the TCC chart rack and commence a literature search...

PICO Question
Population: Adult patients presenting to the Emergency Department (ED) with chest pain in whom there is clinical concern for acute coronary syndrome (ACS)
Intervention: The application of a Clinical Decision Rule (CDR) to assess patients at such low risk that discharge home without stress testing is warranted
Comparison: Standard practice and clinical gestalt
Outcome: Death, myocardial infarction, life-threatening arrhythmia, quality of life

Search Strategy

After searching PubMed using multiple strategies and identifying an abundance of articles addressing various decision rules for low-risk chest pain, you instead email Dr. Erik Hess, Associate Professor of Emergency Medicine and Critical Care at the Mayo Clinic in Rochester Minnesota. A known expert in acute coronary syndrome research, he recommends the four selected articles to address the topic.

Article 1: Than M, Cullen L, Reid CM, et al. A 2-h diagnostic protocol to assess patients with chest pain symptoms in the Asia-Pacific region (ASPECT): a prospective observational validation study. Lancet. 2011 Mar 26;377(9771): 1077-84. Answer Key.

Article 2: Mahler SA, Hiestand BC, Goff DC Jr, Hoekstra JW, Miller CD. Can the HEART score safely reduce stress testing and cardiac imaging in patients at low risk for major adverse cardiac events? Crit Pathw Cardiol. 2011 Sep;10(3):128-33. Answer Key.

Article 3: Kline JA, Zeitouni RA, Hernandez-Nino J, Jones AE. Randomized trial of computerized quantitative pretest probability in low-risk chest pain patients: effect on safety and resource use. Ann Emerg Med. 2009 Jun;53(6):727-35. Answer Key.

Article 4: Aldous SJ, Richards M, Cullen L, Troughton R, Than M. A 2-hour thrombolysis in myocardial infarction score outperforms other risk stratification tools in patients presenting with possible acute coronary syndromes: comparison of chest pain risk stratification tools. Am Heart J. 2012 Oct;164(4):516-23. Answer Key.

Bottom Line

Chest pain remains a common chief complaint among patients presenting to the Emergency Department, accounting for more than 10 million visits annually in the US. According to data from the Physician Insurers Association of America, more than a quarter of all money paid in closed malpractice claims from 1985 to 2003 involved patients with a chief complaint of "chest pain." Given the high risk of malpractice, and increased morbidity and mortality associated with missed diagnosis of ACS, many Emergency Physicians have a low threshold to perform extensive testing in these patients, frequently including provocative testing. The 2010 American Heart Association Scientific Statement on testing in low-risk chest pain patients in the ED supports this practice, recommending confirmatory testing in patients with negative or nondiagnostic ECGs and negative serial cardiac biomarkers prior to hospital discharge. Such confirmatory testing can include exercise treadmill testing, myocardial perfusion imaging, or coronary angiography (invasive or computed tomography).

Unfortunately, this recommendation does not take into account the potential downsides to such confirmatory testing in low-risk patients, and does not consider the impact of the test threshold on clinical decision making. Potential downsides include both monetary issues (cost of the test, prolonged hospitalization, time off work) and false positive risk. A simple exercise can demonstrate the high theoretical incidence of false positive stress testing in low risk patients. Using reported accuracy measures

Table 1. Prevalence = 5%

	CAD +	CAD -
Test +	41	100
Test -	9	850

for treadmill stress echocardiography (positive LR 7.94 and negative LR 0.19, Banerjee 2012), we can draw 2X2 tables for a hypothetical group of 1000 patients with a prevalence of coronary artery disease (CAD) of 5% (Table 1). We see that of the 50 patients with CAD, 41 will have a positive stress test, while 9 will have a false negative test. Equally as important, we see that 100 patients *without* CAD will have a *false positive* stress test. Over two-thirds of patients a with a positive stress test *do not* have CAD in this example. These 100 patients will likely be subjected to further testing, many undergoing invasive coronary angiography as a result. If we instead take a group of patients with a 2% prevalence of disease, we see that the false-positive risk increases, and potential for harm (relative to the potential for benefit) increases significantly (Table 2).

Table 1. Prevalence = 2%

	CAD +	CAD -
Test +	16	108
Test -	4	872

Studies have demonstrated this high false positive rate in both "low risk" and "intermediate risk" patient populations. This high risk of false positive stress testing is underscored by its recent inclusion as part of the American College of Cardiology contribution to the Choosing Wisely campaign. While these recommendations were targeted at screening in asymptomatic patients rather than symptomatic ED patients, the same risks of "invasive procedures" and "excess radiation exposure" applies to any population at significantly low risk. It is therefore imperative to identify ED patients at sufficiently low risk of ACS such that further cardiac imaging is unnecessary. The use of clinical decision rules (CDRs) and accelerated diagnostic protocols (ADPs) may help solve this crisis.

The ASPECT trial looked at an ADP that consisted of a thrombolysis in myocardial infarction (TIMI) score of 0 and normal cardiac biomarkers (troponin and CK-MB) at presentation and 2 hours later. This ADP identified a population with a 0.9% risk of a major adverse cardiovascular event (MACE) at 30 days, with a sensitivity of 99.3% and a negative predictive value (NPV) of 99.1%. There were 3 patients in the study with a false negative ADP, 2 of whom required coronary stenting and one of whom underwent radiofrequency ablation for a 30-minute episode of stable ventricular tachycardia; none died or had serious morbidity. A follow-up study (Aldous 2012) looked at several CDRs and ADPs in patients from one institution in the ASPECT trial. Three ADPs were found to be superior, including the 2-hour TIMI (sensitivity 99.2%, NPV 98.1%), an ADP reported by Hess et al (sensitivity 99.7%, NPV 98.9%), and an ADP reported by Christensen et al (sensitivity 99.4%, NPV 93.8%). Of these, the 2-hour TIMI had the highest specificity (23.8%) while the ADP by Christensen had the lowest (4%), and would likely have limited clinical utility as a result.

An evaluation of the HEART score from Wake Forest Baptist Medical Centre (Mahler 2011) demonstrated a high NPV (99.4%). It's poor sensitivity (58.3%) was

due to the inclusion of only low-risk patients in the cohort (those with a TIMI score < 2 and low clinical suspicion of ACS). Combination of the HEART score with a negative 4 to 6-hour troponin increased both the sensitivity and NPV to 100%. Unfortunately, the study protocol required the use of two CDRs (TIMI and HEART) for inclusion, making application to everyday practice difficult. Poor methodology also makes the study's results unreliable.

Beyond ADPs and CDRs, Jeff Kline has looked at the use of attribute matching to provide pre-test probabilities for patients at risk for ACS. A recent randomized controlled trial assessed the impact of providing these pre-test probabilities to patients and clinicians in the ED. While this practice reduced the rate of negative testing associated with significant radiation exposure (> 5 mSv), this effect was not the result of reduced provocative testing, but rather a shift from radiologic testing to non-radiologic testing in the intervention group. It is unclear why attribute matching would cause such a shift in the type of tests ordered by the clinician. Further benefit should be shown prior to widespread implementation of the tool in clinical practice, especially given its proprietary nature and the associated cost.

Consensus:

While most present agreed that reducing stress testing in patients at very low risk of adverse outcomes would likely benefit both patients and society, the quantification of what constituted significantly low risk was variable, ranging from 0% up to 5%. Medicolegal risk was cited as the primary concern when discharging low-risk patients without provocative testing. Ongoing research into shared decision making may help remove some of these barriers, decrease healthcare utilization, reduce the risk of false-positive stress testing, and improve patient care.