MAYO CLINIC

Disrupting Common Practice: Retiring Stress Tests for Acute Chest Pain Presentations

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Each year, more than 6 million patients are evaluated for coronary artery disease (CAD) and acute coronary syndrome (ACS) in emergency departments (EDs) across the United States. Yet, the vast majority of patients are at low-to-intermediate-risk of ACS, creating a high-stakes challenge to identify the few patients at high risk of short-term major adverse cardiovascular events (MACE). CAD is the inductive etiology for ACS, which is a syndrome of acute heart injury that produces symptoms, electrocardiogram (ECG) changes, or imaging findings characteristic of acute coronary hypoperfusion. ACS consists of acute myocardial infarction (AMI) and unstable angina (UA), where AMI causes myocyte death and can be identified by an increase, and if presenting late after symptom onset, a decrease in myocardial biomarkers such as troponin I or T.[1]

Historically, biomarker assays could not reliably detect small, but clinically meaningful heart injury, and clinicians worried about UA, that is, troponin-negative ACS. Consequently, stress testing was used to identify CAD and infer that ACS was the cause of chest pain. However, contemporary high-sensitivity troponin (hsTn) assays can reliably determine troponin levels in half of the general population and can reclassify a majority of UA as AMI. These highly sensitive assays have led experts to question if ACS can occur without an elevation of hsTn.[2] However, current guidelines continue to recommend routine stress testing.

CURRENT APPLICATIONS OF STRESS TESTING

Despite improvements in diagnostic tests and risk factor mitigation, stress testing use has increased, while rates of inducible ischemia have plummeted. As the prevalence of ACS is low, especially after serial troponin and ECG testing, application of Bayes' theorem would intuit that many patients will have false-positive stress test results leading to increased downstream costs. In a prospective cohort of 4181 patients with chest pain undergoing stress testing, abnormal results were found in only 11% of patients, most of whom did not undergo invasive angiography. Despite the risk of verification bias in which higher-risk patients preferentially underwent angiography, 50% of positive stress test results were false-positives, and less than 1% of the cohort benefited from testing and revascularization.[3]

Clinicians may believe that revascularization in patients without AMI, that is those with CAD, improves outcomes and deploy stress testing to identify patients who may benefit. However, the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE), Objective Randomised Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina (ORBITA), and International Study of Comparative Health Effectiveness With Medical and Invasive Approaches (ISCHEMIA) trials have shown that the addition of percutaneous coronary intervention (PCI) to optimal medical therapy (OMT) does not improve mortality or MACE in patients with stable CAD. Although PCI improved anginal symptoms in the COURAGE and ISCHEMIA trials, ORBITA showed that sham PCI eliminates the symptomatic benefit of PCI, thus attributing at least some of the benefit to placebo effect.[4] Given the absence of improved cardiovascular outcomes, doubts about symptomatic relief, and the safety of OMT alone, regularly stress testing patients to identify

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candidates for PCI should not be performed urgently.

STRESS TESTING AND OUTCOMES

Large administrative datasets provide evidence that stress testing increases risk of admission, invasive angiography, and PCI without improving AMI risk. Notably, observational studies can have residual confounding, although as clinicians are more likely to obtain stress testing in higher risk patients, it would make stress testing appear to be a stronger testing strategy. A large, private insurance database study attempted to control for case-mix confounding by comparing outcomes between weekend and weekday presentations for chest pain and found stress testing within 2 or 30 days of presentation increased rates of invasive angiography and revascularization with no change in AMI admissions at 1 year.[5] Further, a post hoc analysis of 118 patients who did not undergo stress testing or cardiac computed tomography angiography (CCTA) in the ROMICAT II trial found that further testing with either CCTA or stress testing resulted in increased length of stay, costs, rates of angiography, and radiation exposure without a difference in readmissions or MACE.[6] Although observational studies and post hoc analyses have limitations, these findings add to the body of evidence suggesting that routine stress testing may not be necessary in patients with low- or intermediate-risk chest pain.

ALTERNATIVE STRATEGIES TO STRESS TESTING

Risk Stratification Scores

HEART (History, ECG, Age, Risk factors, Troponin) score is a 10-point risk stratification system that classifies undifferentiated chest pain into low (0-3 points), moderate (4-6 points), and high (7-10 points) risk of MACE at 6 weeks by incorporating information available at initial ED presentation, including a conventional troponin level. In a systematic review of 30 studies and 44,202 patients presenting with chest pain where MACE occurred in 12%, HEART score greater than 3 had 96% sensitivity of detecting short-term MACE with a negative likelihood ratio of 0.09, a negative predictive value of 98%, and a miss rate of 1%.[7] The HEART score is increasingly used in EDs worldwide as it has a better area-under-the-curve and misses fewer patients at risk for short-term MACE than the Thrombolysis in Myocardial Infarction and Global Registry of Acute Coronary Events scores.

High Sensitivity Biomarkers

High sensitivity troponin offers an additional opportunity to identify low-risk patients who do not need further testing. In a large cohort of 22,651 patients with chest pain where 15.6% had AMI, more than half of patients had initial hsTn I or T less than 6 ng/mL with a change in (delta) hsTn less than 4 ng/mL at 45 to 120 minutes. These patients could be ruled out for AMI with a 99.5% negative predictive value and are at less than 0.2% risk of MACE in the next 30 days. The COMPASS-MI risk calculator was derived from the cohort and provides the sensitivity, specificity, and predictive values across a range of initial and delta troponin values during early and late resampling periods using two commercially available hsTn assays.[8] Clinicians must also be cautious to attribute all hsTn elevations to AMI, as it lacks sufficient specificity. Elevated troponin values can be found in a number of conditions other than ACS, such as pulmonary embolism, congestive heart failure, or even CAD and thusly, the universal definition of myocardial infarction recommends careful history-taking and serial measurements to identify an increase and/or decrease in troponin values to understand the etiology and acuity of myocardial injury.[1] Nonetheless, low hsTn values can reliably exclude significant myocardial injury and reliably rule out ACS.

Other Diagnostic Strategies

If serial ECG and troponin testing are negative, reviewing existing diagnostic studies provides an opportunity to identify patients with CAD and ensure they are receiving OMT. As chest pain has a broad differential, patients often undergo computed tomography

of the chest which can reveal coronary artery calcification, identifying a cohort of patients with CAD. Further, reviewing ECGs for signs of prior infarcts and echocardiograms for segmental wall motion abnormalities may identify patients with underlying CAD who can benefit from risk factor management and medication optimization.

Cardiac Computed Tomography

The management of CAD is best suited for the ambulatory care setting where longitudinal disease monitoring and counseling can be provided. A study of community practice found that clinicians appear to incorporate the patient's whole picture in the evaluation of chest pain when deciding to pursue further testing.[9] The study found that the majority of patients with normal ECGs do not need further testing and those in whom further testing was deferred did not have any preventable CAD-related deaths at 5 years.

If access to routine follow-up is challenging, diagnosing CAD during a chest pain presentation may remain a priority for the patient and the clinician. In these situations CCTA should be considered the first test in low-to-intermediate risk patients, as it has higher accuracy in detecting significant coronary stenosis, has lower radiation exposure, and is faster to obtain than stress tests. For instance in the ROMICAT II trial, two patients in the CCTA arm had short-term MACE, both of whom had significant lesions on CCTA but negative stress testing and thus did not undergo further treatment.[10] Further, CCTA reduced the risk of AMI compared with stress testing through increased use of aspirin and statins.[11]

Caution is warranted when using CCTA in the evaluation of low-to-intermediate risk chest pain as it increases costs, leads to more invasive angiography, and may not improve outcomes. Furthermore, CCTA is not helpful in high-risk patients or older patients with calcified coronary lesions. However, when the need for diagnosing CAD during the chest pain presentation remains a priority, rather than stress testing, CCTA should be considered as the preferred strategy for low- or intermediate-risk patients.

CONCLUSION

ACS is diagnosed and excluded based on history, biomarkers, and ECG, whereas CAD is routinely diagnosed with stress testing. With the absence of evidence of improved cardiovascular outcomes, routine stress testing should be avoided in patients with chest pain at low-to-intermediate risk for ACS given the significant costs and limited benefits. Instead, hsTn, in conjunction with the HEART score, identifies patients at low risk and who may be candidates for early discharge, thereby reducing costs, length of stay, and downstream testing. If you must diagnose CAD during a presentation for chest pain, consider CCTA over functional stress testing as it is faster and may improve subsequent risk of AMI from increased use and adherence to OMT.

Abbreviations and Acronyms: **ACS** = acute coronary syndrome; **AMI** = acute myocardial infarction; **CAD** = coronary artery disease; **CCTA** = cardiac computed tomography angiography; **ECG** = electrocardiogram; **ED** = emergency department; **hsTn** = high sensitivity troponin; **MACE** = major adverse cardiovascular event; **OMT** = optimal medical therapy; **PCI** = percutaneous coronary intervention; **UA** = unstable angina

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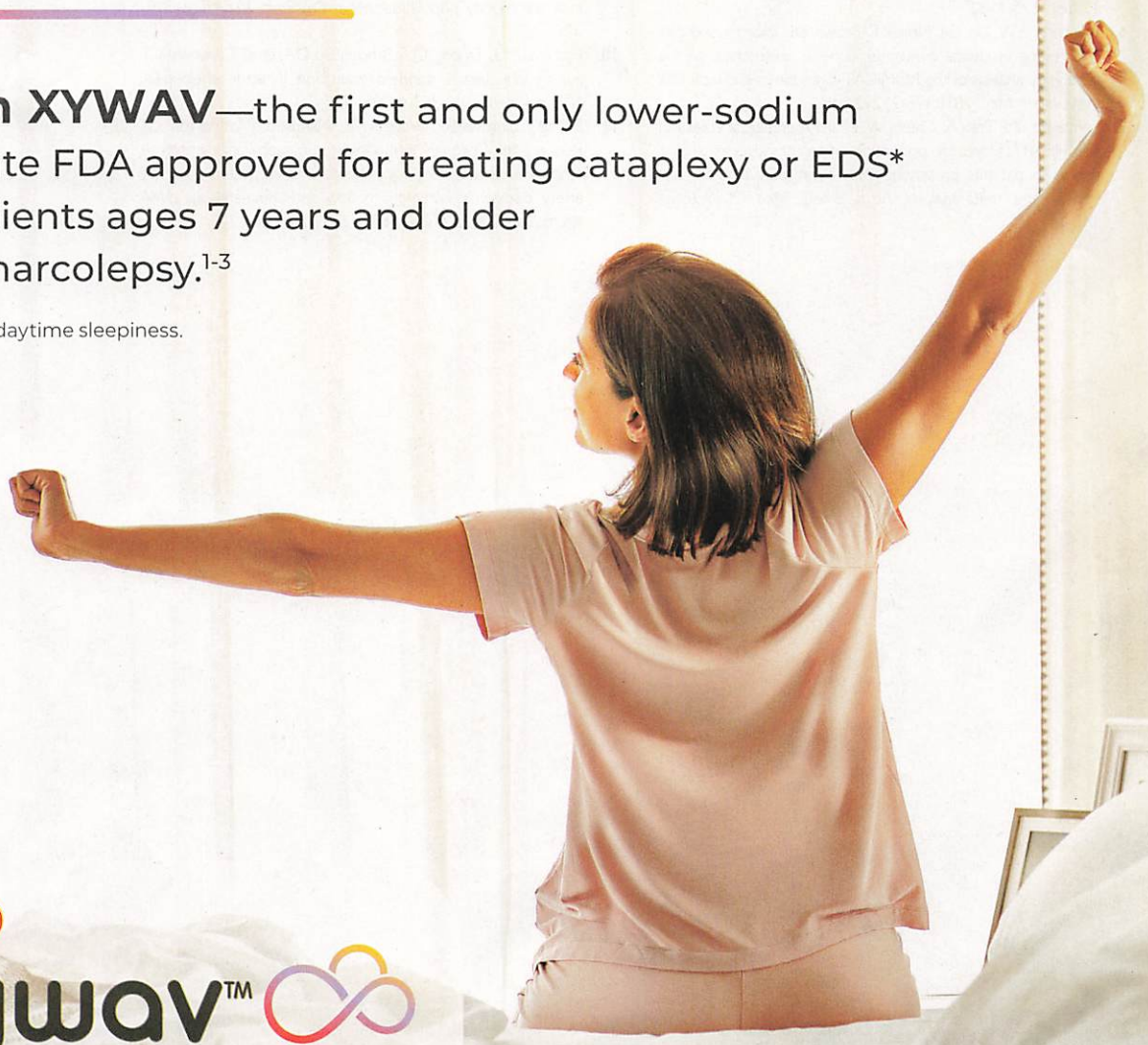

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