Among Low-Risk Patients, Does Functional Testing Decrease Referrals for Invasive Coronary Angiography Compared With Coronary Computed Tomographic Angiography?

TAKE-HOME MESSAGE

Functional testing in patients with symptoms suggestive of low risk for acute coronary syndrome is associated with decreased invasive coronary angiography compared with coronary computed tomography (CT) angiography.

METHODS

DATA SOURCES

Authors searched MEDLINE, MEDLINE in process, EMBASE, PubMed, Web of Science, SCOPUS, World Health Organization International Clinical Trial Registry Platform, ClinicalTrials.gov, and the Cochrane Library, with no language restrictions for studies, from 2005 to November 2015, which is the date the meta-analysis authors conducted the literature search. A second search of only PubMed evaluated for relevant studies before 2005.

STUDY SELECTION

Authors included diagnostic randomized controlled trials comparing any noninvasive anatomic or functional strategies for detection of coronary artery disease in patients at low risk for acute coronary syndrome. The meta-analysis defined as low risk patients with chest pain (or anginal equivalent) lasting at least 5 minutes at rest within the past 24 hours and without history of known coronary

EBEM Commentators
Brit Long, MD
Michael D. April, MD, DPhil
Department of Emergency Medicine
San Antonio Uniformed Services Health
Education Consortium
Fort Sam Houston, TX

This review does not reflect the views or opinions of the US government, Department of Defense or its Components, US Army, US Air Force, or SAUSHEC EM Residency Program.

Jestin N. Carlson, MD, MS, and Alan Jones, MD, serve as editors of the SRS series.

Results

Results of included trials.

Grouped Functional Testing* vs Anatomic Testing†	OR (95% CI)	Heterogeneity (τ^2)
ICA	0.71 (0.53–0.96)	0.032
Downstream testing	0.58 (0.17–1.92)	1.23
Revascularization	0.57 (0.42–0.78)	<0.001
MI	1.59 (0.60–4.23)	<0.001

ICA, Invasive coronary angiography; *MI*, myocardial infarction.

*Functional testing included exercise ECG, stress echocardiography, or single-photon-emission CT–myocardial perfusion imaging.
†Anatomic testing included noninvasive coronary CT angiography.

Of 19,674 potentially relevant studies identified, authors included 18 trials (11,329 patients) evaluating patients at low risk for acute coronary syndrome. The meta-analysis included 6 different imaging modalities. In patients with low risk of acute coronary syndrome, several diagnostic tests were associated with fewer

artery disease, ECG findings diagnostic of cardiac ischemia, hemodynamic or clinical instability, or an initial troponin level greater than the assay 99th percentile.

DATA EXTRACTION AND SYNTHESIS

Meta-analysis authors extracted data in regard to the effect of noninvasive diagnostic modalities on downstream testing as defined by invasive angiography, rates of revascularization, death, and myocardial infarction. Noninvasive modalities included exercise ECG, stress echocardiography, single-photon-emission CT–myocardial perfusion imaging, real-time myocardial contrast echocardiography, coronary CT angiography, and cardiovascular magnetic resonance imaging (MRI). If data from included studies were incomplete, meta-analysis investigators contacted primary study authors. The meta-analysis predefined analyses separately for each study population group and each outcome and evaluated each study with the Cochrane risk-of-bias tool.[1] Authors synthesized study-specific odds ratios (ORs) with random-effects pairwise and network meta-analyses with 95% confidence intervals (CIs) and calculated heterogeneity. In primary analyses, authors considered each diagnostic strategy separately, and in secondary analyses, authors grouped traditional functional tests and compared them with coronary CT angiography as an anatomic test and cardiovascular MRI as an advanced modality. Authors conducted sensitivity analysis and calculated number needed to treat and number needed to harm for each outcome and group of patients.

invasive referrals for angiography compared with coronary CT angiography, including stress echocardiography (OR 0.28; 95% CI 0.14 to 0.57), cardiovascular MRI (OR 0.32; 95% CI 0.15 to 0.71), and exercise ECG (OR 0.53; 95% CI 0.28 to 1.00). Standard care was associated with the highest rate of downstream testing (OR 4.11; 95% CI 1.74 to 9.74). Pairwise meta-analysis found functional testing resulted in fewer referrals for invasive testing than coronary CT angiography, and functional testing resulted in fewer revascularization procedures (Table). No difference was found in functional- or anatomic-based strategy for myocardial infarction or death; however, estimates of associations between alternative diagnostic tests and myocardial infarction or death were not precise. Heterogeneity was moderate to high (τ^2 ranged from <0.001 to 1.23). Meta-analysis authors considered most trials to be at low risk for bias in 5 of the assessed areas of potential bias, although risk of bias was often unclear because of limited reporting.

Commentary

Chest pain is a common emergency department (ED) presentation and admission diagnosis, with many patients admitted from the ED for risk stratification.[2,3] A significant number of patients undergoing cardiac testing ultimately receive diagnoses of noncardiac causes for their chest pain, yet these patients nevertheless remain at risk for subsequent cardiovascular complications and even death.[4,5] Current guidelines recommend functional testing for

risk stratification, although this testing demonstrates only a modest association with subsequent actionable diagnostic findings.[6] Coronary CT angiography represents a noninvasive anatomic imaging test that investigators hoped might overcome the limitations of functional testing.[7-9] However, randomized controlled trial data have not yet definitively established the superiority of either functional or noninvasive anatomic testing in regard to downstream testing or clinical outcomes.

This meta-analysis evaluated the current available randomized controlled trial data of strategies to evaluate patients with chest pain who are at low risk for acute coronary syndrome. Results suggest that in these patients, associations exist between initial functional testing and decreased downstream angiography and revascularization compared with anatomic testing with coronary CT angiography. This is further demonstrated with the number needed to treat of 49 patients (95% CI 30 to 364) for functional testing versus anatomic testing to reduce invasive angiography, whereas the number needed to treat to prevent revascularization was 79 (95% CI 58 to 155). Two trials, Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) and CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART), advocate coronary CT angiography,[8,9] although the 2012 American College of Cardiology Foundation/American Heart Association guidelines

continue to recommend functional testing as the first-line diagnostic strategy in this patient population.[6] This meta-analysis supports the latter recommendations.

This meta-analysis has several limitations. Individual patient data were not available, preventing further subgroup analyses. The overall rates of death and myocardial infarction were low, so it may have been underpowered to assess differences in these outcomes. The primary outcomes of invasive coronary angiography and revascularization are more subjective and may have been influenced by provider preferences. No information on cost-effectiveness was available. Although many studies included standard of care, the specific definition of this strategy varied across studies. Several of the studied testing modalities may be unavailable in the EDs of many institutions. Finally, few trials evaluated the use of high-sensitivity troponin assays.

According to this meta-analysis, coronary CT angiography is associated with greater downstream testing and revascularization compared with functional testing in patients with chest pain and low risk for acute coronary syndrome. Further research should focus on outcomes when synthesizing alternative functional and anatomic diagnostic strategies with decision support tools such as the HEART (History, ECG, Age, Risk factors and Troponin) score and tests such as high-sensitivity troponin assays.[10]

1. Higgins JP, Altman DG, Gotzsche PC; Cochrane Bias Methods Group Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:d5928.
2. Amsterdam EA, Kirk JD, Bluemke DA, et al. American Heart Association Exercise, Cardiac Rehabilitation, and Prevention Committee of the Council on Clinical Cardiology, Council on Cardiovascular Nursing, and Interdisciplinary Council on Quality of Care and Outcomes Research. Testing of low-risk patients presenting to the emergency department with chest pain: a scientific statement from the American Heart Association. Circulation. 2010;122:1756-1776.
3. Benjamin EJ, Blaha MJ, Chiuve SE, et al. American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2017 update: a report from the American Heart Association [published corrections appear in Circulation. 2017;135:e646; Circulation. 2017;136: e196]. Circulation. 2017;135:e146-e603.
4. Sekhri N, Feder GS, Junghans C, et al. How effective are rapid access chest pain clinics? prognosis of incident angina and non-cardiac chest pain in 8762 consecutive patients. Heart. 2007;93:458-463.
5. Jordan KP, Timmis A, Croft P, et al. Prognosis of undiagnosed chest pain: linked electronic health record cohort study. BMJ. 2017;357:j1194.
6. Fihn SD, Gardin JM, Abrams J, et al; Foundation/American Heart Association Task Force. 2012 ACCF/AHA/ACP/AATS/PCNA/ SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons [published correction appears in Circulation. 2014;129:e463]. Circulation. 2012;126:e354-e471.
7. de Azevedo CF, Hadlich MS, Bezerra SG, et al. Prognostic value of CT angiography in patients with inconclusive functional stress tests. JACC Cardiovasc Imaging. 2011;4: 740-751.
8. Douglas PS, Hoffmann U, Patel MR, et al. PROMISE Investigators. Outcomes of anatomical versus functional testing for coronary artery disease. N Engl J Med. 2015;372:1291-1300.
9. SCOT-HEART Investigators. CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open-label, parallel-group, multicentre trial. Lancet. 2015;385: 2383-2391.
10. Oliver JJ, Streitz MJ, Hyams JM, et al. An external validation of the HEART pathway among emergency department patients with chest pain. Intern Emerg Med. 2018; https://doi.org/10.1007/s11739-018-1809-y.

Annals' Impact Factor

5.008	12.4 days	1.8 million
2017 Impact Factor	Time to First Decision	full-text downloads in 2017