American Heart Association | American Stroke Association

Initial Diagnostic Evaluation of Stable Coronary Artery Disease: The Need for a Patient-Centered Strategy

Robert C. Hendel, MD; Ahmad Y. Jabbar, MD; Indrajeet Mahata, MD

The diagnosis and subsequent management of coronary artery disease (CAD) represents a major challenge to our healthcare systems, affecting millions of patients each year. Despite many years and literally thousands of publications, the optimal approach for the evaluation of stable ischemic heart disease remains unclear. Functional or stress testing to detect inducible ischemia has been the "gold standard" and remains the most common noninvasive test used to diagnose stable CAD. However, the advent of coronary computed tomography angiography (CCTA) has created a genuine debate regarding the best initial modality for the workup of stable CAD. Furthermore, simple and low-cost diagnostic options, such as ECG stress testing (GXT), should be considered, given extensive clinical experience and current pressures on healthcare resources.

In this issue of *JAHA*, Roifman and colleagues evaluated initial testing strategies for stable CAD with anatomical versus functional stressing modality in a nonselected general population.[1] The cohort consisted of 15 467 patients who had undergone a noninvasive test, with the end point being obstructive coronary artery disease on invasive coronary angiography. The authors demonstrated that neither stress imaging nor CCTA resulted in a higher diagnostic yield for obstructive CAD than GXT, a rather surprising result. Outcome data were also provided and did not demonstrate superior risk discrimination with cardiac imaging, as compared with GXT.

The design of the current study has inherent selection biases that limit the conclusions and utility of these data. Patients had to have undergone both a noninvasive test and then invasive coronary angiography within 6 months of the index test to be included. Additionally, patients who had a noninvasive study during the preceding year were excluded. Depending on the testing modality, only 3.8% to 6.5% of patients having noninvasive testing underwent invasive angiography for the definitive diagnosis of CAD. In aggregate, only 3.3% of the initial cohort undergoing stress testing or CCTA were included in this retrospective trial.

A major concern regarding this article was the use of the Framingham Risk Score rather than a determination of the pretest probability for coronary artery disease; this is critically important as Framingham Risk Score does not include an assessment of symptoms and should be used for evaluation of the 10-year risk for developing coronary heart disease.[2] The use of the Framingham Risk Score for something other than prognosis is therefore an incorrect application of this measure.

The authors do quote existing guidelines but do not stress that these guidelines offer specific scenarios for some of the recommendations; they also seem to overstate the impact of their findings. It is clear that not all patients with suspected CAD are the same and risk factors, pre-existing diagnoses, ability to exercise, the interpretability of an ECG, and the purpose of the evaluation should be considered in the selection of noninvasive testing. The European Society of Cardiology Guidelines clearly base noninvasive test selection for the initial diagnosis of CAD on the pretest likelihood of CAD and actually make a Class I recommendation for GXT in patients with an intermediate likelihood of CAD who have an interpretable ECG and can exercise.[3] A virtually identical recommendation is made by the 2012 American College of Cardiology/American Heart Association guidelines, as supported by the appropriate use criteria.[4,5] Thus, it appears that no guidelines recommend cardiac imaging procedures as the initial test in this population, although the European Society of Cardiology document does indicate that stress imaging is an initial testing option depending on local expertise. Both guidelines suggest stress imaging when the pretest likelihood is higher than intermediate or when the resting ECG is uninterpretable. It also is obvious that GXT cannot be considered the initial testing option when patients are unable

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

From the Section of Cardiology, Department of Medicine, Tulane University; Heart and Vascular Institute, Tulane University School of Medicine, New Orleans, LA.

Correspondence to: Robert C. Hendel, MD, 1430 Tulane Ave, Suite 7550, New Orleans, LA 70115. E-mail: rhendel@tulane.edu

J Am Heart Assoc. 2017;6:e006863. DOI: 10.1161/JAHA.117.006863.

to exercise and pharmacologic stress imaging or CCTA would clearly be rational and appropriate.[3,4] Thus, while GXT may well serve as the first-line test in some patients, all guidelines indicate that cardiac imaging (stress echocardiography, stress cardiac magnetic resonance, stress radionuclide myocardial perfusion imaging, and CCTA) may be selected and in fact preferable in many patients.

Some of the findings in this trial merit additional comments. The selection of detection of obstructive CAD may be a reasonable end point but should not be considered an "outcome" measure. Fortunately, the authors also included some data on cardiac events, although the follow-up period was limited to 2 years and not all events were included. It is a surprising finding that among the patients who had CCTA, only 54% were found to have obstructive CAD during invasive coronary angiography. This is certainly disparate to the findings of many who have shown the very high diagnostic accuracy of CCTA[6,7] for the detection of obstructive CAD and begs the question of who got invasive coronary angiography and who did not and the reasons for these evaluations. It is also surprising that stress echocardiography and stress single-photon emission computed tomography myocardial perfusion imaging did not demonstrate higher diagnostic accuracy than GXT, which is very much in conflict with the existing literature.[8–10] Additionally, the concern raised by the author about the apparent discordance between stress imaging procedures and invasive coronary angiography is not new, as there is an abundance of evidence highlighting the difference between the anatomic assessment of CAD and the results of functional testing, which are based on coronary physiology.[11,12] Increasing emphasis is now placed on the hemodynamic assessment of coronary stenosis, which is clearly valuable from a prognostic standpoint and is critical to direct therapeutic interventions.[12] Of note, the ability to noninvasively obtain both data related to obstructive coronary disease and the physiologic significance of a coronary stenosis has great promise.[13] Related to the current article, the known disparity between functional testing and coronary anatomy raises concern about the selection of the presence of obstructive CAD as the primary end point for this trial.

We agree with the authors that there are few data on the comparative effectiveness of different noninvasive testing strategies, literature that would be most welcome.[14] These should, however, focus on prognosis, not the mere detection of disease. The PROMISE (Prospective Multicenter Imaging Study for Evaluation of Chest Pain) trial suggests clinical equipoise regarding outcome between functional (stress single-photon emission computed tomography, stress echo, and GXT) and anatomic (CCTA) but did not examine differences among the stress modalities, and initial testing with GXT was performed in only 10.2% of the study cohort.[15] Although cardiac events were similar between functional and anatomic approaches, there were more coronary revascularization procedures performed with CCTA. However, the SCOT-HEART trial demonstrated that a CCTA-based approach to the detection of CAD results in a decline in subsequent myocardial infarction, albeit not a statistically significant reduction.[16] In one of the few comparative effectiveness trials performed, we previously demonstrated that the addition of single-photon emission computed tomography myocardial perfusion imaging did not add prognostic value beyond that obtained with GXT in a population of women, although this was a low-risk cohort.[17] Overall, most trials support the notion that commonly performed diagnostic modalities are often similarly effective, emphasizing the need for continued studies of clinical and cost effectiveness.

In conclusion, while the authors are to be commended for their efforts to assess the diagnostic efficacy of various noninvasive tests, issues related to referral/selection bias, known discordance of anatomic and physiologic factors, and absence of patient-specific approaches based on risk ECG and exercise abilities limit the conclusions offered in this article. While it is true that these results "do not support the routine initial use of stress imaging or CCTA," this conclusion is based on an inhomogeneous cohort of patients and must be tempered with the application of patient-centered imaging strategies.

Disclosures

None.

References

1. Roifman I, Wijeysundera HC, Austin PC, Rezai MR, Wright GA, Tu JV. Comparison of anatomic and clinical outcomes in patients undergoing alternative initial noninvasive testing strategies for the diagnosis of stable coronary artery disease. *J Am Heart Assoc*. 2017;6:e005462. DOI: 10.1161/JAHA.116.005462.
2. D'Agostino RB, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, Kannel WB. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. *Circulation*. 2008;117:743–753.
3. Montalescot G, Cechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, Bugiardini R, Crea F, Cuisset T, Di Mario C, Ferreira JR, Gersh BJ, Gitt AK, Hulot JS, Marx N, Opie LH, Pfisterer M, Prescott E, Ruschitzka F, Sabaté M, Senior R, Taggart DP, van der Wall EE, Vrints CJ; ESC Committee for Practice Guidelines, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S; Document Reviewers, Knuuti J, Valgimigli M, Bueno H, Claeys MJ, Donner-Banzhoff N, Erol C, Frank H, Funck-Brentano C, Gaemperli O, Gonzalez-Juanatey JR, Hamilos M, Hasdai D, Husted S, James SK, Kervinen K, Kolh P, Kristensen SD, Lancellotti P, Maggioni AP, Piepoli MF, Pries AR, Romeo F, Rydén L, Simoons ML, Sirnes PA, Steg PG, Timmis A, Wijns W, Windecker S, Yildirir A, Zamorano JL. 2013 ECC guidelines on the management of stable coronary artery disease of the European Society of Cardiology. *Eur Heart J*. 2013;34:2949–3003.
4. Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, Douglas PS, Foody JM, Gerber TC, Hinderliter AL, King SB III, Kligfield PD, Krumholz HM, Kwong RY, Lim MJ, Linderbaum JA, Mack MJ, Munger MA, Prager RL, Sabik JF, Shaw LJ, Sikkema JD, Smith CR Jr, Smith SC Jr, Spertus JA, Williams SV; American College of Cardiology Foundation; American Heart Association Task Force on Practice Guidelines; American College of Physicians; American Association for Thoracic Surgery; Preventive Cardiovascular Nurses Association; Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons. 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. *J Am Coll Cardiol*. 2012;60:e44–e164.

5. Wolk MJ, Bailey SR, Doherty JU, Douglas PS, Hendel RC, Kramer CM, Min JK, Patel MR, Rosenbaum L, Shaw LJ, Stainback RF, Allen JM; American College of Cardiology Foundation Appropriate Use Criteria Task Force. ACCF/AHA/ASE/ASNC/HFSA/HRS/SCAI/SCCT/SCMR/STS 2013 multimodality appropriate use criteria for the detection and risk assessment of stable ischemic heart disease: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and Society of Thoracic Surgeons. *J Am Coll Cardiol*. 2014;63:380–406.
6. Budoff MJ, Dowe D, Jollis JG, Gitter M, Sutherland J, Halamert E, Scherer M, Bellinger R, Martin A, Benton R, Delago A, Min JK. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. *J Am Coll Cardiol*. 2008;52:1724–1732.
7. Nielsen LH, Ortner N, Nørgaard BL, Achenbach S, Leipsic J, Abdulla J. The diagnostic accuracy and outcomes after coronary computed tomography angiography vs. conventional functional testing in patients with stable angina pectoris: a systematic review and meta-analysis. *Eur Heart J Cardiovasc Imaging*. 2014;15:961–971.
8. Fleischmann KW, Hunink MG, Kuntz KM, Douglas PS. Exercise echocardiography or exercise SPECT imaging? A meta-analysis of diagnostic test performance. *JAMA*. 1998;280:913–920.
9. Underwood S. R., Anagnostopoulos C., Cerqueira M., Ell PJ, Flint EJ, Harbinson M, Kelion AD, Al-Mohammad A, Prvulovich EM, Shaw LJ, Tweddel AC; British Cardiac Society; British Nuclear Cardiology Society; British Nuclear Medicine Society; Royal College of Physicians of London; Royal College of Radiologists. Myocardial perfusion scintigraphy: the evidence. *Eur J Nucl Med Mol Imaging*. 2004;31:261–291.
10. Mahajan N, Polavaram L, Vankayala H, Ference B, Wang Y, Ager J, Kovach J, Afonso L. Diagnostic accuracy of myocardial perfusion imaging and stress echocardiography for the diagnosis of left main and triple vessel coronary artery disease: a comparative meta-analysis. *Heart*. 2010;96:956–966.
11. Min JK, Shaw LJ, Berman DS. The present state of coronary computed tomography angiography-a process in evolution. *J Am Coll Cardiol*. 2010;55:957.
12. De Bruyne B, Pijls NH, Kalesan B, Barbato E, Tonino PA, Piroth ZX, Jagic N, Mobius-Winkler S, Rioufol G, Witt N, Kala P, MacCarthy P, Engström T, Oldroyd KG, Mavromatis K, Manoharan G, Verlee P, Frobert O, Curzen N, Johnson JB, Jüni P, Fearon WF; FAME 2 Trial Investigators. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. *N Engl J Med*. 2012;367:991–1001.
13. Min JK, Leipsic J, Pencina MJ, Berman DS, Koo BK, van Mieghem C, Erglis A, Lin FY, Dunning AM, Apruzzese P, Budoff MJ, Cole JH, Jaffer FA, Leon MB, Malpeso J, Mancini GB, Park SJ, Schwartz RS, Shaw LJ, Mauri L. Diagnostic accuracy of fractional flow reserve from anatomic CT angiography. *JAMA*. 2012;308:1237–1245.
14. Shaw LJ, Philips LM, Nagel E, Newby DE, Narula J, Douglas PS. Comparative effectiveness trials of imaging-guided strategies in stable ischemic heart disease. *JACC Cardiovasc Imaging*. 2017;10:321–334.
15. Douglas PS, Hoffman U, Patel MR, Mark DB, Al-Khaliki HR, Cavanaugh B, Cole J, Dolor RJ, Fordyce CB, Huang M, Khan MA, Kosinski AS, Krucoff MW, Malhotra V, Picard MH. Outcome of anatomic versus functional testing for coronary artery disease. *N Engl J Med*. 2015;372:1291–1300.
16. 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.
17. Shaw LJ, Mieres JH, Hendel RH, Boden WE, Gulati M, Veledar E, Hachamovitch R, Arrighi JA, Merz CN, Gibbons RJ, Wenger NK, Heller GV; WOMEN Trial Investigators. Comparative effectiveness of exercise electrocardiography with or without myocardial perfusion single photon emission computed tomography in women with suspected coronary artery disease: results from the What Is the Optimal Method for Ischemia Evaluation in Women (WOMEN) trial. *Circulation*. 2011;124:1239–1249.

Key Words: Editorials • cardiac computed tomography • diagnostic testing • noninvasive imaging • radionuclide imaging • stress echocardiography • stress testing