Coronary Computed Tomography Angiography in Stable Chest Pain to Prevent Myocardial Infarction and Reduce Costs—Seeing Is Believing

Erin D. Michos, MD, MHS; Philip Greenland, MD

Seeing is believing and believing is knowing and knowing beats unknowing and the unknown.

Philip Roth, Zuckerman Bound: A Trilogy and Epilogue

Cardiovascular disease (CVD) remains the leading cause of mortality in the United States, causing 1 in 3 deaths, and is associated with an estimated $316 billion in health care-related costs and lost productivity. Patients with coronary artery disease (CAD), both obstructive and nonobstructive, require a comprehensive approach to optimize lifestyle and medical therapy to mitigate the effects of adverse risk factors and reduce the risk of major adverse cardiovascular events (MACEs). Statin therapy plays a key role in slowing atherosclerosis progression, stabilizing plaque, and reducing MACEs and all-cause mortality.1 In symptomatic patients, knowledge of the coronary anatomy, such as that demonstrated by coronary computed tomography angiography (CTA), has the potential to improve triaging of health care resources, with prompt ruling out of high-risk coronary anatomy (ie, left main, >50%) and allocation of preventive medications for those identified as having atherosclerotic disease.

The benefits of seeing is believing were most clearly demonstrated in the SCOT-HEART trial,2 an open-label study comparing the utility of coronary CTA with usual care among patients with stable chest pain symptoms (47% of patients had established CAD at baseline). A coronary CTA–guided early diagnostic strategy resulted in a 41% relative reduction in subsequent MACEs (2.3% vs 3.9%) at 5 years.2 Patients in the coronary CTA–randomized group were 40% more likely to initiate preventive therapies compared with patients receiving usual care (hazard ratio, 1.40; 95% CI, 1.19-1.65).2 Other studies of asymptomatic patients at risk of CAD have also shown that a patient’s awareness of their coronary artery calcium (CAC) score by noncontrast CT, a measure of total atherosclerotic burden, is associated with better adherence to preventive medications and behavioral lifestyle changes.3

Each year in the United States, an estimated 8 million nuclear stress tests are performed with the goal of identifying obstructive CAD in patients with chest pain who are suspected of having myocardial ischemia. The cost-effectiveness of such a functional strategy in terms of quality-adjusted life-years (QALYs) gained is unclear. Most patients with stable CAD have few or no symptoms of angina, and most CVD events occur among individuals without angina or evidence of ischemia.4 These observations emphasize the role of a prevention-driven strategy with appropriate medical therapy rather than a symptom-driven or even ischemia-driven strategy.5

In this issue of JAMA Network Open, Karáday et al6 evaluated the short-term, mid-term, and long-term cost-effectiveness of anatomic vs functional strategies for the evaluation of stable chest pain using data from the Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) trial.7 PROMISE7 randomized 10 003 symptomatic patients (88% of patients with chest pain or dyspnea on exertion) with a mean (SD) age of 61 (8) years and pretest probability of CAD of 53% to a strategy of coronary CTA (anatomic) or stress testing (functional). Because women are more likely to have angina without obstructive CAD than men, we applaud the investigators for enrolling women as more than half (ie, 53%) of study participants. Additionally, 23% of patients belonged to minority racial or ethnic groups. The main finding of PROMISE was that the rate of the primary clinical outcome (a composite of death, myocardial infarction, unstable angina...
hospitalization, or major procedural complication) at a median follow-up of 2.1 years was relatively low (approximately 3%) and similar between the 2 testing strategies.

In the current analysis, Karáday et al\(^6\) used a Markov microsimulation model for the economic evaluation of stable chest pain, comparing anatomic vs functional approaches. Their model was derived from observed outcomes in the PROMISE trial\(^7\) at 6 months and 2 years and used real costs for testing strategies and downstream procedures (i.e., invasive coronary angiography [ICA] with or without revascularization) observed in PROMISE (expressed in 2014 US dollars). The outcome was an estimation of cost differences at 5 years and over the lifetime, benchmarked to QALYs gained.

Their key finding was that an anatomic testing approach with coronary CTA (with or without the addition of CT-fractional flow reserve [FFRCT] for stenosis 30%-69%) was cost-effective compared with the functional approach, in the range of incremental cost-effectiveness ratios (ICER) of approximately $1900 to $3500 per QALY across varying sensitivity analyses.\(^6\) The anatomic approach resulted in higher costs at 2 years and 5 years, associated with higher rates of ICA and revascularization, but still had higher QALYs at both points (with a 1.5-month gain of perfect health). However, over the lifetime, coronary CTA was associated with lower costs and was more cost-effective than functional testing, with an ICER of $2743/QALY and 6 months gained of perfect health. The coronary CTA strategy was cost-effective for both men and women (discounted ICER/QALY, $3559 and $1912, respectively) vs functional strategy, with similar 6 months life years gained for both sexes.\(^8\)

The benefits of coronary CTA were associated with better diagnostic accuracy for obstructive and nonobstructive CAD, resulting in more statin use in those assigned to the anatomic group than the function group (8539 [85.4%] vs 6702 [67.0%]). The authors' model assumed a mortality reduction with statins only for those with CAD (30% reduction for both obstructive and nonobstructive CAD) and 0% mortality benefit for those with no CAD. Their cost estimates may even be conservative because the authors assumed full adherence with the statin therapy assigned in the functional arm; however, adherence may be greater with anatomic assessment (seeing is believing, after all). Their sensitivity analyses confirmed cost-effectiveness even if statin adherence declined over time.

This new analysis from PROMISE aligns with the UK National Institute for Health and Care Excellences (NICE) clinical guideline\(^8\) and the European Society of Cardiology (ESC) guideline for chronic coronary syndromes,\(^9\) which have endorsed coronary CTA as first-line test (NICE) or as a class I recommendation (ESC) for evaluation of patients with stable chest pain. A prior analysis conducted by NICE also concluded that the use of coronary CTA as first-line test would be cost-effective, with an estimated annual savings in the United Kingdom of £16 million through prompt exclusion of significant CAD and more efficient triaging of National Health Service resources.

While CAC (by noncontrast CT) has been reserved by guidelines as a shared decision-making tool among asymptomatic individuals, given CAC's much lower cost (approximately $100) compared with a coronary CTA, CAC may be an even more cost-effective gatekeeper in the initial triaging of low-risk chest pain and applying preventive therapies, although this strategy was not modeled in the current analysis.\(^6\) In the anatomic arm of the PROMISE trial,\(^7\) most events (84%) occurred in individuals with a CAC score of greater than 0.\(^10\) In asymptomatic patients with intermediate risk, assessment of CAC also appears to be a cost-effective strategy for guiding decisions about statin initiation, especially when there is a strong patient preference for avoiding statin medication.\(^11\)

In the PROMISE study,\(^7\) there were initial greater rates of ICA and revascularization at 2 years with coronary CTA compared with functional testing, given that more CAD was observed. The addition of FFR\(_{CT}\) incorporates a functional assessment of vessel-specific ischemia to the anatomic assessment of coronary CTA and can improve the revascularization-to-ICA ratio. Furthermore, the prior PLATFORM study\(^12\) had suggested that FFR\(_{CT}\) reduces the need for ICA. More recently, preliminary data from the FORECAST trial\(^13\) reported that a FFR\(_{CT}\) strategy vs usual care in stable chest pain did not reduce costs at 9 months but did reduce the rate of ICA by 22%. The cost-effectiveness of adding FFR\(_{CT}\) was also examined in the analysis of PROMISE from Karáday et al.\(^6\) The
addition of FFR\textsubscript{CT} to coronary CTA added an upfront cost of approximately $1000 but conferred less lifetime cost among the 3 strategies and dominated functional testing because of fewer ICAs and more targeted revascularizations. However, the QALY of with coronary CTA with FFR\textsubscript{CT} was similar to coronary CTA alone.

Notably, costs could be further reduced with an anatomic strategy (coronary CTA with or without FFR\textsubscript{CT}) if less subsequent ICAs and revascularizations were performed in lieu of an initial conservative approach of optimal medical therapy for the management of obstructive CAD after high-risk anatomy was excluded. Stable CAD may be managed more effectively and safely with medical therapy than revascularization, as shown in the COURAGE trial and the ISCHEMIA trial.\textsuperscript{5,14} Perhaps an even more cost-effective strategy would be the use of first-line coronary CTA to confirm the diagnosis of CAD and exclude high-risk anatomy, followed by an initial conservative course of intensive medical therapy for CAD and/or angina, lasting for at least several months, then an assessment of symptoms with a tool such as the Seattle Angina Questionnaire and referral for ICA and revascularization only if symptoms are refractory. For cost savings and QALYs to be maximally realized, there needs to be clear guidance regarding the appropriate clinical management strategy after coronary CTA is performed.

CAD is best addressed through a multipronged approach combining lifestyle and pharmacotherapy interventions to halt or slow the progression of atherosclerosis and prevent thrombosis. The data show that coronary CTA leads to greater uptake of preventive measures than usual care among patients with stable chest pain symptoms,\textsuperscript{2} and this new economic model\textsuperscript{6} suggests it is cost-effective over a patients’ lifetime compared with functional-based stress testing. In sum, an anatomy-driven strategy confers the greater promise for ensuring at-risk patients are appropriately treated with risk-reducing preventive therapies.


