CLINICAL DECISIONS
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Imaging in Coronary Artery Disease Risk Stratification

This interactive feature addresses the approach to a clinical issue. A case vignette is followed by specific options, neither of which can be considered either correct or incorrect. In short essays, experts in the field then argue for each of the options. Readers can participate in forming community opinion by choosing one of the options and, if they like, providing their reasons.

CASE VIGNETTE

A Woman with Possible Coronary Artery Disease

Siri R. Kadire, M.D.

A 58-year-old woman presents to the emergency department with epigastric pain, left shoulder and jaw pain, and shortness of breath, which have been ongoing for 2 days. Her symptoms are worse when she climbs stairs. She has not had these symptoms before. She reports no diaphoresis, nausea, or vomiting. She works as a bank teller, and she reports no new stressors or recent changes to her lifestyle. She has a history of diabetes, hyperlipidemia, and hypertension, which are managed with metformin, atorvastatin, and lisinopril, respectively. Her most recently measured cholesterol levels were 200 mg per deciliter (5.2 mmol per liter) for total cholesterol and 100 mg per deciliter (2.6 mmol per liter) for low-density lipoprotein cholesterol. Her father had a myocardial infarction at age 60. On physical examination, her heart rate is 90 beats per minute, her blood pressure is 110/90 mm Hg, and her oxygen saturation is 100% while she is breathing ambient air. Her electrocardiogram shows sinus rhythm with nonspecific T-wave changes. On laboratory examination, her complete blood count and complete metabolic panel are within normal limits. Her glycated hemoglobin level is 7.0%. The high-sensitivity troponin T level is 0.04 ng per liter (normal value, <14) on the initial blood test and remains unchanged when the test is repeated 6 hours later.

You suspect that the patient may have or may be at risk for coronary artery disease, and you and the other members of the medical team elect to do further workup to determine the patient's risk. The two main imaging options to assist in risk stratification are radionuclide myocardial perfusion imaging and coronary computed tomographic (CT) angiography. You must advise the team on the appropriate imaging method for this patient.

TREATMENT OPTIONS

Which one of the following approaches would you take? Base your choice on the literature, your own experience, published guidelines, and other information sources.

1. **Recommend radionuclide myocardial perfusion imaging.**
2. **Recommend coronary CT angiography.**

To aid in your decision making, we asked two experts in the field to summarize the evidence in favor of approaches assigned by the editors. Given your knowledge of the issue and the points made by the experts, which approach would you choose?

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From the Department of Cardiology, University of North Carolina, Chapel Hill.

OPTION 1

Recommend Radionuclide Myocardial Perfusion Imaging

James Udelson, M.D.

In this patient presenting to an emergency department, the focus of the initial evaluation should be on the diagnosis of an acute coronary syndrome. Although the symptoms are not those of classic ischemic substernal chest pressure, ischemia may manifest in an atypical manner more commonly in women.

The absence of ischemic ST-segment elevation or depression leaves the risk of acute coronary syndrome in the 8-to-12% range. Serial negative high-sensitivity troponin levels across 6 hours are associated with a risk of myocardial infarction or death from cardiovascular causes at 30 days after presentation of less than 1%.[1] The remaining clinical questions involve whether the

symptoms may represent unstable angina or whether coronary artery disease is present at all and if it is present, what the future risk is.

Myocardial perfusion imaging uses radioisotopes injected while the patient is at rest, during stress, or both to noninvasively image myocardial blood flow. Since the proximate cause of an acute coronary syndrome is a reduction in myocardial blood flow caused by an obstructive and unstable plaque, perfusion imaging while the patient is at rest (rest perfusion imaging) can identify the substrate. In a large multicenter trial, patients randomly assigned to a strategy in which their care was informed by the results of rest perfusion imaging had fewer unnecessary admissions than those cared for without such information.[2] Rest perfusion imaging, though, is most useful when the patient is having ongoing symptoms or within 2 to 3 hours after presentation. In the case of this patient, more than 6 hours have elapsed.

In this situation, perfusion imaging performed during stress (stress perfusion imaging) will generally answer the clinically relevant questions and is considered an appropriate test after results of serial troponin tests have been negative.[3] Exercise stress may reproduce the patient's symptoms (reported here as worsening with exercise) and allow correlation with perfusion defects. A positive stress imaging test suggests that the preceding symptoms may have been due to coronary artery disease and myocardial ischemia. The extent and severity of perfusion defects is predictive of the future risk of myocardial infarction and death from cardiovascular causes and enables a discussion with the patient about the potential role of catheterization and revascularization. A negative test makes unstable angina and obstructive coronary artery disease very unlikely.

Coronary CT angiography can also answer questions here but may not do so as consistently in the majority of patients. Selection of appropriate patients for CT angiography is important, and such selection has been applied in clinical trials involving patients presenting to the emergency department.[4] Patients with allergies to contrast material cannot receive the required contrast. The heart rate would need to be controlled with beta-blockers to enhance the quality of the image, which may be problematic in patients with asthma. In patients with many risk factors, as in this case, substantial coronary calcification may undermine the accuracy of the contrast angiography portion of the test in identifying stenoses, and that will not be known until the patient is already being scanned. If moderate stenoses are found, their relation to symptoms may not be evident. The use of fractional flow reserve techniques with coronary CT angiography (FFR-CT) is useful in that regard, but this imaging method is not yet universally available, and another test might be needed.

Hence, stress and rest myocardial perfusion imaging will provide actionable information to answer the relevant clinical questions and will do so in virtually all patients, with minimal radiation exposure when contemporary techniques are used. This imaging method is widely available, and its use is supported by decades of reports and evidence in the literature.

Not to be lost in discussions about the pros and cons of various cardiac imaging methods is the importance of local experience and expertise. Imaging of any type must be of high quality and must be interpreted by experienced personnel to provide the information needed to drive management decisions affecting patients.

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From Tufts Medical Center, Boston.

OPTION 2

Recommend Coronary CT Angiography

Matthew J. Budoff, M.D.

This 58-year-old woman who presents with acute chest pain has low-to-intermediate probability of obstructive coronary artery disease. This observation strongly favors the use of coronary CT angiography over myocardial perfusion imaging. CT angiography affords direct visualization of the coronary arteries, with a negative predictive value approaching 100% for exclusion of obstructive coronary artery disease. Multiple studies have shown that CT angiography is significantly more accurate diagnostically than myocardial perfusion imaging.[5,6] The SCOT-HEART (Scottish Computed Tomography of the Heart) trial showed that the rate of death or nonfatal myocardial infarction was 41% lower when anatomical testing (e.g., CT angiography) was the imaging method used than when stress testing was used.[7]

The use of CT angiography in patients with acute chest pain has been studied extensively. In six randomized trials involving patients with

acute chest pain, CT angiography was compared with myocardial perfusion imaging, standard care, exercise treadmill testing, and high-sensitivity troponin measurement. Each study showed the superiority of CT angiography over the comparator with respect to cost, time to discharge from the emergency department, or both. One prospective, randomized, multicenter study, CT-STAT (Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment), showed a 54% shorter time to diagnosis and 38% lower cost with CT angiography than with myocardial perfusion imaging, with no difference in safety (cardiovascular) end points.[8] Overall, a diagnostic strategy that uses early CT angiography is safe and results in significantly lower cost and shorter length of hospital stay than those associated with other approaches, most notably myocardial perfusion imaging.

CT angiography now has capabilities to assess ischemic burden as well, by estimating fractional flow reserve. FFR-CT has emerged as a powerful tool to provide important prognostic information and further inform treatment strategies (because it provides information on the anatomical and hemodynamic significance of stenosis). FFR-CT affords considerably better discrimination of ischemia than that provided by other noninvasive tests, including myocardial perfusion imaging and positron emission tomography (PET).[6] In addition, radiation doses are significantly lower with CT angiography than with myocardial perfusion imaging (an important consideration in this younger woman), making CT angiography the preferred test in the 2020 American College of Radiology Appropriateness Criteria guidelines for acute nonspecific chest pain.[9]

Another compelling reason to choose CT angiography over myocardial perfusion imaging was highlighted by the recent ISCHEMIA trial. Risk stratification that used functional imaging (predominantly myocardial perfusion imaging) failed to identify patients who would benefit from coronary revascularization. The anatomical extent and burden of coronary artery disease as assessed on coronary CT angiography was highly predictive of death and myocardial infarction ($P<0.001$), whereas severity of ischemia was not ($P=0.33$).[10]

CT angiography affords information related to stenosis (including discrete information about location, calcification, length, and complexity) and simultaneously the severity of underlying atherosclerosis. Positive outcomes from multiple randomized trials favoring CT angiography over functional imaging have been linked to the ability of CT angiography to identify nonobstructive coronary artery disease,[7] leading to increased use of effective preventive therapy such as statins, aspirin, and angiotensin-converting–enzyme inhibitors, as well as improved adherence to these therapies.

In summary, at a lower cost and radiation burden, CT angiography (with or without fractional flow reserve measurement) will deliver higher diagnostic accuracy for ischemia-causing lesions and left main coronary artery disease, improve risk prediction leading to better outcomes, identify subclinical atherosclerosis (coronary-artery calcification and mild stenosis), allow appropriate initiation of and adherence to preventive therapies, and reduce downstream resource utilization (e.g., subsequent testing).

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