Computed Tomography Coronary Angiography

A Noninvasive Escape When Stress Tests Fail (Caught Between Guidelines and Gut Feeling)*

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Computed tomography coronary angiography (CTCA) has evolved into a robust coronary imaging technique because of improvements in temporal and spatial resolution, short scan times, and ever lower patient radiation exposure. Although CTCA has demonstrated excellent accuracy for excluding obstructive coronary artery disease (CAD), its role in the diagnostic work-up of patients with symptoms suspicious for CAD, in relation to established noninvasive stress (imaging) tests is still not well defined.

Assessment of patients with chest pain in general follows an established stepwise approach, as recommended in American College of Cardiology/American Heart Association and European Society of Cardiology guidelines (1,2). The first step involves careful history taking, physical examination, and risk factor assessment to determine the pre-test likelihood of CAD, in an explicit manner using established or contemporary prediction algorithms (3–5). Further management depends on whether a patient is classified in the low, intermediate, or high pre-test likelihood category. The second step involves stress testing to confirm myocardial ischemia as the cause of symptoms and to identify patients who may merit medical treatment to relieve symptoms or who may merit selective invasive coronary angiography (ICA) and consideration for revascularization to relief symptoms and improve prognosis.

Traditionally, stress testing includes exercise electrocardiography, stress echocardiography, or myocardial perfusion scintigraphy. Although simple and straightforward in conception, “real world” clinical cardiology is more complex, and the low yield of invasive angiography to detect obstructive coronary disease—27% to 49% in women and 47% to 67% in men (6,7)—illustrates the suboptimal performance of the current diagnostic work-up. Reasons for this include the modest correlation between stress tests results and angiographic disease severity, at least in perception, and that an increasing proportion of patients are referred for invasive angiography without even an attempt at noninvasive evaluation (8). There is a need for improved noninvasive evaluation to decrease the number of normal invasive angiograms. The excellent ability of CTCA to exclude significant CAD could make it a more effective gatekeeper to ICA than stress testing (8). While intuitively sensible, there are limited data on the efficacy of CTCA as a second test to confirm or refute the initial functional stress test with equivocal or conflicting results.

Chinnaiyan et al. (9), in this issue of the Journal, evaluated the predictive value of CTCA in patients with inconclusive stress tests, which is in line with guidelines. In addition, they evaluated CTCA in patients in whom initial stress tests outcomes needed adjudication with CTCA because of discordance between symptoms, pre-test likelihood of CAD, and stress test, as perceived by the treating physician. They studied 6,198 patients without known CAD who were undergoing CTCA within 3 months after a stress test, of a total of 22,551 CTCA patients collected from 47 centers by the ACIC (Advanced Cardiovascular Imaging Consortium) in Michigan. The investigators tested the incremental value of clinical information, cardiovascular risk (Framingham Risk Score with additional risk parameter), probability of CAD, and stress testing to predict CAD on cardiac computed tomography using C-statistics. They found that stress testing had no incremental value to clinical information or pre-test likelihood of CAD. In a subset of 621 patients who were referred to ICA, they demonstrated that only CTCA had incremental value compared with clinical information, pre-test likelihood, and stress testing to predict >50% stenosis on ICA. They further demonstrated that presuming that 80% (4,650 of 6,198) of the patients with equivocal or abnormal test would be referred to ICA, adjudication to CTCA decreased referral to 20%, indeed an effective gatekeeper. Overall, the approach of adjudication of conflicting stress results was successful and led to a diagnostic yield of ICA of 57% to detect >50% stenosis, which is an improvement over previous data, but still lower than desirable.

There are a number of other issues that deserve further discussion. While sometimes conflicting, at least in appearance, invasive or noninvasive angiography and functional testing provide complementary data, both of which are important in the management of patients with suspected CAD. Before dismissing functional testing as noncontributing in the risk assessment process, we should also acknowledge that CTCA as the reference outcome has a
tendency to overestimate CAD. As a matter of fact, the positive predictive value of CTCA in this study was only 71% in comparison to that of invasive angiography.

It is also important to reiterate the acknowledged biases in the comparison between CTCA and stress testing in the ACIC registry (9). The population selected leaned toward patients with conflicting or equivocal stress test results—patients with clearly positive or negative results that confirmed clinical suspicion were excluded—thereby potentially inducing a “self-fulfilling prophecy” that CTCA is indeed a better test. That was further amplified by referral and validation bias to ICA by demonstrating the superiority of CTCA to predict angiographic stenosis on ICA. The choice of a moderately severe anatomical endpoint, CTCA >50% stenosis, which is a poor predictor of myocardial ischemia, stacked the cards in favor of a noninvasive anatomical modality. That a moderately stenotic lesion does not cause objective myocardial ischemia does not imply that the functional test result is incorrect, or that the obtained information is meaningless for further management of that patient. Not unlikely, results would have been different if a >70% threshold or fractional flow reserve had been selected as a reference.

Indeed, the present study by Chinnaiyan et al. (9) provides valuable insights into what is the current practice use of CTCA in the management of patients with chest pain. In the original population, 30% (9,348 of 22,551) appear to have undergone CTCA without prior stress tests. While this approach is not yet widely embraced, there are indeed emerging data to suggest that cardiac CT may be a more efficient initial test to rule out CAD (8). More controversial is the referral to CTCA of patients with a history of CAD (25%) and asymptomatic patients (5%). Although these referrals appear to be deviations from current practice guidelines (10–12), the study also teaches us that clinical judgment, although arbitrary and not well defined, does have value, and “gut feeling” may prompt a second test to “correct” tests with a high suspicion of false positive or negative outcomes, thereby avoiding a substantial number of catheterizations. Nevertheless, we should be aware of the potential overuse of cardiac testing, and may want to rethink our current practice of arguably less appropriate first tests in patients with low pre-test probability of CAD, inevitably leading to substantial numbers of false positive results, which consequently necessitate a second test to avoid a likely-to-be-negative invasive examination. The study is interesting, revealing, stimulates our diagnostic thinking, and should prompt a prospective well-designed study in which the need for adjudication with a second test, in case of diagnostic uncertainty after a initial diagnostic test, is based on the post-test likelihood of CAD, with pre-specified levels of diagnostic uncertainty, thereby providing more support to judicious referral to another test to increase the diagnostic yield of ICA to detect obstructive disease.

REFERENCES


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