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REVIEW TOPIC OF THE WEEK

Finding the Gatekeeper to the Cardiac Catheterization Laboratory

Coronary CT Angiography or Stress Testing?

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ABSTRACT

Functional capacity is a robust predictor of clinical outcomes, and stress testing is used in current practice paradigms to guide referral to invasive coronary angiography. However, invasive coronary angiography is driven by ongoing symptoms, as well as risk of adverse outcomes. The limitations of current functional testing-based paradigms might be avoided by using coronary computed tomographic angiography (CCTA) for exclusion of obstructive coronary artery disease. The growth of CCTA has been supported by comparative prognostic evidence with CCTA and functional testing, as well as radiation dose reduction. Use of CCTA for physiological evaluation of coronary lesion-specific ischemia may facilitate evaluation of moderate stenoses, designation of the culprit lesion, and prediction of benefit from revascularization. The potential of CCTA to serve as an effective gatekeeper to invasive coronary angiography will depend, in part, on the adoption of these new developments, as well as definition of the benefit of detecting high-risk plaque for guiding the management of selected patients. (J Am Coll Cardiol 2015;65:2747–56) © 2015 by the American College of Cardiology Foundation.

Invasive coronary angiography (ICA) is the concluding step in the diagnostic work-up of suspected coronary artery disease (CAD), often on the basis of results of noninvasive stress testing. Guideline support of this practice (1) derives from the prognostic value of functional capacity and extent of ischemia, as well as data from >15 years ago evaluating the comparative effectiveness of direct referral to ICA versus selective referral on the basis of stress test findings. These studies suggested cost efficiencies from selective referral and encouraged a noninvasive approach to ICA decision making (2).

However, functional testing prior to ICA is not widespread. Possibly as a consequence, 40% of angiograms in the NCDR (National Cardiovascular Database Registry) detect normal coronary arteries (3). Likewise, less than two-thirds of patients in the NCDR's CathPCI program underwent noninvasive stress testing prior to nonemergent ICA (4). There is substantial geographic heterogeneity in the use of functional testing before coronary intervention (5), with stress testing less likely in women, older patients, those with impaired mobility, situations of competing risk (e.g., cancer), and in the hands of older physicians and those with a high volume

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Listen to this manuscript's audio summary by *JACC* Editor-in-Chief Dr. Valentin Fuster.

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ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome(s)

CAD = coronary artery disease

CCTA = coronary computed tomographic angiography

CI = confidence interval(s)

CP = chest pain

CT = computed tomography

FFR = fractional flow reserve

FFR_{CT} = fractional flow reserve derived from CCTA using computational fluid dynamics

ICA = invasive coronary angiography

MI = myocardial infarction

MPI = myocardial perfusion imaging

NPV = negative predictive value(s)

OR = odds ratio

SE = stress echocardiography

SPECT = single-photon emission computed tomography

of percutaneous intervention. The normal ICA frequency (6) and the frequency of appropriate ICA use show geographical variation that is independent of hospital location, teaching status, or availability of revascularization (7). Overuse, underuse, and misuse may imply poor quality care, providing justification to consider a "gatekeeper" to the catheterization laboratory.

It was hoped that the recently released PROMISE (Prospective Multicenter Imaging Study for Evaluation of Chest Pain) trial would elucidate the relative roles of CCTA and functional testing. This study randomized >10,000 patients between coronary computed tomographic angiography (CCTA) and stress testing (8). A 9% event rate was anticipated in these patients, who had a 53% ± 21% pretest likelihood of obstructive CAD, and the study was powered for a 20% reduction to show superiority, and a 10% margin for noninferiority. However, over a 2-year follow-up, the composite primary endpoint (death, myocardial infarction [MI], hospitalization for unstable angina, or major procedural complication) occurred in only 3.3% of the CCTA and only 3.0% of the functional-testing group (adjusted hazard ratio: 1.04; 95% confidence interval [CI]: 0.83 to 1.29; $p = 0.75$). Although these findings are insufficient to conclude the possibility of either harm or benefit from the use of CCTA, a particularly salient feature was that although catheterization was performed in more CCTA patients in the 90 days following noninvasive testing, the likelihood of nonsignificant CAD was significantly lower in the CCTA group (3.4% vs. 4.3%; $p = 0.02$). Clinicians seeking guidance as to whether a CCTA or functional testing strategy would provide the most favorable outcomes have been disappointed, with interpretations ranging from concluding that CCTA and functional testing strategies are comparable, to emphasizing the inconclusive nature due to limited statistical power (9,10). In this context, there is merit in reviewing published reports comparing CCTA and functional testing in diagnosis of CAD.

RESULTS OF FUNCTIONAL TESTING IN PATIENTS WITH ACUTE CHEST PAIN

Strong evidence supports appropriate use of stress imaging tests for both diagnostic and prognostic assessment of CAD (11). Good evidence supports the use of single-photon emission computed tomography (SPECT) and stress echocardiography (SE) in patients presenting acutely with chest pain (CP) (12–16) (**Table 1**). Nonetheless, use of functional testing after presentation with CP may be nonideal—patients have often been treated with antianginal agents, submaximal treadmill tests are common, and complications are not unusual (17).

Although guidelines recommend the use of stress testing, recent audits in nearly 400,000 such patients showed its impact to be modest (3). Patients with positive tests were only moderately more likely to show obstructive coronary disease (41% vs. 35%; $p < 0.001$; adjusted odds ratio [OR]: 1.28; 95% CI: 1.20 to 1.40). Similarly, in the CathPCI data (4), although abnormal noninvasive test results improved the identification of individuals with anatomically obstructive CAD, the difference in the proportion of testing among patients with obstructive and nonobstructive disease was small. Fewer individuals with nonobstructive CAD—who are at risk of incident MI and mortality—are recognized with a selective referral strategy on the basis of functional testing than with coronary imaging. These findings evoke concerns that the current practice paradigm of stress testing followed by ICA is ineffective at identifying individuals who should start treatment for CAD. CCTA is a promising noninvasive method for identification and

TABLE 1 Studies of Functional Testing (Stress Echocardiography and SPECT) in Acute CP Presentations in Studies of >250 Subjects

	Modality	n	Age (yrs)	Men	Design	Stress	Angio (%)	CAD Patients	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Kontos et al. (12)	SPECT	162	56	50	Negative ECG	Rest	>70 >50	86 86	76	64	71	70
Conti et al. (13)	SPECT	503	62	75	Low-risk, equivocal workup	Rest	>50	94	86	83	54	96
Bholasingh et al. (15)	SE	377	56	58	Negative ECG	Dob	>50	25	44	96	42	96
Bedetti et al. (16)	SE	552	58	58	Negative ECG and enzymes	Dipy/dob	>50	50	88	100	95	99
Conti et al. (14)	New WMA	503	62	75	Negative ECG and enzymes, normal rest echo	Ex	>50	94	85	95	81	97

Angio = coronary angiography; CAD = coronary artery disease; CP = chest pain; Dipy = dipyridamole; Dob = dobutamine; ECG = electrocardiogram; Echo = echocardiogram; Ex = exercise; NPV = negative predictive value; PPV = positive predictive value; SE = stress echocardiography; SPECT = single-photon emission computed tomography; WMA = wall motion abnormality.