PROMISE: Anatomic and Functional CAD Testing Comparable in Clinical Outcome and Cost

Written by Alla Zarifyan

Pamela S. Douglas, MD, Duke University Medical Center, Durham, North Carolina, USA, presented results of the PROMISE trial [Douglas PS et al. *N Engl J Med*. 2015], demonstrating that a strategy of initial computed tomographic angiography (CTA) in symptomatic patients with suspected coronary artery disease (CAD) who required noninvasive testing did not improve clinical outcomes over a median follow-up of 2 years when compared with functional testing. Daniel B. Mark, MD, Duke University Medical Center, Durham, North Carolina, USA, also reported the results of an economic substudy, revealing that the difference in net cost between the 2 testing strategies was not significantly different.

Dr Douglas highlighted that new-onset stable chest pain leads to approximately 4 million stress tests annually in the United States in patients without diagnosed heart disease [Ladapo JA et al. *Ann Intern Med*. 2014]. CTA has the potential to reduce unnecessary invasive testing and improve outcomes due to higher accuracy when compared with functional testing and its ability to detect prognostically important nonobstructive CAD. However, the relative impact of data derived from noninvasive anatomic testing vs functional testing on subsequent management and clinical outcomes had not been elucidated.

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The PROMISE trial was a multicenter randomized pragmatic comparative effectiveness trial analyzing whether anatomic testing with CTA, as compared with functional testing with a stress test (ie, exercise electrocardiogram, stress echocardiography, or stress testing with nuclear imaging), would improve the health outcomes of patients with symptoms of potential CAD who require further testing [Douglas PS et al. *N Engl J Med*. 2015]. The primary end points were all-cause mortality, nonfatal myocardial infarction (MI), hospitalization for unstable angina, and major complications from cardiovascular (CV) procedures (eg, stroke, bleeding, renal failure, or anaphylaxis). The secondary end points included the primary end point plus invasive catheterization without obstructive CAD, other components of the primary end point, invasive catheterization without obstructive CAD, cumulative radiation exposure at ≤ 90 days, and an economic analysis that was reported separately by Dr Mark.

The study included patients with clinically necessary, nonurgent, noninvasive CV testing; no history of CAD or recent CAD evaluation; men who were aged > 54 years or women aged > 64 years; or men aged 45 to 54 years or women aged 50 to 64 years with ≥ 1 major cardiac risk factor.

A total of 10 003 patients were enrolled: 4996 were randomized to CTA and 5007 to a functional testing strategy. Baseline characteristics were similar between the groups. The median follow-up time was 25 months, with a maximum follow-up of 50 months. Nearly 94% of patients received the testing to which they were randomized. At 12 months, loss to follow-up was 2.4% and 3.2% in the CTA and functional-testing strategy arms, respectively, and withdrawal of consent was 2.5% and 4.9%, respectively.

During follow-up, 3.3% of patients in the CTA group and 3.0% in the functional testing group had a primary end point event (HR, 1.04; 95% CI, 0.83 to 1.29; $P = .75$; Table 1). Results of the prespecified subgroup analyses were consistent with those in the overall population.

Results were also not significant for the secondary end point of the composite of the primary end point plus invasive cardiac catheterization (HR, 0.91; 95% CI, 0.78 to 1.06; $P = .22$) or for death or nonfatal MI (HR, 0.88; 95% CI, 0.67 to 1.15; $P = .35$). A lower-than-anticipated event rate may have contributed to these null findings.

However, the exploratory secondary end point of catheterization showed no obstructive CAD at ≤ 90 days and occurred in 3.4% of patients in the CTA group vs 4.3% of those in the functional

Table 1. Clinical End Point Events

	CTA (n = 4996)	Functional (n = 5007)	Adjusted HR (95% CI)	*P* Value
Primary end point composite	164	151	1.04 (0.83 to 1.29)	.750
All-cause death	74	75		
Nonfatal MI	30	40		
Unstable angina hospitalization	61	41		
Major procedural complications	4	5		
Primary end point plus catheterization without obstructive CAD	332	353	0.91 (0.78 to 1.06)	.217
Death or nonfatal MI	104	112	0.88 (0.67 to 1.15)	.348
Death, nonfatal MI, or unstable angina hospitalization	162	148	1.04 (0.84 to 1.31)	.703

CAD, coronary artery disease; CTA, computed tomographic angiography; MI, myocardial infarction.

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Source: Douglas PS et al. *N Engl J Med*. 2015.

testing group ($P = .022$). The difference in the cumulative radiation exposure at ≤ 90 days was driven by the type of functional test ordered. A comparison of CTA vs stress testing with nuclear imaging revealed lower radiation in the CTA group (10.1 vs 12.0 mSv); however, in comparison to those patients undergoing a stress electrocardiogram or stress echocardiography, radiation in the CTA group was higher. No ionizing radiation exposure was received by 4% of patients in the CTA group vs 33% in the functional group ($P < .001$).

Dr Mark reported results of the economic substudy, whose primary objective was to measure and compare cumulative total costs of each strategy and to estimate the cost-effectiveness of anatomic strategy if it was shown to be superior. Medical costs considered in the calculation included initial diagnostic test technical fees, hospital-based facility costs, and physicians' fees for testing and hospital services. A total of 96% of patients were included in economic substudy across both testing groups. The results demonstrated that despite somewhat lower testing fees for CTA compared with functional testing, the net cost for CTA was higher, although the increase was not statistically significant (no *P* value reported). However, Dr Mark cautioned that outpatient medication costs were not included in the cost calculation, and the analysis of data on quality of life and the employment status was not yet completed.

Dr Douglas concluded that an initial strategy of CTA was not associated with better clinical outcomes than functional testing over a median follow-up of 25 months in this large, community-based population of symptomatic patients with suspected CAD who required noninvasive testing.

Percutaneous Treatment of Valvular Heart Disease, Atrial Fibrillation Examined in Various Studies

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The results of trials of the percutaneous treatment of aortic stenosis (AS) and mitral regurgitation (MR), including PARTNER 1 and CoreValve US Pivotal, showed a reduction in mortality, and registry data supported the safety of the MitraClip System. The AATAC-AF study showed that catheter ablation was superior to amiodarone for the treatment of persistent atrial fibrillation (AF).

PERCUTANEOUS TREATMENT OF VALVULAR DISEASE

Michael Mack, MD, The Heart Hospital Baylor Plano, Plano, Texas, USA, reported the results from long-term follow-up of the PARTNER 1 trial [Mack MJ et al. *Lancet*. 2015]. At 5 years, high-surgical-risk patients with severe AS who underwent transcatheter aortic valve replacement (TAVR) had similar mortality and other major clinical outcomes to those who were treated with surgical aortic valve replacement (SAVR).

The PARTNER 1 trial was an international, multicenter, randomized controlled trial that randomized patients who were at high surgical risk to either TAVR with the Edwards Sapien valve or SAVR. The primary end point of the trial was mortality at 1 year. Other key end points included valve performance and stroke rate.

A total of 699 patients were randomized to either TAVR (n = 348) or SAVR (n = 351). The median survival was 44.5 months in the TAVR group vs 40.6 months in the SAVR