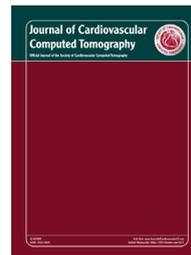




ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofCardiovascularCT.com

From the Desk of the President

President's page - The promise of coronary CT angiography: Precision medicine



Dear Colleagues,

The field of cardiac imaging was recently presented with two important prospective multi-center randomized trials comparing an initial strategy with Coronary CT Angiography (CCTA) vs a traditional strategy with functional testing.^{1,2} PROMISE¹ and SCOT-HEART² trials were conducted in intermediate risk patients presenting with stable chest pain in the outpatient setting.

The PROMISE Trial randomized 10,003 symptomatic patients to an initial evaluation with CCTA or to functional testing (exercise ECG, nuclear stress testing or stress echocardiography). The median follow-up was 25 months. The composite primary end-point was death, myocardial infarction, hospitalization for unstable angina or major procedural complication. Secondary end-points included hard events alone, invasive cardiac catheterization without obstructive CAD and radiation exposure. The main results of the trial showed no difference for the primary end-point, demonstrating that CCTA is a viable alternative to stress testing for assessment of stable chest pain patients. Interestingly, an initial strategy with CCTA was associated with a significant lower rate of invasive catheterization without obstructive CAD (28%) as compared to a functional strategy with stress test that demonstrated 52% of invasive catheterization without obstructive CAD. If you want to present the data in a different way, there was very good correlation to detect obstructive CAD between CCTA and invasive coronary angiography in 72% of patients compared to only 48% with the functional testing strategy. This data in a prospective randomized trial confirms prior data from a recently updated publication from the National Cardiovascular Data Registry about prevalence of obstructive disease in the United States, as defined by cardiac catheterization in 661,063 patients.³ The rate of obstructive CAD by cardiac catheterization in patients undergoing stress SPECT and stress Echo was only 44.5% and 43.8% respectively, when compared to 70% of patients who had obstructive CAD by CCTA.⁴ These data should significantly impact daily clinical practice, with CCTA being an effective gate-keeper to the catheterization lab and with



potential to dramatically reduce the number of unnecessary invasive angiograms and stress tests.

Now, the (*second and*) most important question that comes to mind is, does it change patient management? Does it improve patient outcomes? Does it reduce hard events? Surprisingly, in the PROMISE Trial there was a significant early benefit from the CCTA strategy over functional strategy for decreasing hard events (death or non-fatal MI) in 12 months. The data was statistically significant ($P = .049$) and the hazard ratio was 0.66. The overall median follow-up of 25 months did not show this difference. However, fewer patients were present in the later analysis and a longer follow-up could potentially show a significant difference for hard events.

SCOT-HEART was a large prospective multi-center trial in 4146 patients presenting with suspected angina due to coronary heart disease in twelve cardiology outpatient clinics in

Scotland. Patients were randomized to standard of care (including functional imaging) or standard of care PLUS CCTA. Even more surprisingly, the use of CCTA led to changes in diagnosis and subsequent treatment strategies, resulting in a 38% reduction on cardiac death and non-fatal myocardial infarction (MI) when compared to the standard of care. This makes an impact on clinical care. Even if just borderline significant, the findings are very encouraging and will need to be confirmed by longer-term follow-up.

So, what would explain that two prospective randomized trials both demonstrated that a strategy with CCTA achieved borderline statistically significant reduction in hard events (cardiac death and non-fatal MI)? Is it just a statistical fluke or can a strategy with CCTA save lives? We need either more patients in these trials, more hard events or longer follow-ups. We will definitely have longer follow-ups in both trials and this may lead to a more definitive answer. As a matter of fact, both trials demonstrated an increase in cardiac catheterizations in the CCTA arm, but here I would speculate that this data is positive. Actually, CCTA is leading to more precise diagnosis (better correlation with cardiac catheterization for obstructive CAD is a fact, as described above) resulting in better triage of patients to the catheterization lab and leading to revascularization in appropriate patients, which can potentially have an impact on patient outcomes. On the other hand, CCTA uniquely identifies patients who have non-obstructive atherosclerosis and who will benefit from medical therapy. A strategy with CCTA in the SCOT HEART Trial increased the certainty (RR 2.56, 95% CI 2.33–2.79; $P < .0001$) and frequency (1.09, 1.02–1.17; $P = .0172$) of the diagnosis of coronary heart disease at 6 weeks. Overall, the 6-week diagnosis of coronary heart disease changed in 27% of participants assigned to CCTA compared with 1% assigned to standard care, and the 6-week diagnosis of angina due to coronary heart disease changed in 23% of participants assigned to CCTA compared with 1% assigned to standard care ($P < .001$ for both). These changes were mainly the result of the exclusion or identification of obstructive coronary heart disease, leading to a more precise diagnosis. The changes in diagnoses and investigations were associated with changes in the subsequent recommendations for preventive (18% vs 4% respectively; $P < .0001$) and anti-anginal (9% vs 1% respectively; $P < .0001$) treatments. Overall, reclassification happened in one in four patients and addition of CCTA to standard care clarified the diagnosis of angina due to coronary artery disease and this is clearly important for the subsequent investigation and treatment of these patients. Moreover, the CCTA strategy reduced the need for additional stress testing, increased the use of invasive coronary angiography in appropriate circumstances, and led to more focused treatment. Overall, these findings were associated with a 38% reduction in cardiac death and non-fatal myocardial infarct in the CCTA arm. All this data summarizes the concept of precision in diagnosis, leading to precision in treatment and translating in better patient outcome.

On the PROMISE Trial, the median cumulative radiation exposure per patient was lower in the CCTA group than in the functional-testing group (10.0 mSv vs 11.3 mSv), but 32.6% of the patients in the functional-testing group had no exposure,

so the overall exposure was higher in the CCTA group (mean, 12.0 mSv vs 10.1 mSv; $P < .001$). The radiation exposure in patients that had SPECT study was significantly higher when compared to the CCTA group (14.1 mSv for SPECT and 12.0 mSv for CCTA; $P < .001$). On the SCOT HEART trial, the median radiation dose for CCTA was only 4.1 mSv, continuing the rapidly accelerating downward trend thanks to technological advances and rigorous professional training. We can summarize that both CCTA and Functional strategies will expose patients to radiation with Nuclear SPECT leading to the highest radiation exposure, and with recent technological advances in CCTA decreasing significantly the radiation exposure, as demonstrated in the SCOT HEART study.

In summary, both SCOT HEART and PROMISE trials provide compelling evidence that CCTA should be part of the everyday testing armamentarium and support expanded use of CCTA for evaluation of patients with stable chest pain. These studies provide convincing evidence to revise coverage and medical necessity decision rules. CCTA should be considered an appropriate test for assessing symptomatic intermediate-risk patients presenting with stable chest pain and the Guidelines should be changed to level of evidence A and class I.

The promise of CCTA is precision in Diagnosis. We can see scientific evidence confirming such promise, but we need to continue to foster high quality training, excellence in education and service, advances in technology, and continue to explore further research trials. The investigators of PROMISE and SCOT HEART Trials should be commended for their efforts. The future of CCTA is bright with more standardization in reporting and linking to specific treatment recommendations. CCTA needs to continue to make an impact on the field with not only “intent to diagnosis”, but also “intent to treatment” trials based on specific CCTA findings. This was the main difference between PROMISE (intent to diagnosis trial) and SCOT HEART (intent to treat trial) and therefore more favorable results of SCOT HEART trial towards a CCTA strategy. As the CCTA field matures (remember we are still a young 10-year-old field) with more standardization and the incorporation of new technologies and techniques, such as CT Perfusion and FFR-CT, the CCTA PROMISE of Precision in Diagnosis will further translate into precision in treatment and better patient outcomes. Precision and personalized medicine, this is what CCTA is all about!

REFERENCES

1. Douglas PS, Hoffmann U, Patel MR, et al. PROMISE Investigators. Outcomes of anatomical versus functional testing for coronary artery disease. *N Engl J Med*. 2015;372(14):1291–1300.
2. SCOT-HEART investigators. CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open-label, parallel-group, multicentre trial. *Lancet*; 2015 Mar 13 [Epub ahead of print].
3. Patel MR, Dai D, Hernandez AF, et al. Prevalence and predictors of non-obstructive coronary artery disease identified with coronary angiography in contemporary clinical practice. *Am Heart J*. 2014;167(6):846–852.e2.

4. Cury RC. President's page: coronary CT angiography as a gatekeeper to the catheterization laboratory. *J Cardiovasc Comput Tomogr.* 2014;8(6):480–482.

Ricardo C. Cury, MD, FSCCT, FAHA, FACC*
Miami Cardiac and Vascular Institute
Baptist Health of South Florida
8900 North Kendall Drive
Miami, FL 33176, USA

* Corresponding author.

E-mail address: rcury@baptisthealth.net

Available online 11 April 2015

1934-5925/\$ – see front matter

© 2015 Society of Cardiovascular Computed Tomography.

All rights reserved.

<http://dx.doi.org/10.1016/j.jcct.2015.04.001>