Coronary Computed Tomography in the Evaluation of Symptomatic Patients With Suspected Coronary Artery Disease

– Coronary Calcium Scoring (CAC) and Computed Tomography Angiography (CTA) –

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Coronary artery disease (CAD) is a leading cause of mortality worldwide.¹ In countries where appropriate medical resources are available, preventive and therapeutic strategies can significantly reduce this disease burden.² This requires reliable diagnosis of acute and chronic disease and identification of risk for future events. Based on current consensus, the assessment of future risk depends predominantly on clinical history, serum markers of inflammation, and lipid metabolism.³ While carotid ultrasound and computed tomography (CT) calcium scoring allow identification of latent, asymptomatic plaque burden, population-wide screening with these modalities is currently not recommended.⁴

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In contrast, imaging plays a central role in the assessment of symptomatic patients with suspected or known CAD. Guidelines recommend an initial rapid clinical assessment with risk stratification based on electrocardiogram (ECG) and serum markers (troponin, creatine kinase).³ High-risk patients will subsequently undergo conventional X-ray coronary angiography and revascularization if necessary. Lower risk patients are observed with serial assessment of ECG and enzymes. A large percentage of these patients will eventually undergo diagnostic imaging, with the goal of identifying (hemodynamically) significant disease, and stratification of risk for future cardiovascular events. Using stress-imaging (echocardiography, nuclear perfusion imaging), impairment of left ventricular ejection fraction, extent of ischemia, and scar are strongly associated with future adverse outcomes.⁵ Clinical trials demonstrate that such stratification allows differentiation of subgroups of patients that would benefit from revascularization vs. intensive medical management.⁶

Similar to these more established diagnostic imaging modalities, non-invasive imaging with magnetic resonance imaging and CT angiography (CTA) allow identification/exclusion of significant stenosis and risk stratification of patient with suspected CAD.⁷ A meta-analysis of coronary CTA data, including almost 10,000 patients and 449 major adverse cardiovascular events (MACE) during 20 months follow-up, demonstrated an

event rate of 4.7% and 2.4% for MACE and death or myocardial infarction (MI), respectively.⁸ The pooled annualized event rate for obstructive (any vessel with >50% luminal stenosis) vs. normal coronary CTA was 8.8% vs. 0.17% per year for all MACE and 3.2% vs. 0.15% for death or MI ($P<0.05$). Strata of 'absent CAD', 'non-obstructive CAD' (worst stenosis <50%), or 'obstructive CAD' demonstrated incremental increase of MACE (0.17%, 1.41%, 8.84%). Adverse cardiovascular events among patients with normal findings on coronary CTA were rare, similar to the background event rate among healthy low-risk individuals (<1%). Recent data from the ROMICAT trial reports 2-year follow up data of 368 patients presenting to the emergency department with acute chest pain syndromes and negative initial troponin and ECG.⁹ During follow-up, 25 patients had 35 MACE (0 cardiac deaths, 12 MI, 23 revascularizations), consistent with an event rate of 6.8% for MACE and 3.3% for death or MI. Cumulative probability of 2-year MACE increased across CT strata for CAD (no CAD 0%, non-obstructive CAD 4.6%, obstructive CAD 30.3%, $P<0.0001$). The C statistic for predicting MACE was 0.61 for clinical Thrombolysis In Myocardial Infarction risk score, and improved to 0.84 by adding CT CAD data ($P<0.0001$).

In this issue of the Journal, Yamamoto et al examine the potential role of coronary calcium scoring (CAC) in a similar population of Japanese patients.¹⁰ The authors followed 317 patients (205 men and 112 women) who underwent both coronary angiography and CT calcium scoring. Indication for coronary angiography included chest pain in 82% of patient, and ECG abnormalities or positive stress test in the remaining 18%. Out of these patients, 58% had angiographical evidence of CAD and 42% needed revascularization. In patients with CAC scores of 0 to >1,000, the frequency of angiographic CAD increased from 5% to 94%, and revascularization from 5% to 69% ($P<0.001$). Over an average follow-up period of 6.0 year (range 1–10), 34 patients died, including 13 from cardiac causes. After adjustment for age, gender, traditional coronary risk factors, previous MI, and the need for revascularization, the hazard ratio for cardiac mortality in patients with a CAC score >1,000 was 2.98 (95%CI: 1.15–9.40) compared with those with a CAC score <100. The data demonstrates the predictive

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value of CAC scoring for angiographical CAD and long-term mortality in Japanese high-risk patients. The authors suggest that CAC allows risk-stratification of patients presenting with chest pain, acting as a gatekeeper to invasive coronary angiography. However, because performance of conventional angiography was not conditional on the results of the CAC score, it is unclear if the results of CAC could have resulted in a change in patient management that would have yielded improved patient outcomes. This will need to be examined in future prospective trials. In fact, similar hypotheses are currently examined with coronary CTA in several prospective trials.^{11,12}

While outcome data for individual imaging modalities is accumulating, the relative value of different modalities (eg, CAC vs. CTA) in specific clinical scenarios such as chest pain has not been systematically compared. Such an assessment will also need to weigh the risk of the test, including potential downstream consequences of false-positive results, contrast administration, and radiation exposure. The evaluation is further complicated, because many studies of post-imaging outcomes fail to control or risk-adjust for post-imaging patient management.

Comparing the relative value of CAC and CTA in the diagnostic workup of patient with chest pain is complex, and the data presented by Yamamoto et al suggests that a potential benefit of CTA over CAC in these patient populations is not clearly documented. While CTA can differentiate lumen and vessel wall and therefore identify presence and severity of luminal stenosis, false-positive results are frequent in patients with advanced calcified CAD secondary to calcium blooming. This might lead to unnecessary diagnostic and therapeutic intervention. In comparison to CAC, coronary CTA (even if performed with low-dose protocols) is associated with the need for intravenous contrast administration and higher radiation exposure (CTA <3 mSv CAC <1 mSv).

Comparative effectiveness data needs to be collected and analyzed in prospective clinical trials, national, and international databases. As discussed in the study by Yamamoto et al, comparison of results in patient populations from individual countries or different ethnic backgrounds will be important to understand geographic variation. Over the next several years, these data will define the relative role of invasive and non-invasive modalities, their cost-effectiveness, and environmental impact^{13,14} and will allow to direct patients to the most appropriate diagnostic test.

Disclosures

None.

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