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EDITORIAL

Good news on coronary computed tomographic angiography: answers that have questions!

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This editorial refers to 'Non-invasive diagnosis of ischaemic heart failure using 64-slice computed tomography'† by S. Ghostine *et al.*, on page 2133

An increasing number of studies have examined the role of coronary computed tomographic angiography (CCTA) in assessing patients with known or suspected coronary artery disease (CAD) relative to established evaluation approaches. The diagnostic and predictive value of stress electrocardiography, stress imaging, and invasive, selective coronary angiography (SCA) is documented by a large body of evidence, and their use to guide patient management is codified in clinical guidelines. To date, no convincing evidence suggests that the diagnostic or predictive value of CCTA is superior or even equivalent. Consequently, no first-line indications for CCTA exist.[1,2] However, there may be niche applications where CCTA could be a potentially effective and cost-saving alternative to more established imaging techniques.

Studies comparing CCTA with SCA have universally shown a high negative predictive value (NPV).[3] As a result, a 'negative' CCTA excludes CAD with very high certainty if image quality is diagnostic and most coronary segments are well seen, particularly in populations with a low prevalence of CAD. A valid argument can be made that patients with low pre-test probability do not need testing at all. However, there are clinical scenarios in which SCA is often performed because proving the absence of CAD has important diagnostic or therapeutic implications, or because the diagnostic accuracy of conventional stress testing is reduced. Ghostine *et al.*[4] address the potential use of CCTA in one of these scenarios.

CCTA for the assessment of unexplained cardiomyopathy

The authors examined the role of 64-slice multidetector CCTA in non-invasively classifying symptomatic left ventricular (LV) dysfunction as ischaemic or non-ischaemic. They determined, in 93 consecutive heart failure patients without known CAD, the diagnostic accuracy of CCTA in predicting >50% diameter stenoses detected on SCA. Cardiomyopathy was classified as ischaemic if coronary stenoses were present in the left main coronary artery or the proximal left anterior descending artery, or in ≥2 of the remaining coronary artery segments.

Based on the SCA findings, 43 patients (46%) had at least one >50% diameter stenosis. Of those, 31 patients (33%) had a degree of CAD suggesting ischaemic cardiomyopathy. Sixty-two patients (67%) had non-ischaemic cardiomyopathy. CCTA correctly identified 42 of 43 patients (sensitivity, 98%) with any significant CAD and correctly classified 28 of 31 patients (sensitivity, 90%) with presumably ischaemic cardiomyopathy. Absence of any significant CAD was correctly predicted by 45 of 46 negative CCTAs (NPV, 98%), and CAD suggesting ischaemic cardiomyopathy was correctly excluded by 59 of 62 negative CCTAs (NPV, 95%).

This work expands current knowledge on the use of cardiac CT in patients with cardiomyopathy. Coronary artery calcification on cardiac CT imaging without contrast enhancement can identify ischaemic cardiomyopathy with a sensitivity of 97–98% and an NPV of 95– 98%.[5] However, information on the severity and distribution of CAD provided by coronary calcium imaging alone is limited. A previous study of CCTA in a lower number ($n = 61$) of heart failure patients[6] used older 16-slice multidetector CT scanners but found results similar to the current study: at a prevalence of 28%, the sensitivity for detecting CAD in 870 coronary segments was 99%, and the specificity 96%.

A few aspects of the current work by Ghostine *et al.*[4] deserve discussion. The prevalence of CAD in the authors' cohort was higher than in other studies of patients with unexplained cardiomyopathy. Yet, the uncorrected likelihood ratio of ischaemic cardiomyopathy being present was 18.7 for a positive CCTA and 0.1 for a negative CCTA, suggesting good evidence for both ruling in and ruling out disease.

At least moderate renal insufficiency is present in ~50% of patients with heart failure. This frequent association may be an important limitation for the potential role of CCTA because of

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concerns about contrast nephropathy. The current study does not state how many potentially eligible patients were excluded because of renal insufficiency. In a previous study of CCTA in heart failure patients,[6] 14% of eligible patients were excluded because of impaired renal function.

The CT scanning protocol in patients with heart failure needs careful attention: with reduced cardiac output, the circulation time increases, and the delay between the onset of contrast injection and scanning must be adjusted accordingly. Most contemporary scanners can make such adjustments automatically.

As cardiac output decreases, peak attenuation and contrast-to-noise ratio in the aorta and large peripheral arteries increase because less dilution of contrast medium by blood occurs; this should theoretically result in an image quality better than at normal or high cardiac output. However, in our experience, this concept does not hold true for coronary artery attenuation in patients with very low cardiac output, perhaps because coronary perfusion can decrease as LV end-diastolic pressure increases.

As there are important conceptual disadvantages of an anatomic approach to defining the aetiology of cardiomyopathy, CCTA in its current form cannot address the functional significance of coronary stenoses or the likelihood of functional recovery of myocardium after revascularization. However, potential future modifications of cardiac CT scanning protocols that include co-registered radionuclide myocardial perfusion imaging,[7] or repeat CT scanning 5–60 min after initial contrast injection,[8] might aid in identifying non-viable myocardium, at the expense of additional exposure to ionizing radiation.

CCTA to 'rule out' disease

Many patients with cardiomyopathy have left bundle branch block (LBBB) and, conversely, >50% of elderly patients with new-onset LBBB have pre-existing cardiovascular disease. The diagnostic accuracy of stress myocardial perfusion imaging and stress echocardiography in patients with LBBB can be reduced because of heart rate-dependent reversible perfusion defects in the former and because of conduction-related abnormalities of septal motion or thickening in the latter.[9] SCA is needed to exclude the presence of CAD with certainty if indicated. Ghostine *et al.* previously examined the accuracy of 64-slice multidetector CCTA compared with SCA in identifying >50% luminal diameter stenoses in 66 patients with LBBB but without known CAD.[10] At a prevalence of 44%, the sensitivity for identifying patients with at least one 'significant' stenosis was 97%, and the NPV was also 97%. No head-to-head comparison with stress imaging was performed.

SCA is routinely performed in most patients undergoing non-coronary cardiac surgery to exclude the need for concomitant coronary artery bypass grafting. The prevalence of CAD in this heterogeneous patient group depends on indication for surgery, average age of the patients, and geographic location.[11] In several small series of consecutive patients ($n = 40–145$) referred for pre-operative SCA,[12] 13–33% of patients were not suitable candidates for 16- or 64-slice multidetector CCTA. At a prevalence of CAD of 20–42% based on SCA findings, the sensitivity for detecting stenoses, in the coronary segments that could be assessed confidently, was 78–100% and the NPV was 95–100%. Severe coronary calcification was present in many of the elderly patients undergoing surgery for severe aortic valve stenosis. This is a problem because the objective of pre-operative CCTA, detecting all major epicardial branches that require bypass grafting, is more vulnerable to limitations of image quality in individual coronary segments than the detection of 'at least one' significant stenosis anywhere in the coronary tree.

Most cardiac transplant centres perform annual SCAs to address the possibility of transplant vasculopathy. Because of the diffuse and concentric nature of transplant vasculopathy, identification of focal luminal stenosis on SCA is not the only predictor of event-free survival. Tomographic techniques that can image not only the coronary lumen but also the arterial wall are potentially well suited for the assessment of cardiac transplant patients. Several small studies[13,14] ($n = 11–122$) have examined the diagnostic performance of CCTA in post-transplant patients. Up to 17% of patients were not candidates for CCTA because of co-morbidities. Compared with SCA, the sensitivity for identifying >50% luminal stenoses was 83–100% and the NPV was 95–100%. Compared with intravascular ultrasound, the sensitivity for detecting intimal thickening >1 mm was 70%, and the NPV was 77%.

Co-morbidities and the well-established limitations of diagnostic accuracy imposed by heart rate and coronary calcification may well be barriers to routine use of CCTA in patient groups where conventional imaging modalities falter or where SCA is performed as a matter of course irrespective of pre-test likelihood of CAD. However, in the current era of scrutiny of the comparative efficacy of new diagnostic and therapeutic strategies, examining the value of CCTA for such indications may be an important opportunity for CCTA to establish itself. The experience with CCTA to date is limited to studies representing diagnostic accuracies that are specific for observer expertise, makes of scanners, and local prevalence of CAD. Designing appropriately powered multicentre studies with scanners from various vendors that examine focused clinical questions is an important frontier in establishing and expanding the role of CCTA in the contemporary practice of cardiology.

Conflict of interest: none declared.

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