The clinical role of 'non-invasive' coronary angiography by multidetector spiral computed tomography: yet to be defined

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This editorial refers to 'Detection of coronary artery stenoses using multidetector CT with 16 × 0.75 collimation and 370 ms rotation'† by S. Achenbach et al., on page 1978 and 'Limited diagnostic yield of non-invasive coronary angiography by 16-slice multidetector spiral computed tomography in routine patients referred for evaluation of coronary artery disease'‡ by C. Kaiser et al., on page 1987

'Medicine is a science of uncertainty and an art of probability'

Sir William Osler (1849–1919)

Seeing is believing. The great attraction of coronary angiography for both patient and doctor is the direct view of those small structures whose integrity may dictate life or death. In patients with suspected coronary artery disease (CAD), myocardial perfusion imaging or stress echocardiography may provide good and clinically meaningful distinction between those who are at risk and those who are not, but a shade of doubt remains. For those who find such doubts unacceptable, yet fear the small but definite risks of invasive coronary angiography, multislice spiral computed tomography coronary angiography (CTCA) comes as a deus ex machina—ready to solve all problems. The promise of cardiac CT is no less than the best of all worlds: high-resolution coronary images are able to give a definite answer beyond all doubts, yet avoiding unpleasant groin haematoma and the threatening atmosphere of a hospital. However, are these expectations justified? Two seemingly contradictory answers to this question are offered by Achenbach et al.1 and Kaiser et al.2 Although Achenbach et al.1 demonstrate a high diagnostic accuracy of the technique and recommend CTCA for limited clinical application, Kaiser et al.2 find both sensitivity and specificity of multislice CT unacceptably low for applying CTCA in daily clinical life. To put these statements into perspective, one needs to have a closer look at the patient populations in the two studies, details of image acquisition, and some aspects of data analysis.

The Erlangen group1 confirms previous data, indicating that 16-slice multidetector spiral CT is well suited to distinguish between patients with and without coronary lesions obstructing the lumen by ≥50%. However, just as in the reports by Kuettner et al.3 and Mollet et al.4 the patients had been referred for a first invasive diagnostic coronary angiography because of suspected, stable CAD. When compared with the large group of patients with known coronary disease, such patients are usually younger, have a higher proportion of single vessel disease, and less coronary calcifications. Such clinical features make it easier to obtain high-quality images and hence a correct diagnosis. In contrast, the group from Basel included both patients with the clinical question whether CAD was present and patients with known CAD. Moreover, the Basel patients were older.

Technical progress in image acquisition is another key factor explaining some of the differing degrees of optimism between the two studies. The newer machine used by Achenbach et al. enables a gantry rotation time of 370 ms when compared with 420 ms in the slightly older machine available to Kaiser et al. This reduces the temporal resolution for a scan from 210 to 185 ms, with a concomitant improvement in image quality. The newer machine also permits an increase in the tube current. This will, on the one hand, increase the radiation burden of CTCA, but, on the other hand, improve image quality by boosting contrast-to-noise ratio. The protocol employed by Achenbach et al. partially compensates for the increase in tube current by using ECG-gated tube modulation. Nevertheless, improved image quality comes only at the cost of further increases in radiation burden.

Another procedural factor which may explain the better results of Achenbach et al. is the consistent use of beta-blocking agents before the scan to keep their patients’ heart rates below 60. Consequently, the mean heart rate in Achenbach et al.’s patients was 58 b.p.m., whereas it was 63 b.p.m. in the patients from Basel (despite the fact that 70% of them were on chronic beta-blocker medication). One needs, however, to keep in mind that the routine
application of beta-blockers may be problematic in a setting of outpatient scanning performed by radiologists in patients with left ventricular dysfunction and chronic obstructive lung disease.

Maximizing the diameter of the coronary arteries by isosorbide dinitrate helps to maximize the differences between normal and stenosed segments. At a spatial resolution of approximately $0.5 \text{ mm} \times 0.5 \text{ mm} \times 0.6 \text{ mm}$, the strategy used by Achenbach et al. increases the diameter of the proximal coronary arteries by 1–2 pixels. In contrast, Kaiser et al. did not use vasodilatation. Moreover, their reconstruction time points were selected only every 100 ms, which is rather crude and may not be optimal for minimizing motion artefacts.

When interpreting sensitivity and specificity values of CTCA studies, one needs to consider the specific restrictions used in the analysis. Interpretation and comparison between studies are further complicated as values are reported for segment-based, vessel-based, patient-based, and lesion-based analyses. Achenbach et al. excluded segments of the coronary arterial tree with diameters of $\leq 1.5 \text{ mm}$. About 10% of stenoses in their patients were located in the excluded segments. Indeed, small vessels do not lend themselves to interventions. However, by excluding those segments, one may miss the diagnosis of CAD if a stenosis is located in the distal LAD or in a smaller diagonal branch. Thus, it may not be clinically justified to exclude such segments, as it is an important motivation of the diagnostic process to find out what causes the patient’s symptoms. In contrast, Kaiser et al. included all coronary segments which could be adequately assessed by the gold standard, invasive coronary angiography. Surprisingly, only 89% of segments fulfilled this requirement, but Kaiser et al. did not explain this suboptimal performance of catheter-based angiography.

How can the low specificity in the study of Kaiser et al. be reconciled with the high specificity in the study of Achenbach et al.? The sensitivity and specificity values of Achenbach et al. (94 and 96%, respectively) refer to the evaluable segments (exclusion of 128 segments with a diameter $< 1.5 \text{ mm}$, nine segments distal to a chronic occlusion, 13 with severe calcification, 15 with motion artefacts leaving 79.4% of all segments in the analysis). In contrast, the respective values of Kaiser et al. refer to all segments which could be evaluated by invasive angiography (irrespective of whether they were evaluable by CTCA). In fact, all segments which could not be evaluated by CTCA because of motion artefacts or calcification (23% of those evaluable by invasive angiography) were counted as normal in their study. Consequently, the segmental analysis of Kaiser et al. is fraught with a high number of false negatives, resulting in a high specificity of 91% but a disappointingly low sensitivity of just 30%. Calculations look rather different for the patient-based analysis. Kaiser et al. now find a low specificity of just 49% but a high sensitivity of 86%, whereas the corresponding numbers in the study of Achenbach et al. remained consistently high at 83 and 100%. The high sensitivity in the patient-based analysis of Kaiser et al. is most likely the result of the high prevalence of severe CAD. By chance, most (86% = 97 patients) of the 113 patients with CAD (with a total of 432 stenoses) must have had just one of the 128 true-positive segmental stenoses. In a healthier population a patient-based analysis might result in a sensitivity much closer to the segmental sensitivity reported by Kaiser et al.

Califications, which are common in patients with advanced CAD, pose a huge problem to the interpretation of CT scans. Blooming effects expand the apparent size of calcified plaques and hence lead to overestimation of plaque volume. In a patient population with advanced CAD similar to the population of Kaiser et al., Kuettner et al. also reported a very low lesion-based sensitivity of 37% at a specificity of 99%. Using an older 4-row CT machine, only 57% of segments were judged to be evaluable, which is even lower than that in the report of Kaiser et al. Their analysis was similar to that used by Kaiser et al., as lesions in segments which could not be evaluated were counted as missed. However, in contrast to Kaiser et al., they found a low diagnostic accuracy of 36% in their patient-based analysis corresponding to their suboptimal lesion-based results.

Where do the data of Achenbach et al. and Kaiser et al. leave us with respect to the clinical applicability of 16-row multislice CTCA? In their special study population, i.e. patients in sinus rhythm with suspected but not pre-existing CAD, Achenbach et al. conclude that multidetector CTCA can reliably (at a sensitivity of 93% and a specificity of 83%) detect patients with a coronary stenosis. As CTCA has a negative predictive value of 100% in patients in whom all segments could be evaluated (96%), they suggest that CTCA may be used in patients who are symptomatic but have a low pre-test likelihood of significant luminal narrowing. In brief, this means that CTCA is good for rather healthy patients. However, it is clear that for this application, CT will be in competition with stress imaging modalities. Thus, before CTCA can be definitely recommended for this limited application, comparative studies of CTCA with stress magnetic resonance imaging, stress echocardiography, or nuclear perfusion imaging are required. One also needs to consider that the impressive numbers for negative predictive value provided by Achenbach et al., Kuettner et al., and Mollet et al. for 16-row multidetector CT were obtained in a population with a high prevalence of CAD (50% in the study of Achenbach et al.,). Therefore, the applicability of CTCA in a low prevalence population as recommended by Achenbach et al. is yet to be shown.

Before advocating a broad use of CTCA for excluding stenoses in a low prevalence population, one needs to ask another important clinical question in this special patient population: how useful is a negative CTCA in a convincingly symptomatic patient with a history of chest pain classified anginal by his doctor? Does the lack of significant stenoses really exclude the presence of heart disease, especially if this patient also has subtle abnormalities in the resting ECG? This question has recently received renewed interest from the cardiology community, and various degrees of endothelial dysfunction or myocarditis were found to be common in this patient population. Establishing the mechanism of chest pain in patients with normal coronary arteries, which often presents as unstable or atypical angina, usually requires invasive functional testing.

It is important to give these patients a definite diagnosis, as re-admissions for unstable angina and repeated coronary angiograms despite previous demonstration of normal coronary arteries are common. The exclusion of flow-limiting stenoses
in the large epicardial vessels by CTCA should thus not be the final step in the evaluation of such patients.

Are Kaiser et al. too pessimistic when they conclude that the accuracy of CTCA is not good enough in any subgroup of patients in their study to be clinically useful? As discussed previously, some of their disappointing results may be explained by technical and procedural factors. However, important limitations will remain even in the setting of optimized scanning and interpretation. CTCA is currently not useful in patients without stable sinus bradycardia, those who are not able to perfectly hold their breath (and their diaphragms), and those with heavy calcifications (or coronary stents). Thus, Kaiser et al. illustrate that CTCA is currently not useful in the sicker patient population with coronary disease.

The ultimate value of CTCA in the evaluation of patients has not been clarified by these two articles. A sensible take-home message might be that in rather healthy people with typical exercise-induced angina, 16-row CTCA is very good for excluding flow-limiting stenoses. However, at the other end of the spectrum of coronary disease, in those patients with known severe coronary disease, it is unlikely that adequate clinical decisions can be based on the images provided by 16-row CTCA. Technical improvements such as the 64-row CT may overcome some of these limitations. However, even then we need to accept that the non-invasive diagnosis of CAD will always require some artistic handling of probabilities and yet always leave physicians with a trifle of uncertainty.

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References


