Coronary computed tomographic angiography (CTA) is establishing itself as a method that allows robust visualization of the coronary arteries in a noninvasive fashion. It is certainly not a widespread replacement for diagnostic invasive coronary angiography, nor a screening technique, but if image quality is adequate (which requires that state-of-the-art equipment is used and adequate imaging protocols are applied) and patients are appropriately selected, coronary CTA is considered clinically useful in a number of well-defined situations (1–3). Such situations include patients presenting with acute chest pain at an intermediate likelihood of coronary artery disease, with an absence of electrocardiographic (ECG) changes and normal troponin values, or patients with stable chest pain at intermediate likelihood of coronary artery disease, but with equivocal stress test results. In numerous trials and meta-analyses, it has been shown that after appropriate patient selection and with sufficient experience, coronary CTA has a high sensitivity to detect coronary artery stenoses (4–11). Consequently, in most published studies, the negative predictive value approaches 100%: if a coronary CTA study shows coronary arteries without plaque or stenoses, the false-negative rate is very low.

On the other hand, there are obvious drawbacks to coronary CTA. It cannot be reliably performed in all patients, and its somewhat limited spatial resolution makes it difficult to accurately assess stenosis degree (12–15). Overestimation of stenosis degree is not uncommon, and false-positive findings do occur, especially if image quality is not optimal. In addition, coronary CTA is an anatomic imaging method and as such shares the limitations of invasive angiography: when a stenosis is seen, it is still uncertain whether this specific lesion causes ischemia (16–19)—usually considered a prerequisite to justify revascularization.

Contrast-enhanced computed tomography (CT) imaging of the heart shows not only the coronary arteries, but also the myocardium. It has been shown that chronic hypoperfusion can easily be seen by CT, for example, in patients after myocardial infarction (20,21). Early data suggest that CT may also be able to detect stress-induced perfusion defects (22,23), and in this issue of the Journal, Blankstein et al. (24) present the first series of patients studied by adenosine-induced stress myocardial perfusion imaging using contrast-enhanced dual-source CT. In fact, their examination protocol was comprehensive and approached what some may be referring to as a “1-stop shop.” Thirty-three patients who had a nuclear stress test and underwent invasive coronary angiography were studied by CT. The scan protocol consisted of an initial contrast-enhanced scan acquired during adenosine infusion, a second contrast-enhanced scan acquired at rest, and a third scan performed without additional contrast. The initial adenosine stress contrast-enhanced scan served to visualize the coronary arteries and identify coronary artery stenoses, as well as to identify areas of hypoenhancement in the left ventricular myocardium. The data were acquired in high resolution using spiral acquisition and retrospective ECG gating. The investigators used reconstructions in multiple phases of the cardiac cycle to differentiate perfusion defects from artefacts that can be caused by motion. The second contrast-enhanced scan, acquired at rest, served to identify resting perfusion defects and was acquired at a substantially lower dose (using prospective triggering). Similarly, the final scan, without additional injection of contrast, used a low-dose protocol. It was performed to visualize late enhancement, which in CT—similar to cardiac magnetic resonance imaging—can help identify scar tissue (25,26).

The investigators report that CT myocardial perfusion assessment at stress had a high sensitivity (93%) to identify coronary artery stenoses that were associated with a single-photon emission computed tomography perfusion defect. Also, sensitivity for the detection of very high-grade stenoses on invasive angiography (≥70% diameter stenosis) was high (96%). Sensitivities were higher than for CTA alone.

This is a small, initial study, with inherent bias because of the trial design and a rather preliminary nature, but it constitutes an important step in a new direction: CT imaging of the heart is moving away from pure visualization of coronary anatomy, and data acquisition and interpretation protocols become more complex and sophisticated, allowing the gain of additional information, now including myocardial perfusion, as has previously been shown for the assessment of left ventricular function (27,28), analysis of valvular disease (29,30), and imaging of late enhancement (25,26). Certainly, many additional steps will follow: now that the door for CT has been opened to a field as vitally important as myocardial perfusion, animal and human...
studies will be performed that teach us about the best scan sequences and image reconstruction protocols (for all those who consider performing similar scans, note the small but important details provided by the expert group around Blankstein et al. [24], such as using a very soft reconstruction kernel to make perfusion visible amidst the otherwise high image noise and performing the rest scan after the stress scan to allow a stronger contrast gradient between myocardium perfused at first pass and myocardium that may enhance in a delayed fashion), which provide more definitive validation of the accuracy for detection of disease, and that will help to identify patients who might benefit from this test. Indeed, before CT myocardial perfusion imaging will be backed by data even remotely as strong as for single-photon emission CT many giant steps will still need to be taken.

As interesting as the results of this initial study may be, and despite the excitement it may create, as usual, new research creates new questions. What is the optimal scan protocol? Is it really necessary to add resting perfusion and late enhancement? Does the sensitivity hold up in a patient group without selection bias? Does performing a stress scan to obtain perfusion outweigh the potential negative effects brought about by the higher heart rate, which reduces image quality for coronary CTA? Certainly, many answers will be provided in future trials, and even more questions will arise.

Also, it must be pointed out that although Blankstein et al. (24) found a high sensitivity for stress CT myocardial perfusion, specificity was a bit disappointing, hovering around 75%. Specificity is a problem of coronary CTA to begin with, and it seems that adding another test with limited specificity may be a bit problematic. We will need to better understand the true accuracy of stress CT myocardial perfusion before it can be used clinically. In this respect, layering of tests must be avoided. Automatically adding another layer to CT coronary angiography by performing CT perfusion imaging “because it is there” would not make sense because a CT angigram that clearly shows an absence of stenoses has such a high negative predictive value, both for the presence of stenoses (5–11) and for the occurrence of adverse cardiac events in future years (31–33). Adding layers to testing for coronary artery disease in general, by performing CT myocardial perfusion imaging in patients who already had other forms of testing for ischemia “just to make sure,” would similarly be undesirable.

Blankstein et al. (24) have opened a door. They have provided an important report that highlights the potential of contrast-enhanced CT to visualize stress myocardial perfusion. Now, the work begins. Steps need to be taken, questions need to be answered—and additional layers need to be avoided.

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REFERENCES


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