Computed Tomography Coronary Angiography for Screening Asymptomatic Subjects

A Bridge Too Far?*

Pim J. de Feyter, MD, FACC,†‡
Carl J. Schultz, MD†
Rotterdam, the Netherlands

Multislice computed tomography (MSCT) coronary angiography (CA) has emerged as a powerful noninvasive diagnostic modality to visualize the coronary arteries and the manifestations of coronary atherosclerosis (1). Many reports have demonstrated that 64-slice computed tomography (CT) CA is a viable diagnostic modality to detect or rule out the presence of significant coronary stenoses, but the precise role of MSCT-CA in the diagnostic work-up of patients with suspected CAD in relation to existing noninvasive functional tests (electrocardiogram-stress test, stress–single-photon emission CT, or dobutamine echocardiography) is not yet established, and the technique falls short to replace invasive coronary angiography.

Seen page 357

Computed tomography coronary imaging assesses, in addition to coronary integrity, comprehensive anatomical information about location, extent, severity, and tissue composition of coronary atherosclerosis. An intriguing possibility of coronary CT is that the technique can assess the presence of occult atherosclerosis and might develop as a useful tool to screen for early detection of atherosclerosis in asymptomatic subjects. Because CT coronary imaging comprehensively evaluates the composition (calcific and noncalcific) of coronary plaques, it might provide prognostic evidence independent of and incremental to simple CT calcium scoring.

So far, MSCT has not been explored extensively in asymptomatic subjects, and only a few reports have been published indicating the feasibility of the technique (2,3).

Because approximately 50% of all acute coronary syndromes occur in previously asymptomatic subjects, there obviously is a need to identify these subjects before coronary atherosclerosis becomes clinically manifest and irreversible damage occurs by progression to myocardial infarction or cardiac death (4).

It is customary to initially estimate a person’s risk of cardiovascular death or myocardial infarction with traditional risk factors including age and gender to derive a risk score—for instance, the Framingham Risk or European Risk Score (Systemic Coronary Risk Evaluation). However, asymptomatic subjects generally are at low risk score or, in case of the presence of more than 1 risk factor, might be at intermediate risk. In low-risk populations the prognostic accuracy of screening is far from perfect, and the incorporation of CT atherosclerotic imaging data into a coronary artery disease (CAD) risk score might improve existing algorithms for risk stratification.

In this issue of the Journal, Choi et al. (5) evaluated the potential of MSCT coronary imaging in asymptomatic subjects. They investigated 2 important topics. First, they assessed the presence of occult coronary atherosclerosis, and second, they subsequently established the value of CT to predict adverse coronary events. A total of 1,000 middle-aged (50 ± 9 years; range 35 to 75 years) Korean men (n = 626) and women (n = 374) were evaluated who underwent general routine health evaluation. These subjects were self-referrals, but much to the credit of the investigators, all important risk parameters were objectively measured. More than one-half of them were considered at low risk (0 to 1 risk factor), 30% were considered at moderate risk (more than 2 risk factors but 10-year risk between 10% and 20%), and 10% at high risk (10-year risk >20%). These subjects were followed for a period of 17 ± 2 months. The study of Choi et al. (5) raises several questions.

First, is there need for a new noninvasive atherosclerosis imaging technique? Noninvasive atherosclerosis imaging techniques, including ultrasound assessment of intima-media thickness of the carotid artery, cardiovascular magnetic resonance imaging for atherosclerosis, brachial artery endothelial reactivity assessment, measurement of the ankle–brachial index, or coronary calcium scanning, might further enhance the detection and management of patients at risk for coronary heart disease, but they are not perfect. It is recognized that a “detection gap” exists that is defined as the difference between coronary heart disease cases or events currently detected and the total burden of disease or events among the population. (6) This leaves room for the introduction of a new noninvasive atherosclerosis imaging technique.

Second, what is the prevalence of significant CAD in asymptomatic subjects using MSCT-CA? Currently only very few data are available about the diagnostic yield of
MSCT-CA in asymptomatic high-risk subjects. Romeo et al. (3), with MSCT in 168 asymptomatic high-risk subjects (age 60 ± 7 years), found that the prevalence of significant CAD (>50% diameter stenosis) was 27% (1-vessel disease: 16%; 2-vessel disease: 7%; 3-vessel disease: 4%; left main disease: 2.5%). The majority of these subjects were diabetic (100 of 168: 60%), of which 36% had evidence of significant CAD. Bachar et al. (2) investigated 244 asymptomatic high-risk subjects (age 54 ± 8 years). They identified significant obstructive disease in 4.9%, mild- to moderate disease (<50% diameter stenosis) in 51%, and no atherosclerosis in 44.3% of these subjects. The study of Choi et al. (5) revealed similar findings. They identified an atherosclerotic plaque in 22% of the study population, of which 5% had evidence of a significant stenosis (diameter stenosis >50%) and 2% had evidence of a severe stenosis (>75% diameter stenosis). The majority had single-vessel disease, and in 77% a stenosis was located on the left main or proximal/mid left anterior descending artery.

These data show that MSCT coronary imaging not only can document the presence of coronary atherosclerosis but also is able to identify subjects with significant 3-vessel, left main, or proximal anterior descending artery disease. These subjects might benefit from coronary revascularization, although studies are lacking to demonstrate that revascularization might improve prognosis in asymptomatic subjects.

Third, what is the additional diagnostic value of MSCT coronary imaging compared with CT coronary calcium screening? Obviously coronary calcium scoring alone cannot detect noncalcified or mixed plaques. The prevalence of noncalcified plaques as the only manifestation of CAD is rather low. A significant noncalcified obstruction was present in 7% (9 of 125) of the patients evaluated for acute chest pain, between 6.2% to 6.5% in symptomatic subjects, and 4% in asymptomatic subjects (5,7–9) Intuitively comprehensive coronary imaging to assess the total coronary plaque burden with MSCT might be superior to simple calcium screening, but so far no studies are available showing that MSCT coronary imaging in either symptomatic or asymptomatic subjects will result in better risk stratification and improvement of outcome compared with calcium screening alone.

Fourth, what is the value of MSCT coronary imaging to predict adverse coronary events? Because MSCT coronary imaging was introduced just recently, it is too early to expect large long-term follow-up studies to be available. Two recent published reports have demonstrated the predictive value of CT coronary imaging in symptomatic patients (10,11). Both studies clearly showed that the extent and severity of coronary atherosclerosis present on MSCT were associated with a worse prognosis compared with absence of coronary atherosclerosis. In particular the presence of 3-vessel disease and left main disease were associated with worse prognosis.

The strength of MSCT coronary imaging is the fact that this noninvasive technique can identify significant CAD of the left main or 3-vessel disease known to carry worse prognosis, which can be improved by revascularization. This might (so far unproven) open new avenues to treat these patients, including intense lifestyle modifications or risk factor possibly or even revascularization. Although this might be effective for symptomatic patients, or asymptomatic subjects at high risk, this does not necessarily apply to low-risk asymptomatic individuals.

Future well-designed studies need to be conducted to provide substantial evidence that intervention in low-risk asymptomatic individuals is beneficial. The report of Choi et al. (5) underscores that the design of prognostic study in asymptomatic subjects might be flawed. They assessed the prognostic value in their population of 1,000 asymptomatic subjects during a follow-up period of 17 ± 2 months. Fifteen cardiac events occurred in subjects with evidence of CAD, and none occurred in those without CAD. The events consisted of 1 unstable angina episode requiring hospital stay and 14 revascularization procedures. It is of note that no hard events (death, nonfatal myocardial infarction) occurred, but more importantly, the revascularization procedures were triggered by the fact that both patients and physician were unblinded to the CT outcome data. Other outcome studies should follow, with physicians and patients blinded to CT outcome, to provide reliable data about the predictive value of CT coronary imaging with respect to hard outcomes: cardiac death, or nonfatal myocardial infarction.

Fifth, is CT coronary imaging harmful? Computed tomography coronary imaging is associated with radiation exposure and subsequent likelihood of radiation-induced incidence of cancer and cancer mortality (12). Newer CT technology and adapted CT protocols can significantly reduce the radiation exposure, but before embracing CT coronary imaging as a routine screening procedure it needs to be shown that the potential benefits of screening outweigh the potential harmful effects of MSCT-CA.

Another matter of concern is the high likelihood of false positive (i.e., false positive regarding prognostic value) outcomes, turning asymptomatic healthy subjects into “patients” with occult coronary atherosclerosis, which might trigger anxiety, further diagnostic procedures, and possibly unnecessary treatment. Conversely, a negative outcome
might lead to a false sense of security of health and neglect of potentially favorable institution of risk factor modification, and the risk (albeit low) of an acute coronary event cannot be excluded.

In conclusion, despite study design shortcomings, the authors are to be commended for their efforts to provide initial data concerning the role of CT imaging in asymptomatic subjects. They provided new insights into the prevalence, extent, and severity of coronary atherosclerosis before it has become clinically manifest. However, the study also demonstrated that in clinical reality it is difficult to design a study that provides convincing evidence that CT coronary imaging has independent predictive value in addition to common risk factors. In our opinion studies concerning the predictive value of CT coronary imaging should contain the elements shown in Table 1. The report by Choi et al. (5) will hopefully be the first of a large number of studies regarding the establishment of the use of CT coronary imaging in asymptomatic individuals. We agree with Choi et al. (5) that we are far away from recommending CT screening in asymptomatic individuals and abide by the recommendation statement of the U.S. Preventive Services Task Force against routine screening with resting electrocardiography, exercise treadmill test, and electron beam CT in adults at low risk, which should also apply to MSCT coronary imaging screening (13).

Reprint requests and correspondence: Dr. Pim J. de Feyter, Erasmus Medical Center, Departments of Cardiology and Radiology, Postbus 2040, 3000 CA Rotterdam, the Netherlands. E-mail: p.j.defeyter@erasmusmc.nl.

REFERENCES


