Cardiac CT for risk stratification

Coronary calcium scoring and CT angiography together provide a wealth of information that can be used to predict a patient’s risk of cardiac events.

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Cardiac computed tomography (CT) is currently generating a level of excitement that is reminiscent of the 1970s, when echocardiography rapidly came into common clinical use. The number of cardiac CT scans performed in the United States is growing steadily. More than 10,000 were performed in 2003, according to Arlington Medical Resources, Inc., a hospital market research firm in Malvern, PA. By 2005, that number had grown to nearly 46,000. Data from the marketing research firm IMV (Greenbelt, MD) suggests that in 2005, 13% of cardiology practices were equipped with CT technology, as compared with 2% in 2004. Finally, a survey conducted at the 2005 Transcatheter Cardiovascular Therapeutics meeting found that 77% of respondents either had already purchased a cardiac CT system or were planning to do so (Cascade Market Research, Seattle, WA).

Why all the interest in cardiac CT? Because this noninvasive technique has the potential to diagnose heart disease—the number 1 cause of death not just in the United States but around the world—before severe complications arise.1

This article will focus primarily on the use of cardiac CT for risk stratification. This is just one of several potential applications of cardiac CT. Others include screening asymptomatic patients, determining prognoses in patients with established coronary disease, and guiding therapy.

Overview
The Wisconsin Heart Hospital is a 60-bed freestanding heart hospital. It has 5 cardiac catheterization laboratories and 2 cardiac surgical suites, and is the hospital of choice in our geographic area for the treatment of patients with suspected acute myocardial infarction (MI). Approximately half of the patients who undergo cardiac CT at the Wisconsin Heart Hospital come through the emergency room.

Figure 1 shows a 62-year-old man with several risk factors for heart disease who came to the emergency room with atypical chest pain. Coronary CT angiography (CTA) showed calcified and non-calcified plaque in the left anterior descending (LAD) and circumflex coronary arteries, as well as soft plaque in the first diagonal branch of the LAD. The right coronary artery was relatively free of plaque. The patient went to the cardiac catheterization laboratory, where invasive coronary angiography showed a tight stenosis of the distal left main, LAD, and first diagonal branch. The patient successfully underwent stenting.

Cardiac CT is useful not only for identifying candidates for percutaneous coronary intervention (PCI). It also assists in identify those who might benefit from lipid-lowering medications—for example, a patient with an elevated low-density-lipoprotein cholesterol level but a normal stress test. A high coronary calcium score would signal the need for more aggressive medical management in such a patient.

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Coronary calcium scoring
Standard cardiovascular risk factors are very helpful in identifying patients at an increased risk for coronary artery disease (CAD). More than 300 heart-disease risk factors have been identified, the most powerful being family history, obesity, diabetes, sedentary lifestyle, smoking, hypertension, and hyperlipidemia.

There is now ample evidence that coronary calcium scoring predicts the
risk of CAD independently of Framingham risk factors. More-over, the coronary calcium score is proportional to the athero-sclerotic burden and to the risk of future cardiac events. Eventually, CT measurement of soft plaque may prove to be an even better predictor, but such data are not yet available.

Coronary calcium scoring is an increasingly accepted clinical tool, despite initially being the subject of controversy. At the Wisconsin Heart Hospital, we do coronary calcium scoring on physician order or patient demand and charge $149 for the scan, an amount most self-pay patients find acceptable. We do a limited amount of advertising and strive to make it educational in nature, for example, informing patients about how to modify heart disease risk factors. We do not perform coronary CTA for self-referred patients.

Coronary calcium scoring is easy to perform, relatively inexpensive, and safe: The radiation dose is relatively low, and the scan does not involve the use of iodinated contrast material. One shortcoming is that coronary calcium scoring is of limited use in assessing therapeutic response to statins or other therapies. There is enough variability in the calcium score that it is advisable to repeat the scan no more frequently than every 3 to 5 years to assess for disease progression.

Coronary artery disease involves both the vessel wall and the lumen, and is composed of both soft and calcified plaque. Invasive angiography limits the visualization to the arterial lumen. Perhaps the strongest advantage of cardiac CT is its ability to visualize the arterial wall and the plaque within it. An acute MI seldom results from a high-grade stenosis that progresses to a complete occlusion, but rather, from the rupture of the thin, fibrous cap covering a vulnerable plaque. Therefore, imaging technologies that identify luminal obstruction, such as invasive angiography and, indirectly, nuclear imaging, will miss not only the early signs of atherosclerosis but also any evidence of vulnerable plaque.

The vessel wall has an attenuation of 60 to 80 HU; blood, 40 to 60 HU; and fat, -40 to 30 HU. Coronary calcium generally measures >130 HU. The automatic algorithms used to detect calcium in the coronary arteries are very robust; therefore, our technologists review the scans, with overreading by the supervising
physician. Of note, the density of intravenous contrast material is 150 to 370 HU. Therefore, if a patient is scheduled for both coronary calcium scoring and coronary CTA, it is essential to measure the calcium score before injecting intravenous contrast material.

We routinely perform noncontrast CT with coronary calcium scoring before coronary CTA (Figure 3), not to exclude patients from CTA on the basis of a high calcium score, but rather, because the prognostic data it provides improves the interpretation of the CTA. Whereas population studies that establish the prognostic implications of large amounts of soft plaque are still lacking, the prognostic implications of coronary calcium scoring are well established. Numerous large studies of coronary calcium scoring by electron-beam CT in asymptomatic patients have consistently shown that an elevated coronary calcium score is associated with a marked increase in the risk of cardiac events.4

Additional data from Berman et al5 provides insight into the relationship between stress-induced myocardial ischemia and the magnitude of atherosclerosis, as measured by coronary calcium scoring. This study showed that the higher the coronary calcium score, the greater the likelihood of ischemic segments. However, patients with normal myocardial perfusion studies often had extensive atherosclerosis according to the coronary calcium score. The authors concluded that there is a potential role for coronary calcium scoring in the diagnosis of subclinical atherosclerosis in patients who have normal myocardial perfusion imaging examinations.

Raggi et al6 evaluated the progression of coronary calcium scores and their relationship to the risk of first MI in patients receiving cholesterol-lowering therapy. In patients who experienced an MI, the coronary calcium score changed by 42% a year, on average, as compared with an average annual change of 17% among event-free patients (P = 0.0001). Progression of the coronary calcium score increased the risk of MI 17-fold (P <0.0001). A change in the coronary calcium score ≥15% per year was an independent predictor of the time to MI (P <0.001).

Integrated risk assessment

Several years ago, the American College of Cardiology and the American Heart Association reviewed the literature on coronary calcium scoring and issued a conservative recommendation on its use.7 The consensus document noted that selected use of coronary calcium scoring in patients at intermediate risk for coronary disease may be appropriate; however, additional studies were needed to clearly define which asymptomatic people would benefit from the examination.

In the meantime, the Screening for Heart Attack Prevention and Education (SHAPE) group developed an algorithm showing how to integrate the coronary calcium score with other risk factors and to modify treatment accordingly.4 For example, a patient with a coronary calcium score of 0 and no risk factors is judged to be at low risk. At the other end of the spectrum, a patient with a coronary calcium score >400 is referred for further testing for myocardial ischemia, the results of which will determine whether the patient is classified as high risk or very high risk.

Hecht et al9 have developed an algorithm that incorporates coronary calcium scoring into the risk assessment of asymptomatic patients at apparent intermediate risk for heart disease (a 10% to 20% 10-year risk of a cardiac event by Framingham criteria). It integrates the results of clinical studies, the Framingham Risk Score, the National Cholesterol Education Program Adult Treatment Plan III guidelines, the American College of Cardiology/American Heart Association exercise testing and angiographic guidelines, and clinical experience.9 Per this algorithm, a coronary artery calcium score >100 (or >75th percentile for age and sex) moves the patient to a higher-risk status and initiates a recommendation for more aggressive drug therapy. Conversely, a coronary calcium score of 0 to 10 (or <75th percentile) establishes a
lower-than-expected risk, thereby raising the trigger point for drug therapy.

**Coronary CTA**

At the Wisconsin Heart Hospital, we believe—for several reasons—that coronary CTA is not indicated for use in screening asymptomatic patients for atherosclerosis. The first reason is radiation exposure. The radiation dose, while not excessive, is substantially higher than for a plain chest CT and poses an unnecessary risk to people with no symptoms of heart disease.

Similarly, the risk of adverse reactions from iodinated contrast material is small but not justified in a screening population. In addition, the characterization of plaque is not yet validated for clinical use. There is a low incidence of significant findings in a screening population; therefore, CTA may not be cost-effective. Finally, like any screening test, coronary CTA can lead to inappropriate treatment.

A separate question is whether coronary CTA should be the next procedure performed in patients who have a high coronary calcium score. There are no data for the utility of coronary CTA in this population, although anecdotal reports, including our own, have shown significant left main and triple-vessel disease in patients with even moderately elevated calcium scores. We often find significant stenosis outside the area of calcification, which alters clinical management.

It is difficult to justify even a minimally invasive procedure in truly asymptomatic individuals. Some might argue that a more appropriate follow-up would be stress testing to determine whether the patient has myocardial ischemia. In addition, testing may lead to more testing, resulting in overutilization of resources without improvement in patient outcomes.

Despite these objections, coronary CTA often is the best follow-up procedure in patients who have a high calcium score, particularly for those who are elderly or deconditioned. The decision must be individualized, however. A patient who can exercise to 15 or 16 metabolic equivalents (METs) without symptoms and without abnormalities on the echocardiogram has a good prognosis. In such a case, no further testing is necessary.

**Future**

A new paradigm is needed for diagnostic imaging. Although image quality is important, we must stop focusing on incremental advances in image quality and focus instead on how CT imaging can improve patient outcomes. Nuclear cardiology images are neither crisp nor clear, but the technique is valuable nonetheless, largely because of the volume of prognostic and functional data accumulated through years of research. We need to learn from nuclear cardiology and build a similar body of outcomes data for cardiac CT. The results of cardiac CT must lead to improved treatment as well as a longer and better life.

Cardiac CT must be cost-effective as well as efficacious. That means we need to pick our patients carefully. The goal of cardiac CT must be to replace existing diagnostic tests, not to be used in addition to them. To achieve this goal, advances in CT must enable either perfusion imaging or characterization of atheroma.

We also need to pay attention to performance standards. Under the auspices of the American College of Cardiology, a multidisciplinary committee recently released appropriateness criteria for cardiac CT. Because of the vast increase in the cost and volume of imaging, cardiac CT is now being held to a higher standard than were more established imaging technologies. The future will include accreditation of cardiac CT facilities and professional certification of those who perform cardiac CT. We must ensure that we are delivering good value to our patients.

In the era of evidence-based medicine, it may be time to find a standard other than invasive angiography against which to compare cardiac CT. As our focus shifts away from the detection of obstructive lesions to the detection of atheroma in the arterial wall, it may be more appropriate to use intravascular ultrasound as the gold standard, for example.

Research and technologic advances will continue to drive cardiac CT. Future challenges include characterization of plaque morphology, detection of ischemia through perfusion imaging, and—akin to magnetic resonance imaging—detection of MI and fibrosis.

**REFERENCES**

Discussion

ELLIOIT K. FISCHMAN, MD: Thanks very much, Sam. That was a very good approach to using CT in practice. I have a couple of questions. In terms of using calcium scoring, is there a certain score for which you would say, “Okay, I recommend the patient get a CT angiogram”?

SAMUEL WANN, MD, MACC: Such recommendations must be individualized. I have the advantage of talking to these patients, and certainly a score over 400 would definitely get my attention, but I would not say that I would definitely scan everybody over 400. I would still take into account the patient’s age and other risk factors, and what I might do for them. I use calcium scoring mainly as a lifestyle and noninvasive therapeutic intervention tool rather than to recommend that an asymptomatic patient have a CTA. I do CTA, as I said, particularly in the very high scores. If I had, for example, a 45-year-old man with a score of 800, even if he were asymptomatic, I could probably do CTA or a stress test. I’m waiting for trials to tell me which is better, but I would do one or the other.

FISCHMAN: Before we get other comments, is there a certain age at which you recommend your patients get a calcium scoring? All things being equal, do you say a certain age—40, 45, 50, male or female—that they get a calcium scoring?

WANN: Particularly when we’re doing this for the general public, we strongly discourage people younger than the age of 40 from having a calcium score. Certainly for patients in their 30s and 20s, we will just refuse to do it. I guess with a strong family history we do fudge on age a little bit, but the primary age group would be 40 to 60, and we try to stick to that.

MATTHEW BUDOFF, MD: That was a great presentation. I published some compliance data, and that reinforced that what you find anecdotally does work in practice. You show the scans to the patients, or you show them a representative sample, and they’re much more likely to at least adopt better lifestyle practices. We followed them for 3.5 years, and 90% of those with the highest scores still were still taking statins. There is an argument as to whether that’s patient adherence or physicians being more dogmatic about the therapy, but the end result is that the highest-risk patients are being matched with the most therapy. We did a mixed meeting with Dan Berman and somebody from Leiden. We did a presentation on CT plus nuclear, and he gave a case presentation of a person who had a high calcium score. They did a nuclear test to see if he had obstructive disease, which was negative. Then they decided to do a CTA to see if there was a lot of mixed plaque or soft plaque. Because the calcium score was high, the CTA wasn’t that definitive, but it was abnormal. Then they decided to cath the person, which showed no obstructive disease, so they went to IVUS to define the plaque burden...So the rule was don’t go to Leiden for risk stratification!

I think that’s the fear of the practitioner that you can argue functional testing versus anatomic-based assessment. Patients with high scores at least deserve aggressive therapy. If they’re truly asymptomatic, I often stop there and just treat them for their symptoms. There is an argument we made for finding an occult 3-vessel disease or a left main disease and that you can do with either CT or a nuclear study. It would be nice to have a head-to-head study.

FISCHMAN: One question we get asked is about the fact that with cardiac CTA you have to be so very careful about heart rates. In terms of calcium scoring, do you premedicate anybody? Should you premedicate? Is there a time when you shouldn’t do a study if the heart rate is too high? How do you do things in practice?

WANN: We don’t control heart rate, but I’m aware that some do. Jim Adams, in San Francisco, routinely gives beta-blockers. He’s an old EBT guy, and EBT does have fantastic temporal resolution. I do believe that giving beta-blockers probably does improve the reproducibility of the calcium score because of the blooming artifact that Dr. Achenbach talked about. I think we see that quite frequently in calcium scores. We don’t because I’m looking for small, medium, and large. At this time, I’m not doing serial studies. The beautiful thing about a calcium score is that it takes so little time. We use them as fillers in the CT schedule, since there’s no IV to start, really not much prep, and it’s just slick and easy. To complicate it I think makes it too big of a test, at least for clinical practice.

BUDOFF: Do you know how many doctors have failed? You know, the techs can do it, and the techs can score it.

WANN: My interaction with the process of calcium scoring is very minimal, except in difficult cases.

BUDOFF: I’m very happy if they hand me a stack of 12 that were done that day and I’m done 12 minutes later.

STEPHAN ACHENBACH, MD: I would do the same. We don’t use a beta-blocker to get calcium scores, but there’s also the discussion about prospective versus retrospective triggering for calcium. We use retrospective gating and play around with the reconstruction phase, through which we at least try to optimize image quality because there might be the question of somebody coming back, or you might miss something if you all have blurred coronary arteries. So even if it’s only calcium, and it costs only $99, and the radiation score is not so high, we should still try to optimize the image quality.

BUDOFF: Absolutely. But I think that when you’re looking at small, medium, and large, that’s less important, but you’re right. For the people who come back, you might want to compare the score, and there’s a huge question as to whether or not we can track progression with this tool. If so, what can we use to modulate plaque burden with calcium scoring? We don’t know those answers yet. But I think it’s interesting, and I think Dr. Raji’s data that you showed is going to bear out, that people who are progressors have more events. That’s plaque rupture, whether it’s the scar in the healing, you don’t heal if you don’t have a plaque rupture. You have to have an event to heal. So even if calcium is a healing, the only way you get more of it is if you’re healing more...
plagues, and that means you’re having more plaque ruptures. So progression of plaque has to be a bad thing, I think. We need more data, but we’ll have a lot of data. The multiethnic study of atherosclerosis, the Heinz Nixdorf Recall Study in Germany will have huge data sets of tens of thousands of patients that are already collected.

WANN: These are not with beta-blockers?

BUDOFF: None of them have used beta-blockers. So those are 4-slice CTs, and they’re advancing to 16- and 64-slice. You can debate the argument of retrospective versus prospective, and radiation doses, but I think it would be nice to use beta-blockers if you really wanted to track plaque. Jim Adams does track plaque, and I think if you’re serious about that, you should probably maintain the heart rates below 80.

FISHMAN: Right. But one thing I’ve noticed in a few patients in whom I’ve seen this noncalcified plaque is that when you go back and look at the calcium scoring, you see the fatty lesions. Knowing from other things we know in CT, fat is very recognizable as a low density. If we were gating these studies and using beta-blockers in the patients, would we be able to see a lot of that soft plaque routinely on noncalcified CT scans?

ACHENBACH: It’s not only gating. We use considerably lower-resolution scans for coronary calcium. We use a thicker collimation and less radiation. If we wanted to optimize our image quality, we would have to tune our CT scans, even though we don’t use contrast, we would have to make everything else similar to the CTA, so we would end up with a radiation exposure of 24 mSv. Maybe if you don’t care about giving 24 mSv, and you have to use the really thin collimation, then you might as well throw in some contrast and see it even better.

FISHMAN: But the question is, somewhere between those two extremes, it might be interesting to see how much better you can do. When we spend all the time focusing on the calcification, you start looking carefully. It might be interesting to look back.

ACHENBACH: I don’t know if there have been some efforts on this. I remember from the EBT times there have been efforts, for example, by Dr. Teichholz, who tried to read plaque composition out of noncontrast scans, and none of these efforts has really played out.

BUDOFF: Well, that might not be a fair comparison because EBT is even lower resolution.

ACHENBACH: I’m just saying these efforts have been made. I know Mel Clouse of Beth Israel Deaconess Hospital in Boston is doing something similar. On and off, these efforts has been made, and certainly we have not seen a breakthrough in detecting noncalcified plaque in nonenhanced scans. I’m not saying we won’t be able to do this in the future, but I would have some reservations.

CHIP GILKESON, MD: I have a couple of comments. I think you’re right. For the noncalcium scores, it’s instructive to be really careful at looking at the heart. You’ll often see subendocardial fat deposits in these patients. I think it gives a nice measure of possible early ischemic events. That area of fat can be helpful and, I think, is a marker of prior events that we may not have thought about. The other thing we’re talking about is the perfusion. One of the things that’s very interesting in terms of risk factors is the presence of perfusion defect that we are seeing now more and more, not in gated studies, but in the ER patient with PE and chest pain. The presence of perfusion has really been intriguing in terms of being helpful to then suggest if it is myocardial ischemia. Not the high-tech stuff, not the gated stuff, but it’s been very interesting. We had a number of patients who we diagnosed with ischemia on nongated studies now in perfusion who we’re trying to get the data on now. Certainly, it is a good reminder for us to really look at the myocardium.

FISHMAN: I’m going to speak about the ER next. Are you going back and getting 5-minute delayed scans for looking for perfusion, or is it just on the initial run?

GILKESON: These are initial runs at night, but that certainly would be a good idea. I never thought about that.

FISHMAN: This is one of the things I’m sure we’ll play out over time as we get more and more sophisticated. I have a feeling that there was so much more information on the scans that we don’t look at. That’s typical history of CT in general—you look at one thing, and you realize what’s there, and only in retrospect do you notice that you can go back and find even more information.

One of the things you mentioned, and that Matt has written about, was the importance of getting the patients involved in the scans. I think that’s very critical. It’s been charted in lung cancer screening too. If the patients see the information and get involved in the process, the lifestyle changes are more likely to take effect than otherwise.

GILKESON: We were talking about the insurers, and you commented that the insurers would like to know if patients had a calcium score. Do we have any sense yet if an angiogram was negative, if the insurer would see that patient differently after the CTA? The insurers really drive health care. Are we changing how the insurers look at patients because of our sensitivity to disease or noncalcified plaque? It’s intriguing.

WANN: My comment was on life insurance, not health insurance, which is completely different. They’re worried about the patients dying and having to pay, and they’re very proprietary about their information. Life insurance actuaries have very sophisticated proprietary databases that aren’t shared with the general public. They make a business by predicting the company’s risk when someone comes to buy $1 million worth of insurance. They determine how likely they are to die in the next 20 years. These actuaries are incorporating the results of CT calcium scoring in their risk assessments.

Medical insurers, on the other hand, generally are not able to refuse medical insurance based on risk. They can’t reduce their risk of paying claims by refusing to cover someone with a high calcium score. What is standard business practice in life insurance would be inappropriate “cherry picking” in the medical insurance industry. We need
data to convince medical insurance companies to cover calcium scoring and subsequent aggressive preventive measures as cost-effective in the long term.

**FISHMAN:** It’s an important point because with the MESA trials, and some other trials, the patients were anonymous, so that data is not available to insurance companies. We’ve had some patients who pay out of pocket, and they say, “I’m paying for this study. I want the results, but I don’t want it on my medical record, because medical records are discoverable. I want the information, I want it to go to my physician, I don’t want it to go to the insurance company. I paid for it, it’s mine.”

**WANN:** On the other hand, if you deceive your life insurance company when you apply for life insurance and they find out about it, you’re guilty of fraud, and they don’t pay on the $1 million policy. So you best make very sure that nobody finds out.

**FISHMAN:** Of course, we have no choice. We scan it and we report it, we don’t hide information. But it is an interesting issue that, as patients pay for things, they are concerned about the control of information. In many of these trials, like the lung cancer screening trial, all of the information does not go into the subjects’ medical records. We have issues, for example, with the MESA trial: Someone will say, “I was part of that study 5 years ago,” because now there’s a question with a nodule on the chest X-ray. Going back and being able to use that information is in the patient’s best interest, but it’s all hard to find. Do you see that issue with the study?

**BUDOFF:** It’s definitely a challenge when patients want their results. We need to do an overread that we didn’t do initially to do additional testing on the scan itself, so it’s definitely going to be a significant challenge. As time goes on and patients are further from their original scan, it’s going to happen more.