Coronary calcium scan and coronary CT angiography: chalk and cheese

CHRISTIAN HAMILTON-CRAIG MB BS, FRACP, FSCCT
IAN HAMILTON-CRAIG MB BS, PhD, FRACP, FCSANZ, FLS

Management of cardiovascular risk factors is an important part of routine general practice. New advances in noninvasive imaging have improved our ability to pinpoint risk for the individual patient. Two such imaging techniques are a coronary calcium scan (CCS) and coronary CT angiography (CCTA). When should each be used in clinical practice?

Case 1. An asymptomatic patient with CVD risk factors

A 50-year-old businessman presents to your clinic. He is a smoker, with high–normal blood pressure and cholesterol levels, and taking no medical therapy. His father died at a similar age.

'What is my risk of a heart attack, doc?' he asks.

You check his history, risk factors and fasting lipid levels, and using the Australian cardiovascular risk charts estimate he has an 'intermediate' five-year CVD risk of 10 to 15%.[1]

Can we do better at estimating his risk?

Coronary calcium scan

Absolute risk charts have significant limitations when applied to the individual patient. A meta-analysis of 27 trials found underprediction by 57% in high-risk groups and overprediction by 287% in low-risk groups.[2] A coronary calcium scan (CCS) provides one solution to this problem. It is superior to standard risk algorithms for assessing risk in asymptomatic patients,[3-6] and outperforms the Framingham risk score, carotid intima-media thickness (CIMT) and high sensitivity C-reactive protein (hs-CRP)[7] level as methods to determine risk.

A CCS is a noncontrast cardiac CT for measurement of calcified coronary plaque. A score is generated (usually the 'Agatston score', which takes into account both the volume and distribution of calcified plaque, named after Dr Agatston), which allows a specific centile of risk to be allocated, and calculation of a hazard ratio based on multicentre data.

Key points

- **A coronary calcium scan (CCS) is used to answer the related questions: What is the CCS score-adjusted cardiovascular risk of this *asymptomatic* patient? Is modification of lipid-lowering or other therapy required, and if so what is the target LDL-cholesterol level?**
- **Its application is in the primary prevention setting in the asymptomatic patient, and it is a tool for estimation of CVD risk.**
- **Coronary CT angiography (CCTA) is a different test, and addresses the question: Does this *symptomatic* patient have a coronary stenosis or anomaly that explains the presenting symptoms?**
- **Its application (as is the case for routine invasive angiography) applies to diagnosis in the secondary prevention setting, and it is a tool for defining the anatomy of native coronary arteries or of coronary bypass grafts in symptomatic patients.**
- **Both a CCS and CCTA have the potential to change diagnosis and management in selected patients, when used appropriately.**

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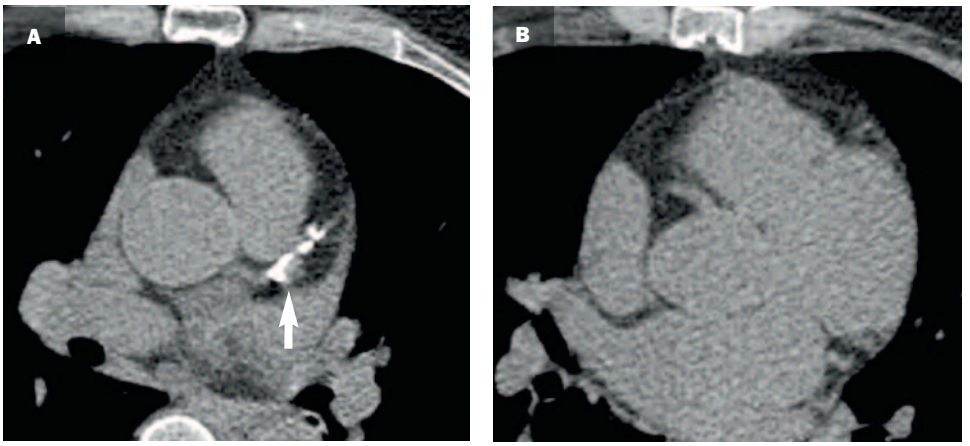
Assistant Professor Christian Hamilton-Craig is a Cardiologist at Prince Charles and Mater Private Hospitals, Brisbane; Senior Lecturer in Medicine at the University of Queensland; and Assistant Professor in Radiology at the University of Washington, Seattle, USA.
Professor Ian Hamilton-Craig is a Staff Cardiologist in the Department of Cardiology, Gold Coast Hospital, and full Professor of Preventive Cardiology and Internal Medicine at Griffith University School of Medicine, Southport, Qld.



Figures 1a and b. Coronary calcium scans (CCS). Noncontrast ECG-gated acquisition in a 50-year-old man, showing established calcified atherosclerosis in the left anterior descending (LAD) artery (a, left; arrow), but no disease in the right coronary artery (b, right). The CCS score was 367, at the 97th centile for subjects of the same age, gender, and race/ethnicity who are free of clinical cardiovascular disease (MESA data). The probability of a positive (1 or greater) calcium score for a white male 50 years of age is 41%.[3]

Case 1 continued

You refer the patient for a CCS. His CCS score is 367, which is at the 97th centile for age, gender and race/ethnicity (Figures 1a and b).

What is the significance of the CCS score?

A CCS score of zero is associated with a very good prognosis and low event rates (about 0.06% major cardiovascular events annually). The detection of any coronary calcium (i.e. a score of 1 or greater) indicates the presence of atherosclerosis and is associated with increased coronary event rates proportional to the degree of calcification (see Table 1).

The rule is the higher the CCS score, the higher the risk. Therapy such as aspirin and statin medications can be commenced, or doses increased, to modify this risk and achieve therapeutic targets.

Importantly, a high CCS score does not indicate coronary artery stenosis, and does not mean that the patient should have an angiogram or functional test, unless he or she develops symptoms. The role of a CCS is as a risk-prediction tool to guide clinical decision making. Recent studies have shown that the CCS score may improve adherence to lifestyle modification and medication by identifying the presence of atherosclerosis.[8]

This patient's CCS score of 367 means that he has established atherosclerosis. This implies a significantly increased risk of future cardiovascular events, and changes his risk profile from intermediate, according the Australian cardiovascular risk chart, to high risk of future events. He now qualifies for aspirin and lipid-lowering (statin) therapy. To put this in context, the estimated probability of any positive calcium score (1 or above) for a white male 50 years of age is 41%, according to the Multi-Ethnic Study of Atherosclerosis (MESA) data.[3]

Case 1 continued

The patient is referred to a cardiologist who discusses the prognostic meaning of this test for the patient. The cardiologist also reassures the patient that he does not require a stress test or angiography at this stage, and commences him on aspirin and statin therapy with a target LDL cholesterol level of less than 2.0 mmol/L.

CCS and plaque detection

A CCS can see the 'chalk' – i.e. calcified plaque (as shown in Figure 1) – but not the 'cheese' (noncalcified plaque). Therefore, it should be considered an extension of risk assessment, and not a 'diagnostic' test. It should not be performed in patients under the age of 45 years who may have noncalcified plaque. In addition, it is not appropriate for patients who have: established coronary disease, had previous heart attack, undergone revascularisation (stent or bypass), or any symptoms consistent with ischaemia.

What is the cost of a CCS?

A CCS is quick, noninvasive and inexpensive. The out-of-pocket cost for a CCS ranges from $100 to $250, depending on the provider. Importantly, there is no Medicare or DVA reimbursement for a CCS when performed alone. Often a CCS is performed

Table 1. Risk of coronary events associated with an increasing CCS score in the MESA trial*[5]

CCS score (number of subjects)	Hazard ratio	Number of individuals with hard MACE events†	MACE % events per annum
0–(3409)	1.0	8	0.06
1–100 (1728)	3.89	25	0.38
101–300 (752)	7.08	24	0.84
>301 (833)	6.84	32	1.10

* Coronary events were adjusted for risk factors. The MESA trial involved 6722 patients followed for a mean period of 3.8 years.
† Hard major cardiovascular events include myocardial infarction, unstable angina, sudden cardiac death and revascularisation (coronary bypass surgery or coronary balloon angioplasty +/- stent).
ABBREVIATIONS: CCS = coronary calcium scan; MACE = major adverse cardiovascular event; MESA = Multi-Ethnic Study of Atherosclerosis.

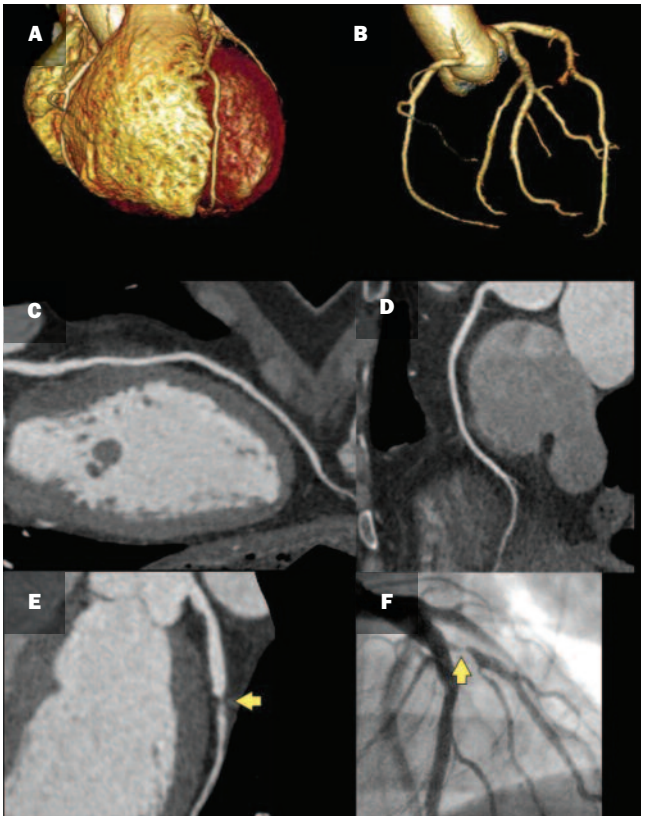
as a preliminary stage as part of a coronary CT angiogram (see below).

Case 2. A patient presents with undifferentiated chest pain

A 63-year-old woman presents with atypical central chest discomfort, occurring both at rest and on exertion. The ECG is normal, and serum troponin and d-dimer tests are both negative. She wants to know if she has a 'blockage' of her arteries, as a friend of hers died suddenly from a heart attack. Does she require any other investigation?

Coronary CT angiography

Coronary CT angiography (CCTA) is a noninvasive coronary angiogram, developed to detect significant coronary artery stenosis and evaluate the coronary anatomy. The early multislice CT scanners were 4-slice systems; the standard-of-care is now a minimum of 64 slices (Figure 2).[9]



Figures 2a to f. Coronary CT angiogram (CCTA) in a 63-year-old woman who presented with atypical central chest discomfort with a normal ECG and negative troponin test. A 64-slice dual-source CCTA was performed using prospective gating, with effective dose of only 2.2 mSv. Three-dimensional reconstructions of the heart (a, top left) and coronary tree (b, top right). No significant disease was present the left anterior descending (c, middle left) or right coronary artery (d, middle right). However, a high-grade (>70%) noncalcified stenosis was present in the first diagonal vessel (e, bottom left). This was confirmed on invasive coronary angiography (f, bottom right), and the lesion was treated with a percutaneous stent.

Accuracy of CCTA

Three, large multicentre trials have established the accuracy and predictive values of CCTA compared with invasive catheter angiography.[10-12] A negative CCTA reliably rules out significant coronary disease, with a negative predictive value approaching 100%. Stenosis and plaque are also accurately detected by CCTA, with high sensitivity, specificity and positive predictive values up to 90%, depending on patient selection.[10-12]

Medicare reimbursement for CCTA

CCTA is reimbursed by Medicare, as of 1 July 2011. A specialist must refer a patient for CCTA, and the test must be performed and reported by an accredited cardiologist, radiologist or nuclear physician (www.anzctca.org). The test must be performed on a minimum of a 64-slice scanner.

Indications for CCTA

The three main indications for CCTA are:

- assessment of patients with symptomatic, undifferentiated (stable) chest symptoms consistent with ischaemia
- assessment of coronary anomalies, and
- evaluation of patients prior to noncoronary cardiac surgery (e.g. valve replacement surgery).

CCTA is highly accurate and appropriate for ruling out significant coronary disease in patients presenting with undifferentiated chest pain, a normal ECG and a negative troponin test.[13-15] It answers the question: 'Does this patient have coronary artery disease or a significant stenosis?' with high accuracy, rapidly and noninvasively.

CCTA may be also useful in patients with ongoing stable chest symptoms despite a 'normal' or 'equivocal' stress test result (nuclear, stress echocardiography or stress ECG), as all of these tests have false-negative rates.[8,16] It may also be useful as a first-line investigation in patients with newly diagnosed heart failure, to exclude significant coronary disease requiring revascularisation.[17]

Importantly, CCTA is not a functional test; to evaluate the functional significance of an intermediate-grade lesion found on CCTA, a stress echocardiography or stress nuclear test, or invasive measurement of fractional flow reserve may sometimes be required.

How is CCTA performed?

CCTA involves a venous injection of iodine-based contrast, much like a CT-pulmonary angiogram. However the scan is 'gated' in sync with the patient's ECG. For the best results it therefore requires a low and stable heart rate. Premedication to control heart rate (such as with oral beta-blockade) is often given before the scan.[18]

In many centres a CCS will be performed before CCTA to provide quantitative risk assessment and allow better planning of the CCTA. Patients with very high calcium scores (e.g. greater than 1000) pose a challenge to accurate assessment of stenosis by CCTA, and may be better served with another test. Importantly, image quality is

Table 2. Cardiac imaging: choosing the right test for coronary artery disease evaluation*

Test	Ischaemia detection	Plaque detection	Stenosis severity	LV function	Limitation of test	Radiation†	Cost (approximate out-of-pocket)
Echocardiography	N/A	N/A	N/A	++++ Also RV, valve and diastolic function	Observer variability	0	$0–100 (rebate ± gap)
Stress echocardiography	+++	N/A	Approximated by degree of wall motion abnormality	++++	Observer variability	0	$0–250 (rebate ± gap)
Nuclear SPECT myocardial perfusion scanning	+++	N/A	Approximated by degree of tracer uptake	++	Poor spatial resolution, misses 'balanced ischaemia'	12–25 mSv	$0–250 (rebate ± gap)
Coronary calcium scan (asymptomatic risk assessment – see Table 1)	N/A	++ Only detects calcified plaque	N/A	N/A	Asymptomatic risk assessment only	1–3 mSv	$100–250 (no rebate if performed alone)
Coronary CT angiography	Implied by severity of stenosis	+++ Visualises stenosis, calcified plaque and noncalcified plaque	+++	+	Radiation dose and accuracy depends on operator experience and patient factors	1–10 mSv	$0–250 (rebate ± gap)
Invasive coronary angiography	If fractional flow available‡	+++	++++ (gold standard)	+ If LV gram performed	Invasive complications	2–6 mSv	$0–2000 (rebate ± gap)

* Information is a guide only, based on expert opinion.
† Radiation doses are indicative, based on current dose-length-product and evidence in 2011. Background global average atmospheric radiation is 2.4 mSv/year.
‡ Fractional flow reserve by intra-coronary pressure wire available in some centres.
ABBREVIATIONS: LV = left ventricular; RV = right ventricular; SPECT = single-photon emission computed tomography.

inversely proportional to heart rate, and in most cases patients with irregular rhythms (such as atrial fibrillation) may be best investigated with an alternative test.

Coronary stenosis and plaque detection

CCTA is able to detect both the 'chalk' and the 'cheese' – i.e. the amount of calcified plaque, partially-calcified plaque ('mixed plaque') and noncalcified plaque ('soft plaque').[19] This is a major strength and allows assessment of 'plaque burden' as well as stenosis, which may have additional prognostic implications to calcium scoring alone.[20,21] However, CCTA should not be performed in asymptomatic patients, in whom simple risk-assessment with a CCS is all that is required.

What is the radiation dose of CCTA?

Radiation doses for cardiac CT have fallen dramatically in recent years. To set the scene, background annual radiation exposure from normal living in Australia is 2 to 3 mSv/year.[22] Most medical radiation exposure comes from nuclear myocardial perfusion imaging (22.1% of the total annual exposure in the USA, with an average dose 16 mSv).[23]

When first introduced, CCTA involved the use of radiation doses similar to that of nuclear perfusion imaging. Recently, however, significant reductions in the radiation dose used for CCTA have been achieved, due to increased public and physician awareness, coupled with major improvements in the technology. In a large multinational registry in 2008, the average dose was 12 mSv,[24] but in

some centres it was much lower (about 4 mSv) and in others, much higher (about 30 mSv). The radiation dose received by the patient is directly proportional to patient size and heart rate and scanner settings, and dose reduction requires appropriate patient preparation and due diligence on behalf of the operators.[25] A recent Australian study showed that using prospective gating, a scan mode which takes single pictures each beat and 'stitches' them together, results in an 85.7% reduction in radiation dose compared with the standard 'helical' acquisition.[26] Most 64-slice scanners are capable of prospective gating, if the software is installed.

The latest generation of scanners, available in a number of sites around Australia, can perform an entire CT angiogram with a dose of less than 1 mSV in selected patients. Importantly, it is not the dose but the image quality that is most important – a scan is only as useful as the information it provides. Remember, it's not just the scanner, it's how it is used.

Appropriate selection and preparation of patients, for the appropriate indication, makes CCTA a safe and effective technology when performed by experienced operators.

Case 2 continued

The patient is referred to a cardiologist, who arranges CCTA with a 64-slice scanner using prospective gating, at a dose of 2.2 mSv. The calcium score is 3, indicating minimal coronary calcium. There is a noncalcified plaque causing severe stenosis of a large diagonal branch (Figure 2e).

After a trial of medical therapy, the patient continues to experience angina and undergoes invasive coronary angiography and successful percutaneous stenting of the lesion. She remains on lifelong aspirin and statin therapy, with clopidogrel treatment for 12 months.

Summary

A diagnosis of coronary artery disease in an individual patient provides an opportunity for therapeutic intervention, whether lifestyle, pharmacological or procedural, depending on the context.

- In *asymptomatic* patients, a CCS is appropriate for risk assessment.
- For *symptomatic* patients with stable, undifferentiated chest pain or ongoing symptoms despite a 'normal' or 'equivocal' stress test result (nuclear, stress echo or stress ECG), CCTA may be appropriate for defining the coronary anatomy.

Clinicians have a range of choices to investigate possible coronary artery disease (Table 2). The choice depends on the indication and the clinical question being asked. A CCS, CCTA, or both, may help in guiding treatment decisions for patients with possible coronary artery disease. **CT**

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