

# Developments in coronary artery disease

This week's Update looks at screening tools and risk factors for coronary artery disease.

## Introduction

ABOUT 50% of acute myocardial infarctions (AMIs) occur in persons with no known history of symptomatic coronary artery disease (CAD). Of these, 40% will die; of those deaths, 50% will die before reaching hospital, and 25% will die in the first hour.

In Australia, an AMI occurs every 11 minutes – that's about 48,000 per year, more than three times the number of deaths attributed to the March 2011 Japanese earthquake and tsunami.

These deaths are not just statistics. They represent fathers and mothers of young children, contributors to society often at their professional peak and in the prime of their lives.

### WHAT ARE WE DOING ABOUT IT?

Traditionally, the 'classical' risk factors that are present are identified and lead to the calculation of a 'score' that evaluates the probability of a cardiovascular event over the next 10 years (for example, the Framingham or Australian Absolute CV Risk).

This might allow the doctor to tell an individual that they have, for example, a 12% chance of an event over the next 5–10 years.

The problems here are:

- Not everyone goes to a GP or cardiologist to have this score calculated, and these people, indeed, may be most at risk (the inverse care law)

- A 'score' like this is vague and non-specific. It does not follow from this data as to who should have aggressive risk factor management and who should have further testing, and thus close ongoing surveillance.

These 'scores', while helpful, don't address these important questions:

Is this patient at real risk of an AMI? Does the patient actually have CAD? How aggressive should we be with risk factor management? How do we motivate the patient to get serious about a risk factor plan?

The primary focus of this Update will be the early detection of coronary disease in at-risk individuals.

## The vulnerable plaque

It is well understood from autopsy studies, and more recently by a new intracoronary imaging technique (optical frequency domain imaging) that CAD involves rupture of atherosclerotic plaques covered by a thin fibrous cap ('vulnerable plaque') and superimposed thrombus.

This may involve a relatively mild plaque.

This process can cause a STEMI, non-STEMI, or be non-clinical but resulting in progression of obstructive coronary disease.

However, it is increasingly recognised that the issue is not the 'vulnerable plaque' but the 'vulnerable patient' – the patient with underlying, undetected and untreated subclinical, asymptomatic atherosclerotic CAD.

These are the patients with a ticking time bomb who often have no idea that they may be at risk (see Figure A).

### WHAT ELSE CAN BE DONE?

It was discovered in the 1970s that while acute ischaemia may be seen on a resting ECG, underlying potential ischaemia may be detected on an exercise stress ECG.

This is because underlying obstructive CAD results in potential ischaemia. There are two problems here:

1. The reliability of standard exercise testing is only about 60% – little better than tossing a coin. This can be markedly improved by combining exercise or pharmacological testing with imaging.

Nuclear perfusion studies have been popular but less so these days because of concerns about radiation exposure – especially where serial testing is necessary, which is often.

Stress echo is now established as the best stress imaging test with no radiation, and therefore suitable for serial testing.

In experienced hands, the reliability

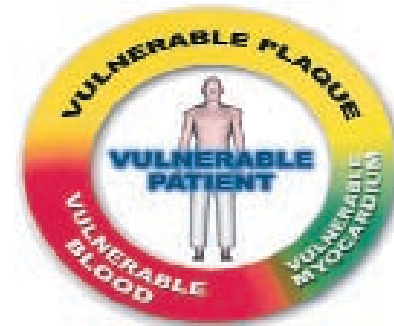


Figure A: The vulnerable patient.

is in the order of 90% or better for diagnostic testing, and it is also of great use following patients with known CAD for prognostic purposes (see Table 1).

In 2011, exercise treadmill testing is no longer recommended by the American College of Cardiology and American Heart Association as a screening tool for CAD in low-risk patients.



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2. This sort of testing picks up only obstructive, advanced CAD. It does not pick up early or extensive non-obstructive CAD, which may have great significance – especially in younger patients. It is recognised that myocardial infarcts often relate to rupture of a fairly mild atherosclerotic plaque. Such a lesion would not show up on exercise testing.

#### RELEVANT QUESTIONS

There are two questions that need to be asked when someone presents for either diagnosis of CAD or the investigation of chest pain.

The first question is: Does this person have obstructive (haemodynamically significant) coronary disease?

If the answer is yes, and in the presence of symptoms, they should proceed to coronary angiography to define their anatomy and suitability for intervention.

The second question that should be asked if the functional testing is negative is: Does this person have evidence of atherosclerosis that will put them at risk of future events?

This would then allow determination for ongoing risk factor modification, treatment, follow-up, and prediction of future risks of a cardiac event.

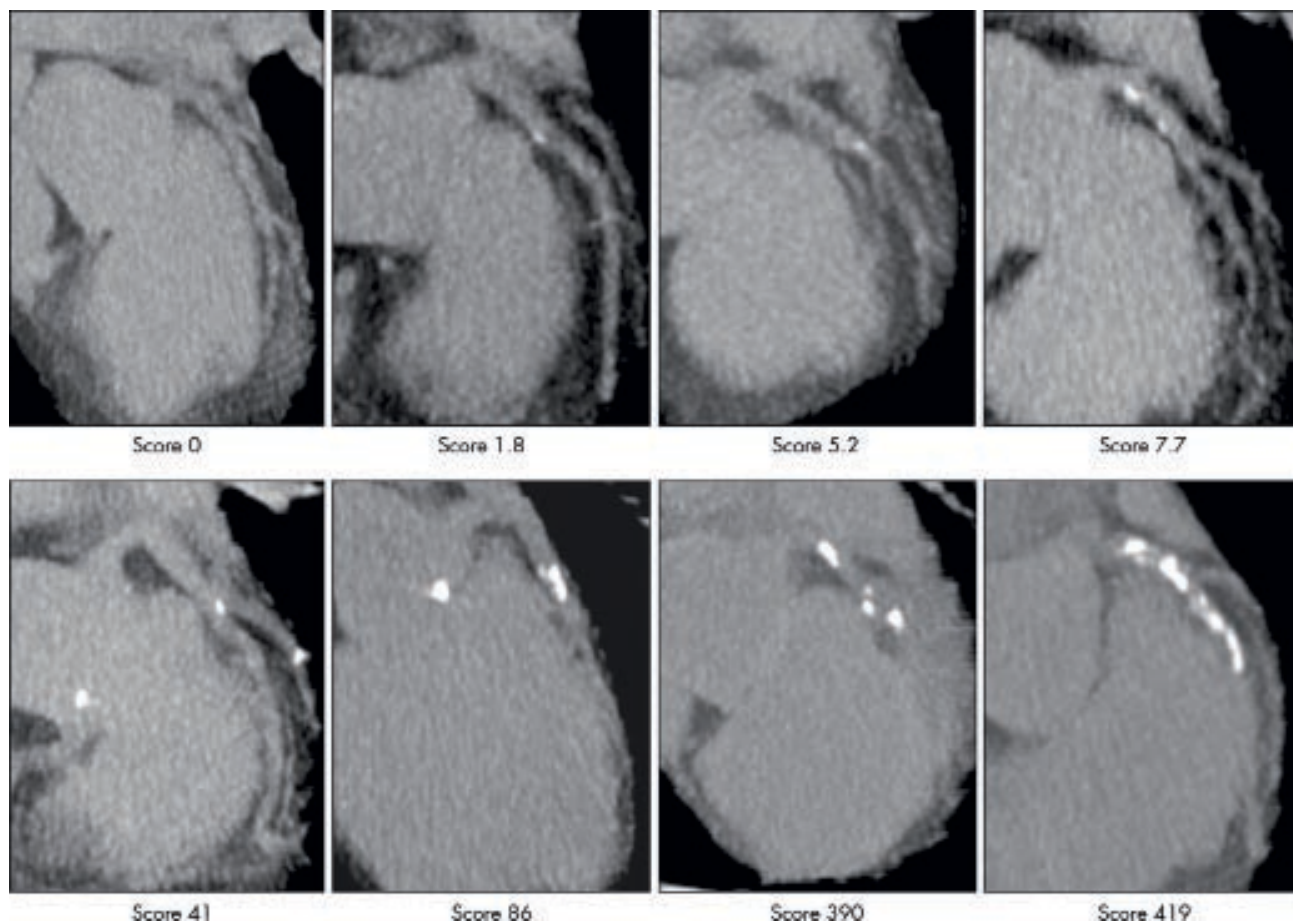
## Detecting atherosclerotic disease

How can early atherosclerotic disease be diagnosed?

The answer is that there have recently been huge advances in this area. The following sections outline two of these developments: coronary calcium scoring and CT coronary angiography.

**Table 1: Comparison of advantages of different stress tests**

Advantages of stress echocardiography	Advantages of stress perfusion imaging
Higher specificity	Higher technical success rate
Versatility – more extensive evaluation of cardiac anatomy and function	Higher sensitivity – especially for single-vessel coronary disease involving the left circumflex
Greater convenience, efficacy, availability	Better accuracy in evaluating possible ischaemia when multiple resting left-ventricular wall motion abnormalities are present
Lower cost	More extensive published database – especially in evaluation
No radiation	N/A



**Figure B: Coronary calcium image and associated score.**

## Coronary calcium scoring

The most economical, best validated and lowest radiation option is coronary calcium scoring (CCS), which is done via multi-detector CT. This has recently been established with the publication of large

multicentre trials conducted within the past 12 months.

The natural history of atherosclerotic coronary plaque is that it starts off as soft plaque and over time calcifies in

the arterial wall to produce calcifications that can be picked up on CT.

CCS can only see calcified plaque, and thus its best use is in the middle age range of patients where plaque has had time to

develop. A key point is that almost always in the presence of calcified plaque, there is soft plaque as well.

Figure B illustrates an example of a calcium score.

**Table 2: General guidelines for interpretation of calcium scores**

MDCT calcium score (Agatston)	Plaque burden and probability of significant CAD	Implications for CV risk	Recommendations
0–10	Cannot exclude the possibility of atherosclerosis. Although negative or extremely low, there is a 5% or lower probability of significant obstructive disease.	Very low to low	No specific further work-up would be recommended in an asymptomatic group. Non-calcified atherosclerosis cannot be excluded. Discussion of primary prevention of CV disease should be emphasised.
11–100	Consistent with mild atherosclerotic burden and, despite the fact that the likelihood of significant obstructive disease is low (less than 20%), atherosclerosis is clearly present.	Low to moderate	Daily use of coated aspirin and guidelines for cholesterol reduction similar to patients with $\geq 2$ traditional CV risk factors should be considered.
101–400	Consistent with at least moderate atherosclerosis and a high likelihood of moderate non-obstructive CAD.	Moderately high	An aggressive approach to lipid lowering (similar to patients with documented CAD by angiography or previous cardiac events), strict control of diabetes and hypertension, smoking cessation, dietary counselling, daily coated aspirin use, antioxidant therapies and regular aerobic exercise should be instituted. Functional testing should be performed.
Over 400	Advanced atherosclerotic plaque present. There is high likelihood of at least one obstructive coronary stenosis and high CVD risk.	High	These patients should undergo the above outlined aggressive risk strategies, and functional testing should be performed with a myocardial perfusion scan or stress echo.

**KEY POINTS OF CORONARY CALCIUM SCORING**

- The entire test takes less than five minutes.
- The entire coronary artery tree is imaged during a 12- to 15-second breath hold.
- This is a non-invasive imaging modality.
- It enables acquisition of thin slices of the heart and coronary arteries to screen for coronary calcium.
- There is no need for exercise, intravenous medications or contrast.
- The average radiation dose for coronary calcium scoring is 0.5 mSv of radiation (about 20 standard chest x-rays; living at sea level in Australia, the average person receives 3.0 mSv).

The ability of CCS to predict future coronary events in symptomatic persons has been demonstrated in multiple large-scale studies to date.

A well-validated scoring system called the Agatston score is used to tally up all the visible calcium seen on the scan and

provide a numerical score that can then be used clinically (see Table 2).

Selected individuals where CCS may be particularly beneficial are demonstrated in Table 3.

Importantly, a calcium score higher than 100 implies a greater than 10-fold increased relative risk for a cardiovascular event as seen in the St Francis Heart Study, and identifies people that need to be monitored closely and treated aggressively.

The great strength in using CCS in addition to traditional risk factors is that it can either upgrade someone from low risk to intermediate based on the CCS score or if the CCS score is zero, it can put people in a lower risk category (see Figure C).

It is the view of the authors that calcium scoring combined with a high-quality functional test such as a stress echo is the most cost-effective and lowest radiation option for the diagnosis of both atherosclerotic coronary disease and obstructive coronary disease.

## CT coronary angiography

CT coronary angiography, which involves the administration of intravenous contrast and often beta blockers to achieve a heart rate of < 60, coupled with higher radiation doses (usually in the range of 2.5–5.0 mSv), is also a very powerful tool in the diagnosis of coronary disease and allows direct visualisation of the coronary lumen, coronary wall and cardiac structures. Its great advantage is that it allows the visualisation of both soft and calcified plaque, and thus is useful in the early stages of disease. Clinically one of the most useful patient populations to use CT coronary angiography is the symptomatic patient with an intermediate risk

for CAD, or an intermediate-risk patient with atypical chest pain. The very high-negative predictive value excludes CAD as the possible cause. It provides prognostic information and helps with risk stratification.

CT coronary angiography is also the imaging modality of choice in coronary anomalies, and the American Heart Association has published a list of criteria: <http://circ.ahajournals.org/cgi/content/full/118/5/586>.


Importantly, it should not be used to screen for coronary disease in patients who have no signs or symptoms suggestive of CAD (see Figure D).

## Conclusion

Although a lot of the latest research and the more acute side of cardiology deals with how to manage the acute events of symptomatic coronary disease such as STEMI and non-STEMI, with the early detection of atherosclerosis, it will allow primary care doctors to intervene with diet, lifestyle and, if needed, pharmacologic therapy at a much earlier stage and prevent events before they happen.

Future primary prevention trials to look out for will involve the detection of early

coronary disease using non-invasive imaging, and then modifying risk factors to see if this alters outcomes.

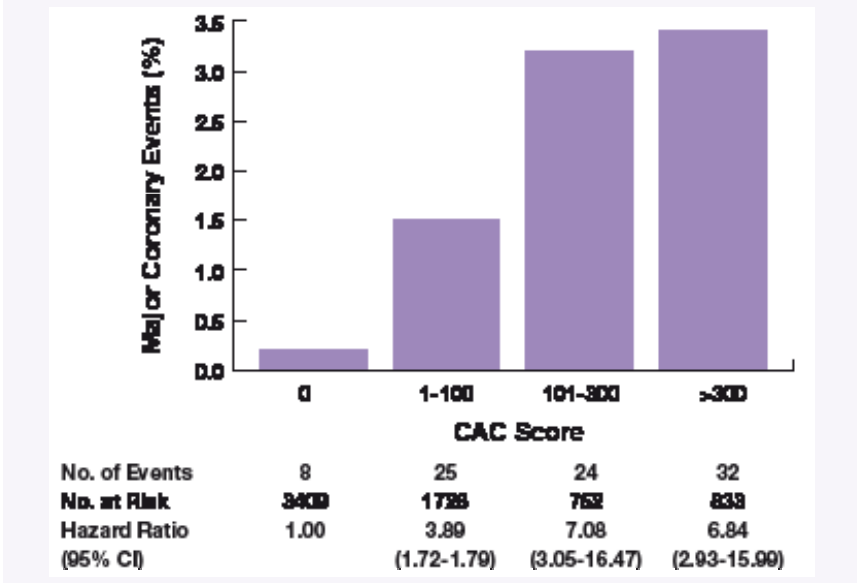
The use of newer imaging techniques in the early detection of asymptomatic disease is being increasingly recognised, with SHAPE (Society for Heart Attack Prevention and Eradication) leading the way with calcium scoring, along with recommendations from all major cardiac societies. 

For the patient handout, 'Exercise electrocardiogram', go to [medobs.com.au](http://medobs.com.au)

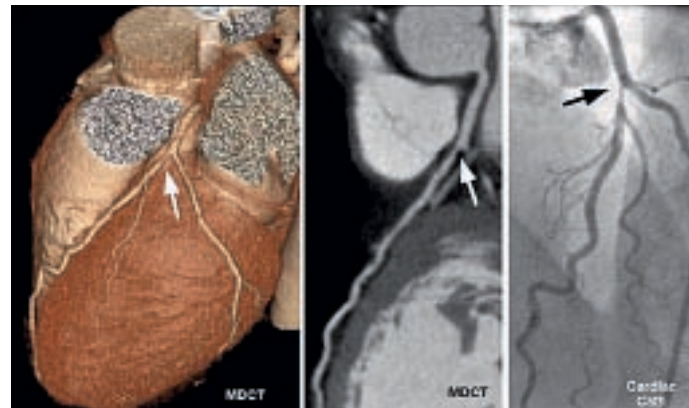
**Table 3: CCS could be used in the following circumstances**

- All asymptomatic males aged 45–75 without known CAD
- All asymptomatic females aged 55–75 without known CAD
- Younger asymptomatic subjects having two or more CAD risk factors
- Added to/integrated with the Framingham risk score in the intermediate- and high-risk groups.
- To improve patient compliance with lipid therapy in non-compliant patients

**Figure C: Risk of major coronary artery events with increasing CCS**



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**Figure D:** CT angiogram demonstrating proximal narrowing of the LAD.

### KEY POINTS

- n In Australia, an acute myocardial infarction occurs every 11 minutes.
- n In 2011, exercise treadmill testing is no longer recommended by the ACC and AHA in low-risk groups as a screening tool for coronary artery disease.
- n Stress echocardiography is now established as the best stress imaging test that doesn't involve radiation.
- n Coronary artery calcium scoring is a major breakthrough in defining at-risk patients and is best applied in the middle-age range of patients (45–65) where atherosclerotic plaque has had time to develop.
- n Future primary prevention trials to watch will involve the detection of early coronary disease using non-invasive imaging.