Cardiac Society of Australia and New Zealand position statement executive summary: coronary artery calcium scoring

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Coronary artery calcium (CAC) scoring is a technique for measuring the amount of calcium in the coronary arteries using an electrocardiogram-gated non-contrast computed tomography (CT) scan of the heart. Its main clinical application is to predict the risk of a future cardiac event in asymptomatic individuals in the setting of primary prevention.

This article summarises the Cardiac Society of Australia and New Zealand (CSANZ) position statement on CAC scoring (http://www.heartlungcirc.org/article/S1443-9506(17)30501-2/fulltext). The position statement covers the available literature at this point in time, and provides expert consensus on clinical decision making based on CAC scores. It was developed by nominated working group members of the CSANZ, incorporating both imaging specialists and general cardiologists. The document was independently reviewed and approved by the CSANZ Imaging Council, the Quality and Standards Committee and the CSANZ Board.

Clinical risk prediction


There are small differences between the NVDPA tool and Framingham Risk Score (FRS). The vast majority of research trials involving CAC scoring have used the FRS as the default risk prediction tool. Traditional FRS has cut-offs on 10-year risk at < 10%, 10–20% and > 20% in classifying low, intermediate and high risk groups (http://cvdrisk.nhlbi.nih.gov/calculator.asp). However, the NVDPA uses 5-year risk levels of < 10%, 10–15% and > 15% for the same groups; importantly, the FRS and NVDPA classifications of absolute cardiovascular risk are broadly similar, and are applicable in identifying intermediate risk patients prior to consideration of CAC scoring.

Certain populations are automatically deemed to be high risk: people with diabetes aged > 60 years or with albuminuria; chronic kidney disease (estimated glomerular filtration rate < 45 mL/min); blood pressure ≥ 180/110 mmHg; familial hypercholesterolaemia; or total cholesterol levels > 7.5 mmol/L. Such patients should be treated with optimal medical management.1 It is important to note that most risk calculators, including the FRS and the NVDPA absolute CVD risk calculator (www.cvdcheck.org.au), do not account for family history, which can be a strong contributor to risk.

Summary

Introduction: This article summarises the Cardiac Society of Australia and New Zealand position statement on coronary artery calcium (CAC) scoring. CAC scoring is a non-invasive method for quantifying coronary artery calcification using computed tomography. It is a marker of atherosclerotic plaque burden and the strongest independent predictor of future myocardial infarction and mortality. CAC scoring provides incremental risk information beyond traditional risk calculators such as the Framingham Risk Score. Its use for risk stratification is confined to primary prevention of cardiovascular events, and can be considered as individualised coronary risk scoring for intermediate risk patients, allowing reclassification to low or high risk based on the score. Medical practitioners should carefully counsel patients before CAC testing, which should only be undertaken if an alteration in therapy, including embarking on pharmacotherapy, is being considered based on the test result.

Main recommendations:

- CAC scoring should primarily be performed on individuals without coronary disease aged 45–75 years (absolute 5-year cardiovascular risk of 10–15%) who are asymptomatic.
- CAC scoring is also reasonable in lower risk groups (absolute 5-year cardiovascular risk, < 10%) where risk scores traditionally underestimate risk (eg, family history of premature CVD) and in patients with diabetes aged 40–60 years.
- We recommend aspirin and a high efficacy statin in high risk patients, defined as those with a CAC score > 400, or a CAC score of 100–399 and above the 75th percentile for age and sex.
- It is reasonable to treat patients with CAC scores ≥ 100 with aspirin and a statin.
- It is reasonable not to treat asymptomatic patients with a CAC score of zero.

Changes in management as result of this statement:

- Cardiovascular risk is reclassified according to CAC score.
- High risk patients are treated with a high efficacy statin and aspirin.
- Very low risk patients (ie, CAC score of zero) do not benefit from treatment.

We acknowledge that certain subgroups of Aboriginal and Torres Strait Islander and Māori peoples who have poorer health outcomes are at increased risk and may warrant primary prevention regardless of risk score.2 CAC score data do not yet exist for Indigenous patients and neither prevalence nor severity has been established in this group.

Coronary artery calcification

A key concept is that coronary artery calcification provides direct visual evidence of coronary atherosclerosis present in an...
individual patient, whereas risk calculators are reliant on antecedent risk factors and epidemiologic calculations. The relationship between coronary artery calcification and major adverse cardiovascular events, including all-cause mortality, cardiovascular events and non-fatal myocardial infarction, has been established in a number of large-scale studies.1,3,4

Importantly, CAC scoring out-performs traditional risk scoring tools, such as the FRS and NVPDA calculators, for the assessment of an individual’s cardiovascular risk.5 CAC scoring is most useful in patients at intermediate risk, allowing reclassification into low or high risk categories based on the score.

Acquisition of CAC scans is relatively quick (less than 10 seconds, one breath-hold), has very low radiation exposure (about 0.5–1.0 mSv; similar to breast mammography) and does not require any intravenous contrast or special preparation. In Australia, Medicare does not currently regulate or reimburse for CAC testing, and the cost usually ranges from $100 to $200.

CAC scores are most commonly reported in Agatston units; the calculation is based on plaque density (> 130 Hounsfield units), the volume of the plaque and a weighting factor. The Agatston score is a highly reproducible, reliable metric that is the most direct in vivo measure of coronary atherosclerotic burden.1,3 A score of zero indicates no detectable coronary atherosclerosis, with a very low event rate (Box 1).

A positive score can be indexed to the patient’s age, sex and ethnicity to give a percentile, based on the Multi-Ethnic Study of Atherosclerosis7 (http://mesa-nhlbi.org/Calcium/input.aspx). This percentile tells us whether a patient has disproportionate atherosclerosis (above average) compared with age- and sex-matched cohorts.

The use of percentiles allows identification of individuals at high risk relative to age- and sex-matched cohorts (Box 2). Box 3 shows a table for easily identifying the patients above the 75th and 90th percentiles, based on age and sex.

Absence of coronary calcification: the power of zero

There have been multiple studies demonstrating the very low event rates in patients with a CAC score of zero.9,12 In a study of 44 052 patients, 45% had a zero score and cardiovascular mortality at 10 years was just under 1%.10 In another large study of 4864 patients with a follow-up of 15 years, a CAC score of zero conferred an annual mortality rate of less than 0.5%.13 Thus, pharmacotherapy is not warranted for asymptomatic patients in this group (Box 1) (note that patients with a CAC score of zero but with symptoms consistent with acute coronary syndrome should be investigated

2 Example: use of percentiles to interpret coronary artery calcium scoring

A 48-year-old woman has a strong family history of premature coronary artery disease. Her coronary artery calcium score is 110 (in the intermediate range). However, when indexed to age and sex, her score is at the 99th percentile (http://mesa-nhlbi.org/Calcium/input.aspx). This means she has disproportionate atherosclerosis for her age and sex, reclassifying her as high risk and warranting primary prevention treatment.◆

Cost-effectiveness of CAC scoring-based primary prevention

There are currently no data in Australia and New Zealand to show that CAC is cost-effective in informing primary prevention decisions. Given the cost of testing is currently borne entirely by the patient, discussion regarding the implications of CAC results should occur before CAC scoring is recommended and undertaken.

Coronary artery stenosis

CAC scoring is a risk prediction tool and is not equivalent to a CT coronary angiogram. It is important to understand that a non-contrast CAC scan does not provide information on stenosis of the coronary arteries, and the presence of calcification on CAC scoring does not equate to stenosis at that site. It is therefore not appropriate to comment on the likelihood of stenosis based on a coronary calcium scan alone. Functional testing for ischaemia is not generally indicated in asymptomatic patients.

3 Indicative coronary artery calcium (CAC) percentiles by score, sex and age*
Recommendations

CAC scoring is **recommended** for patients who:

- are at intermediate risk, aged 45–75 years (absolute 5-year cardiovascular risk, 10–15%) who are asymptomatic and do not have known coronary artery disease. CAC has the ability to reclassify patients into lower or higher risk groups; and
- may also be considered for low and medium risk patients (absolute 5-year cardiovascular risk, < 10%) particularly in those where traditionally risk scores underestimate risk; eg, family history of premature CVD, and in patients with diabetes aged 40–60 years.

CAC scoring is **not recommended** for patients who:

- are at very low risk (absolute cardiovascular 5-year risk, < 5%) or
- are already at high risk (absolute cardiovascular 5-year risk, > 15%), as testing is unlikely to alter the recommended treatment. This includes some patients who are automatically considered to be high risk (eg, people with diabetes aged > 60 years, diabetes with albuminuria, chronic kidney disease [estimated glomerular filtration rate < 45 mL/min], blood pressure ≥ 180/110 mmHg, familial hypercholesterolaemia, or cholesterol levels > 7.5 mmol/L) who should therefore be managed aggressively with optimal medical therapy; or
- have symptomatic or previously documented coronary artery disease (prior myocardial infarction, stent or coronary artery bypass graft surgery).

Recommendations for management based on CAC results for asymptomatic patients are shown in Box 4. An algorithm for the clinical application of CAC scoring for asymptomatic risk assessment is shown in Box 5.

**Very low risk: CAC score of zero**

In asymptomatic patients with a CAC score of zero, the event rate is very low, and no pharmacotherapy is required7,12 (Box 1).

**Intermediate risk: CAC scores of 100–399**

For patients classified as intermediate risk on the basis of CAC score, we recommend statin therapy to be reasonable (but not mandated) and therapy should be tailored to individual risk (Box 2). A CAC score of 100–399 equates to a 10-year risk of 10–20%, with an annual event rate of 1.3%.14 The current American College of Cardiology/American Heart Association blood cholesterol guidelines15 have expanded the indication for treatment with statins to include individuals aged 40–75 years with low-density lipoprotein cholesterol levels > 1.8 mmol/L and a calculated 10-year risk of > 7.5% for primary prevention (Class I indication, Level A evidence), such as patients with CAC scores of 100–399.

Patients with CAC scores of 100–399 but above the 75th percentile are reclassified as high risk (see below).

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**Table: Recommendations for management based on coronary artery calcium (CAC) scores for asymptomatic patients**

<table>
<thead>
<tr>
<th>CAC score</th>
<th>5-year risk</th>
<th>Guidance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Very low</td>
<td>Reassure; maintain healthy diet and lifestyle</td>
</tr>
<tr>
<td>1–99</td>
<td>Low</td>
<td>Maintain healthy diet and lifestyle</td>
</tr>
<tr>
<td>100–399</td>
<td>Moderate</td>
<td>Aspirin recommended</td>
</tr>
<tr>
<td>100–399 and &gt; 75th percentile*</td>
<td>Moderately high</td>
<td>Reclassify as high risk</td>
</tr>
<tr>
<td>&gt; 400 or &gt; 75th percentile*</td>
<td>High</td>
<td>Aspirin recommended</td>
</tr>
</tbody>
</table>

*Percentile based on patient’s age, sex and ethnicity using the Multi-Ethnic Study of Atherosclerosis calculator (http://mesa-nhlbi.org/Calcium/input.aspx). ◆

**Diagram: Algorithm for management based on coronary artery calcium (CAC) scoring**

- **Low risk**: CAC scores of 1–99
  - **<10%**
    - No treatment
  - **10–15%**
    - Strong family history, other concerning features
  - **>100 or > 75th percentile**
    - High risk
      - Recommend treatment

- **Medium risk**: CAC score 100–399
  - Reasonable to treat
    - (reclassify as high risk and treat if > 75th percentile)

- **High risk**: CAC score > 400 or > 75th percentile
  - High efficacy statin recommended to achieve target low-density lipoprotein cholesterol < 2.0 mmol/L
  - Consider functional assessment

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**Low risk: CAC scores of 1–99**

Patients with CAC scores of 1–99 have a relative risk about twice that of patients with a score of zero; however, the evidence for pharmacotherapy is weak, as no observational or prospective trial data are available to guide treatment decisions in this group. We recommend a healthy diet and lifestyle for maintaining a low 10-year risk, unless other clinical factors are present (eg, strong family history of premature infarction at < 50 years of age in a first degree relative; familial hypercholesterolaemia). Some clinicians may elect to offer statin therapy for patients with CAC score of 1–99, in conjunction with counselling patients on the risks and benefits of pharmacotherapy. However, at this point in time, based on the current available data, no strong recommendations can be made for or against treatment in this group.

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**Intermediate risk: CAC scores of 100–399**

For patients classified as intermediate risk on the basis of CAC score, we recommend statin therapy to be reasonable (but not mandated) and therapy should be tailored to individual risk (Box 2). A CAC score of 100–399 equates to a 10-year risk of 10–20%, with an annual event rate of 1.3%. The current American College of Cardiology/American Heart Association blood cholesterol guidelines have expanded the indication for treatment with statins to include individuals aged 40–75 years with low-density lipoprotein cholesterol levels > 1.8 mmol/L and a calculated 10-year risk of > 7.5% for primary prevention (Class I indication, Level A evidence), such as patients with CAC scores of 100–399.

Patients with CAC scores of 100–399 but above the 75th percentile are reclassified as high risk (see below).
High risk: CAC score ≥ 400 or > 75th percentile

For patients reclassified as high risk on the basis of CAC score (>15% absolute 10-year risk), we recommend aspirin and high efficacy statin therapy.

The St Francis Heart Study16 showed that for patients with CAC score > 400, there was a significant reduction in CVD events (8.7% v 15%; P = 0.046) with statin therapy versus placebo. Aspirin and a high efficacy statin (eg, 20–40 mg rosuvastatin or 20–80 mg atorvastatin) to achieve low-density lipoprotein cholesterol levels < 2.0 mmol/L are recommended in this group. Functional testing may be considered on an individual basis, as there are no data to support revascularisation in asymptomatic patients.

Patients with CAC scores of 100–399 but above the 75th percentile are reclassified as high risk. Because age is a main driver of vascular risk, a younger person with a CAC score above the 75th percentile is likely to have an increased lifetime risk of a cardiovascular event, and early therapy is warranted to reduce the risk of future major adverse cardiac events17 (Box 6).

Aspirin
We recommend that patients with CAC scores > 100 will derive net benefit from aspirin.

Routine use of aspirin in the general population for primary prevention is not recommended due to an increased rate of bleeding.19–20 A recent analysis of the Multi-Ethnic Study of Atherosclerosis estimated benefit against risk for aspirin according to CAC scoring results and found that patients with CAC scores ≥ 100 derived net benefit from aspirin, regardless of their traditional risk factors.21

Repeat scanning
Among patients with a zero CAC score, 25% developed CAC over a period of 5 years.22 Therefore, it is reasonable to repeat the scan for such patients to detect coronary calcium conversion and reclassify risk; this is recommended after 5 years.

For a positive CAC score, routine rescanning is not currently recommended. However, an increase in CAC scores of > 15% or scores ≥100 are predictive of increased future myocardial infarction and mortality.23 Calcification progression predicts cardiac events even after adjusting for risk factors and baseline score, thus repeat scanning in low risk patients (CAC scores of 1–99) may be reasonable in circumstances where reassessment of risk is indicated,14 or after 5 years.

Conclusion
CAC scoring is a robust and reproducible way of detecting coronary atherosclerosis and to estimate future risk of cardiac events. It has incremental benefit beyond traditional risk prediction tools. It can be easily performed using current multidetector CT with very low radiation and low cost. It is of greatest benefit when applied to asymptomatic individuals aged 45–75 years who are at intermediate risk as determined by risk calculators (Box 3 and Box 5). CAC scoring helps reclassify patients into either lower risk, with potential cost savings in minimising therapy (CAC score of zero), or higher risk groups (CAC scores ≥ 400, or 100–399 and above the 75th percentile) where early and more aggressive therapies may lead to improved outcomes.

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