CSANZ POSITION STATEMENT ON CORONARY ARTERY CALCIUM SCORING

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1. Background

Atherosclerotic diseases remain the leading cause of death in Western Society, including Australia. Many of these deaths are due to thrombotic complications of the underlying atherosclerotic process,[1] which is largely preventable.[2] A range of risk factors have been identified, including particularly increasing age, male sex, hypertension, diabetes, abnormal cholesterol levels, smoking and a family history of a premature coronary heart disease (CHD) event in a first degree relative.[3] By themselves, these have a variable ability to predict future events such as CHD death or myocardial infarction.[3] However, risk prediction is improved by considering the range and intensity of both non-modifiable and modifiable factors. This approach of absolute risk assessment is usually based on equations derived from prospective follow-up of individuals in Framingham, USA.[4] Better prediction of which people who are asymptomatic but are at high risk of a cardiovascular event is important, as these individuals warrant an aggressive modification of lifestyle and appropriate treatment with medications such as anti-platelet, statin or ACE-inhibitor therapies.

Other approaches have been suggested to 'screen' individuals for high risk or non-invasive evidence of atherosclerosis. These include the measurement of inflammatory markers (e.g. CRP), assessment of endothelial function, exercise stress testing and imaging techniques (ultrasound, CT or MRI, possibly combined with angiography).

This position statement aims to focus specifically on the literature relating to coronary artery calcium scoring with CT-based technologies for assessing cardiovascular risk in asymptomatic individuals.

2. Biology of Coronary Artery Calcification

Coronary calcification is invariably present only if atherosclerotic disease is present in the coronary circulation. Calcification is also closely linked to ageing, the major factor increasing the risk of atherosclerosis. Coronary calcification has been shown to be a good predictor for the burden of atherosclerotic disease, but there is some contention about the role of calcification as it might relate to instability of the atherosclerotic plaque, rupture and subsequent thrombosis (e.g. acute coronary syndromes).[5] However most of the data, including pathological[6-8] and imaging,[9] have shown that the actual sites of coronary artery calcification do not co-locate with culprit coronary lesions associated with myocardial infarction.

3. Role of Coronary Artery Calcium Estimation with CT

There is no evidence to support a role for coronary artery calcium scoring in patients who are already known to have coronary artery disease. While there is some evidence to support the use of coronary artery calcium scoring in patients with acute chest pain

syndromes,[10] the relative effectiveness of this approach versus the various methods available for functional testing for ischaemia has not been fully evaluated. Most attention in the literature has been focused on the potential role of coronary artery calcium scoring as a screening test for coronary artery disease in asymptomatic individuals.

There is now a large body of observational data that shows that coronary artery calcium scoring with Electron Beam Computed Tomography (EBCT) is a predictor for cardiovascular events in asymptomatic individuals,[11-13] including its value above the Framingham risk score.[11] This is despite an initial report suggesting there was no incremental benefit in risk prediction over that achieved using standard risk factor estimation.[14] It is independent of standard cardiovascular risk factors and inflammatory markers such as hsCRP, although less strong a predictor after multivariate analyses.[15, 16] As discussed, it appears to correlate most closely with age among the conventional cardiovascular risk factors. Given the independent risk prediction offered by coronary artery calcium scoring, the obvious role for it is in assisting further risk stratification in those asymptomatic individuals deemed to be at intermediate (0.5 – 2% annual event rate) risk for a cardiovascular event using traditional methods. This may allow more accurate decision making regarding whether or not to instigate aggressive risk factor modification (including medications such as lipid-lowering agents and anti-platelet therapy) beyond life-style modification (see work-flow diagram). However, a number of important caveats remain.

1. It remains a stronger predictor for revascularization (i.e. CABG and angioplasty) than "hard" cardiovascular events (death and non-fatal myocardial infarction).[17] As all of the published data to date are not blinded there is also a potential bias for future management to be based upon the results of the coronary artery calcium score. The benefits of such a strategy are unclear.

2. It is still not proven that knowledge of an individual's coronary artery calcium score can lead to improved outcomes and survival. Although there are many criteria which a screening test should fulfil, the ultimate criterion is that the screening test should lead to a reduction in mortality from the condition in question. In the use of a screening test the balance between adverse and beneficial effects is often delicate. High quality screening is essential if benefits are to outweigh the social and financial costs associated with it, particularly when it is remembered that the social cost of screening (such as the anxiety that results from a false positive test) is borne by a healthy member of the population who will not benefit from the screening program as an individual. No study to date has shown that by managing a person based upon the results of their coronary artery calcium score they are afforded mortality benefit over those patients that are managed without this information. Furthermore, evidence from one study suggests that knowledge about an individual's coronary artery calcium score is not associated with any significant change in factors known to be associated with reduction in cardiovascular events, such as cholesterol and blood pressure levels.[18] However, this was a very low risk cohort.[18] Without any data on reduction in mortality following detection of coronary artery calcification, cost-effectiveness data is not available for the test, although a publication based on the non-randomized data that exist has been reported.[19]

3. CT scanning results in a radiation dose. Although it is a small amount, it does subject the person to around 2msev of radiation (using a MDCT protocol[20]), which should be mentioned in discussion with the patient. This equates to approximately 4 standard chest x-rays (assuming approximately 0.5msev for a standard chest x-ray).

4. It is unclear what role serial coronary artery calcium scoring has to play. Two studies have attempted to address this issue and do provide some information. In one small retrospective sub-study of a randomized controlled trial of statins, it was shown that patients who receive statins have a reduction in coronary artery calcium scores over time compared with patients who did not receive statins.[21] The other study, a small prospective but non-randomised observational study, showed that patients had a more rapid progression of coronary artery calcium scores when not taking a statin compared to when taking this drug.[22] However it is unclear how this information can be used in patient management. The trials were not powered to reliably address the role of serial coronary artery calcium scoring as a tool for monitoring patient risk. In these studies coronary artery calcium scores on serial imaging correlated best with LDL-cholesterol levels rather than statin use per se, and it is not apparent that knowledge of a calcium score affords an additional benefit in patient management.

5. It is still not universally agreed which coronary artery calcification index should be used. Traditionally, the data have been presented as the "Agatston Score", which is an empiric value based upon early work with EBT and shown to be less reproducible (17% interscan variability) than volume scores for example (13% interscan variability).[23] However, many of the studies concerning prognosis continue to use this "Agatston Score", although new standards hopefully will be implemented in the future that may allow greater reproducibility between scanners.[24]

6. All of the published studies have utilized EBCT (electron beam tomography), a technology that at the time of writing of this statement was not available in Australia or New Zealand. Although the EBT units have a faster temporal resolution than even the most recent multi-detector CT units (now 64 detector multi-slice units), it appears from comparative trials that MDCT and EBCT have a good agreement for estimation of coronary artery calcium scoring,[25, 26] although there is still a paucity of data at lower coronary artery calcium scores and the scores between the two systems may be different.[27]

7. It is unclear how to further investigate asymptomatic patients with an elevated score. One concern is that patients with elevated scores may be referred for invasive coronary angiography without further clinical assessment and/or functional testing for ischaemia. This has implications for potential costs both to society and the patient, both financial and in terms of risk of such further investigations. Immediate invasive coronary angiography solely on the basis of a coronary artery calcium score should be avoided, as it remains an unproven strategy. Further investigation is needed to define how best to manage these patients, beyond aggressive risk factor modification, although currently the use of noninvasive stress imaging in the group with high (>400) coronary artery calcium scores

appears preferable and potentially provides incremental information for risk prediction.[28] There is no evidence to support routine functional testing for ischaemia in asymptomatic subjects with coronary artery calcium scores < 400 although clinical judgement remains important in the management of individual subjects. At this stage, there does not appear to be a clinical role for routine repeat coronary calcium scanning in the management of individual patients.

4. Summary

The data from many observational studies of coronary artery calcium scoring show that it is predictive of cardiovascular events. However, there are still a number of questions and issues with its use as a routine screening tool that have been reviewed above.

Accordingly, the position of the CSANZ is that the routine use of coronary artery calcium scoring using CT-based modalities as a screening tool cannot be advocated in unselected asymptomatic patients at this time. However, in those individuals deemed to be at intermediate risk for a cardiovascular event it may be appropriate to undergo such an investigation for the purpose of re-stratifying them into a low or high risk group. This may assist in the identification of individuals how are candidates for pharmacological risk modification atop lifestyle modification (see work-flow diagram). This should only be after consultation with their primary physician before hand about the potential risks, costs and benefits of such an investigation.

5. References

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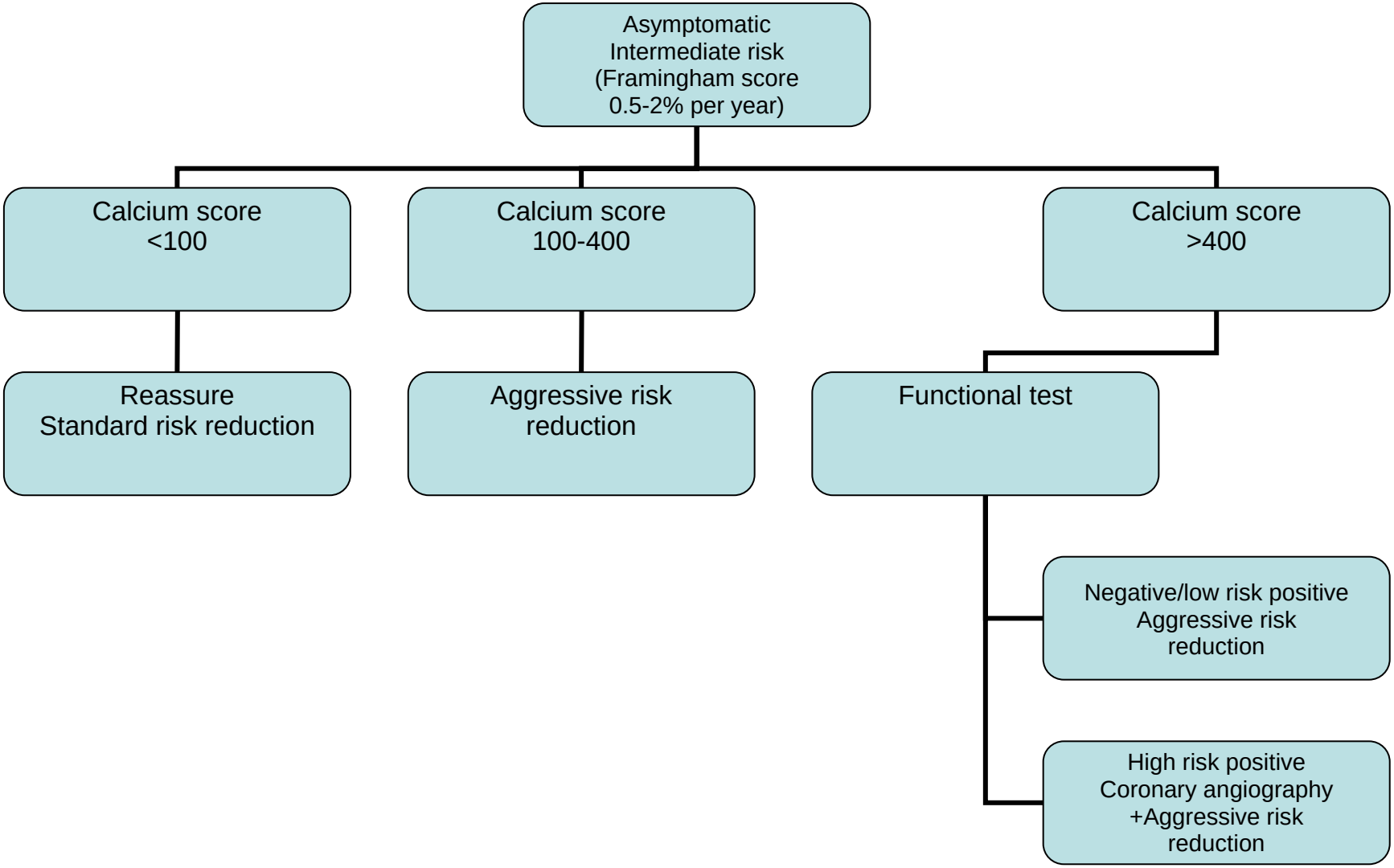
Asymptomatic
Intermediate risk
(Framingham score
0.5-2% per year)
Calcium score
<100
Calcium score
100-400
Calcium score
>400
Reassure
Standard risk reduction
Aggressive risk
reduction
Functional test
Negative/low risk positive
Aggressive risk
reduction
High risk positive
Coronary angiography
+Aggressive risk
reduction