Are we behind the times on cardiovascular risk assessment in Australia?

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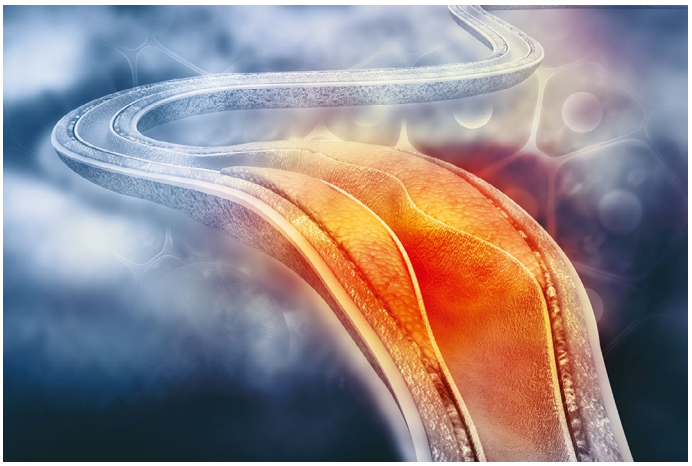
Our approach to estimating risk in some patients should be updated and the role of coronary artery calcium scoring evaluated



While about one in five Australians aged 45–74 years are at high absolute cardiovascular risk, fewer than half of these people are taking lipid- and blood pressure-lowering medications.[1,2] New Medicare Benefits Schedule items for heart health checks (items 699 and 177) were introduced to reduce this gap,[3] but the problem remains that recommended risk calculators are inaccurate and misclassification rates are high.[4]

This is not a new problem. Population risk levels vary over time and between geographic regions, and risk equations based on data from older cohorts may overestimate risk in populations in which cardiovascular event rates have fallen.[5] The Australian Absolute Cardiovascular Disease Risk (ACVDR) calculator is a recalibration of the 1991 Framingham risk equation. Recalibration updates risk equations with cardiovascular event rates from more recent studies. However, a recent assessment of risk prediction algorithms suggests that this approach may be inadequate,[6] as recalibration does not involve incorporating new predictors of risk, many of which are not novel. The factors most frequently recommended for addition to the usual predictors of age, blood pressure, lipid levels, smoking, and diabetes status are ethnic background, socio-economic status, and current treatment of risk factors such as hypertension. Including all possible predictors, however, is not practical, as their relevance varies between populations and across time.

The 2019 American cardiovascular disease primary prevention guidelines introduced the concept of risk-enhancing factors for clarifying risk, especially in people at intermediate or uncertain risk (Box).[7] These guidelines also recommend coronary artery calcium (CAC) scoring as useful if the risk level is uncertain. CAC is a sensitive marker of subclinical coronary atherosclerosis, and evidence is growing that CAC scoring improves risk estimation and reduces misclassification.[8] The United States Preventive Services Task Force (USPSTF) recently reported evidence that adding CAC scoring to risk calculators improved discrimination (the ability to distinguish between people who will or will not experience cardiovascular events) and reclassification. However, USPSTF also concluded that the evidence that CAC scoring leads to lower cardiovascular event rates or improves calibration (agreement between observed and predicted outcomes) was insufficient.[9]

In the Multi-Ethnic Study of Atherosclerosis (MESA). A prospective multicentre cohort study, which measured CAC in an ethnically diverse group of 6814 Americans, CAC level was strongly associated with 10-year risk of atherosclerotic cardiovascular disease events, independent of traditional risk factors;[10] among those eligible for statin therapy according to US guidelines, 41% had zero CAC scores, which was associated with a very low actual cardiovascular event rate (5.2 per 1000 person-years).[11] The EISNER (Early Identification of Subclinical Atherosclerosis by Non-invasive Imaging Research) clinical trial, including 2137 healthy volunteers with coronary artery disease risk factors, found that systolic blood pressure and low-density lipoprotein cholesterol level had improved more in those who had undergone CAC scanning than in those who had not, with no

Cardiovascular risk-enhancing factors*

- Family history of premature cardiovascular disease (men under 55, women under 65 years of age)
- Primary hypercholesteraemia or hypertriglyceridaemia
- Metabolic syndrome
- Chronic kidney disease
- Chronic inflammatory conditions such as lupus and psoriasis
- History of premature menopause and history of pregnancy-associated conditions that increase later cardiovascular disease risk, such as pre-eclampsia
- Ethnic group at high risk, such as Indigenous Australians
- Coronary artery calcium score of at least 100 Agatston units, or at or beyond the 75th percentile (adjusted for age, sex, ethnic background)
- Lipids and biomarkers associated with increased cardiovascular disease risk:
  - Elevated high sensitivity C-reactive protein level
  - Elevated lipoprotein(a) level
  - Elevated apolipoprotein B level
  - Ankle–brachial index below 0.9

* Based on 2019 American College of Cardiology/American Heart Association guideline for the primary prevention of cardiovascular disease,[7] table 3. ◆

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significant difference between the two groups in net medical costs.[12] Evidence from randomised trials for an effect of CAC assessment on cardiovascular event rates has not been reported.

In its recent position statement, the Cardiac Society of Australia and New Zealand proposed that CAC be used to assist treatment decisions by re-classifying patients at intermediate cardiovascular risk as either high or low risk.[13] It was also suggested that CAC scoring could be considered for people at low or intermediate risk, particularly those with family histories of premature cardiovascular disease, a group in which the risk level is often underestimated. CAC scoring is not recommended for patients with high cardiovascular risk, as even a zero CAC score would not reduce the estimated risk to a degree that would modify treatment decisions, and could even be detrimental by suggesting to these patients that risk factor therapy is unnecessary.

In this issue of the *MJA*, Venkataraman and colleagues[14] report their analysis, based on data from a multicentre Australian study including 1059 asymptomatic people with family histories of premature coronary artery disease, of the relationship between cardiovascular risk estimates by the ACVDR and other risk assessment tools and CAC scoring. The authors found that 116 of 151 participants with CAC scores of 100 or more (77%) were deemed to be at low risk by the ACVDR; 14 of 75 patients at intermediate ACVDR risk (19%) had zero CAC scores, and combining the ACVDR and CAC scores lowered the risk classification for a large proportion of participants. This study shows the magnitude by which CAC scoring can change risk classification for people with family histories of premature coronary artery disease.

Accurate risk assessment is pivotal to optimising primary prevention strategies and targeting pharmacotherapy appropriately. Other risk assessment tools may perform better than the ACVDR calculator in Australia, and we need to ask whether it is time to review our approach. There is increasing evidence that CAC scoring improves cardiovascular risk classification, especially in subgroups in which risk estimation is difficult. However, calcium scoring is not subsidised in Australia because of concerns about its cost, radiation exposure, and its implications for further testing. Unanswered questions remain, including whether CAC can be employed for assessing risk in Indigenous Australians and other ethnic groups, and whether it is cost-effective. Given the available evidence, we should consider incorporating coronary artery calcium scoring into risk assessment to improve classification of people for whom the risk level is uncertain (eg, those in the intermediate risk group) or existing tools are inaccurate (eg, people with family histories of premature coronary heart disease).

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