Diagnostic and prognostic value of absence of coronary artery calcification

CRD summary
This review concluded that the absence of coronary artery calcification was associated with a very low risk of future cardiovascular events. Despite the numerous limitations of this review, the results across the 49 studies appeared to be consistent and the conclusion seems to be appropriate.

Authors' objectives
To assess the diagnostic and prognostic value of the absence of coronary artery calcification in individuals with or without symptoms.

Searching
MEDLINE was searched for English-language studies from 1990 to March 2008; search terms were reported. References of identified articles were also searched.

Study selection
Studies that examined the association between coronary artery calcification and adverse cardiovascular events or invasive coronary angiography in people with or without symptoms were eligible for inclusion as were those that reported the value of coronary artery calcification in predicting cardiovascular events. Studies in asymptomatic people had to have a follow-up of at least one year. Significant stenosis was defined as a narrowing of over 50% in studies of coronary angiography.

Most of the included studies assessed coronary artery calcification using electron-beam computed tomography. Where reported, the mean age of participants ranged from 48 to 62 years, the male percentage ranged from 33 to 90, and the prevalence of coronary artery calcification ranged from 10 to 91%.

The authors did not state the number of reviewers who selected studies.

Assessment of study quality
The authors did not state that study quality was assessed.

Data extraction
Data were extracted on the event rates for people with and without coronary artery calcification, from which relative risks or odds ratios and 95% confidence intervals were calculated. Where no events were observed, one was added. For diagnostic accuracy, two-by-two tables of test performance were extracted and from these the sensitivity, specificity, and positive and negative predictive values were calculated. Authors were contacted where data on patients without coronary artery calcification were not provided.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Pooled relative risks or odds ratios and 95% confidence intervals were calculated using the Mantel-Haenszel fixed-effect model. Heterogeneity was assessed using the $X^2$ statistic. Pooled estimates of sensitivity, specificity, and positive and negative predictive values were calculated, but the method used was not specified. Publication bias was assessed in a funnel plot.

Results of the review
Forty-nine studies met the inclusion criteria (n=90,022 participants; range 30 to 25,253).

Prognostic value (20 studies, n=75,519): The risk of experiencing a cardiovascular event was significantly lower in both
asymptomatic (RR 0.15, 95% CI 0.11 to 0.21; 13 studies) and symptomatic (RR 0.09, 95% CI 0.04 to 0.20; seven studies) patients, who did not have coronary artery calcification, compared with those who did.

Diagnostic accuracy (29 studies, n=14,503): Compared with findings from coronary angiography, coronary artery calcification had a pooled sensitivity of 98%, specificity of 40%, positive predictive value of 68% (95% CI 64 to 72) and negative predictive value of 93% (95% CI 88 to 95) in symptomatic patients (18 studies, n=10,355). For the detection of acute coronary syndromes in the emergency department (three studies, n=431), scanning for coronary artery calcification had a sensitivity of 99%, specificity of 57%, positive predictive value of 24% and negative predictive value of 99%. The risk of acute coronary syndrome was significantly less where coronary artery calcification was not present (RR 0.07, 95% CI 0.026 to 0.187). Myocardial perfusion imaging showed a significantly greater incidence of myocardial ischaemia in patients with coronary artery calcification (OR 0.086, 95% CI 0.024 to 0.311; eight studies, n=3,717).

Significant heterogeneity was observed for the analyses of asymptomatic patients. The funnel plots suggested the presence of publication bias.

Authors’ conclusions
The absence of coronary artery calcification was associated with a very low risk of future cardiovascular events. There was modest incremental value from other diagnostic tests in this very low-risk group.

CRD commentary
The authors addressed a clear, but broad, research question, supported by appropriate inclusion criteria. Only one database was searched and this search was limited to published studies in English. Therefore publication and language bias might have been present; the funnel plots suggested that publication bias was present. No methods to reduce error and bias during the review process were reported and these cannot be ruled out. Study quality was not assessed and insufficient information was provided for an assessment. Investigations into potential heterogeneity were limited. Receiver-operating-characteristic plots were not presented for the studies of diagnostic accuracy and the potential for a threshold effect could not be assessed, which means the reliability of the pooled estimates of diagnostic accuracy was unclear. No measures of variance were provided for most of the pooled estimates of diagnostic accuracy.

Despite the limitations of the review, the results across the individual studies were consistent, and the conclusion for coronary artery calcification seems to be appropriate.

Implications of the review for practice and research
Practice: The authors stated that aggressive management in asymptomatic patients who did not qualify according to the National Cholesterol Education Program guidelines was not warranted. They also stated that care should be taken when evaluating patients with symptomatic coronary artery disease, who were younger than 50 years, as 2% of them might not have evidence of coronary artery calcification.

Research: The authors stated that further studies were needed to identify the true role of coronary artery calcification in symptomatic individuals and to determine how to incorporate coronary artery calcification information into the risk stratification algorithm, in combination with information from other diagnostic tests.

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