Carotid plaque, compared with carotid intima-media thickness, more accurately predicts coronary artery disease events: a meta-analysis

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CRD summary
This review concluded that ultrasound assessment of carotid plaque had higher diagnostic accuracy than assessment of carotid intima-media thickness when used to predict future coronary artery events. The difference between assessments was generally small and overall accuracy relatively low for both. Given the limitations of the review and included studies, the conclusions should be treated with caution.

Authors' objectives
To compare the diagnostic accuracies of carotid plaque and carotid intima-media thickness (CIMT) measured by B-mode ultrasonography for the prediction of coronary artery disease events.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and Cochrane Database of Systematic Reviews were searched without language restrictions to April 2011. Conference proceedings from two relevant associations and reference lists of retrieved articles were searched for additional studies.

Study selection
Population-based and diagnostic cohort studies that recruited participants with clinically suspected coronary artery disease were eligible for inclusion. Studies had to use carotid artery ultrasound and either report a cardiovascular event outcome (population-based studies) or compare the results of the ultrasound with coronary angiography (diagnostic cohort studies). Studies had to report the number of true-positives, false-positives, false-negatives and true-negatives. The primary outcome was myocardial infarction for population-based studies and presence of coronary artery disease for diagnostic cohort studies.

Most of the included population-based studies assessed intima-media thickness in the common carotid artery; a large proportion also assessed the internal carotid artery. Where reported, the mean age of participants ranged from 52 to 73 years, the proportion males from 38 to 100% and mean prevalence of carotid plaque was 44%. The assessments made in the cohort studies varied more, though intima-media thickness in the common carotid artery were the most frequently assessed. Where reported, the mean age of the participants ranged from 47 to 85 years; one study was restricted to women; the proportion males ranged from 47 to 100% across the other studies. Most of the cohort studies recruited patients suspected of coronary artery disease; some recruited patients with known coronary artery disease, post-percutaneous coronary intervention or bypass grafting or after a cardiac event. Coronary artery disease was defined as 50% coronary artery stenosis in most of the cohort studies.

Two authors independently conducted the search, but it was unclear how many reviewers applied the inclusion criteria during study selection.

Assessment of study quality
Study quality was assessed using established quality assessment tools; population-based studies using Downs and Black, and the diagnostic cohort studies using QUADAS. Methodological details were identified during the data extraction process.

It appeared that two reviewers assessed study quality.

Data extraction
Data were extracted to construct 2x2 tables of test performance from which sensitivity, specificity, positive and negative likelihood ratios and the diagnostic odds ratio with 95% confidence intervals (CIs) were calculated; disagreements were resolved by consensus. Annual event rates were calculated using the number of events divided by the length of follow-up.
Two reviewers independently extracted data.

Methods of synthesis
Summary receiver operating characteristic (SROC) curves were produced and the area under the curve (AUC) calculated; the model used was not reported. Multivariate meta-regression analyses were used to compare the diagnostic performance between carotid plaque and CIMT after the adjustment for mean age, sample size, publication year, duration of follow-up and study quality. Summary estimates of sensitivity, specificity, likelihood ratios and diagnostic odds ratio were calculated using the DerSimonian and Laird random-effects model. Prevalence rates were pooled using the formula of logit event rate. Subgroup analyses were conducted to investigate the effect of different CIMT measurement sites (common carotid artery with or without carotid bulb or internal carotid artery). Heterogeneity was investigated using $I^2$; 25% was considered to have been low heterogeneity, 50% moderate and 75% high. Publication bias was examined using funnel plots, the Egger's linear regression test and trim and fill method.

Results of the review
Eleven population-based studies (54,336 patients) and 27 diagnostic cohort studies (4,787 patients) met the inclusion criteria. Follow-up ranged from 0.1 to 15.1 years in the population-based studies. The quality score ranged from 16 to 27 out of 27 for population based studies and eight to 14 out of 15 for diagnostic cohort studies.

Population-based studies: Ultrasound assessment of carotid plaque had a higher diagnostic accuracy for the prediction of future myocardial infarction than that of CIMT; the AUC for carotid plaque was 0.64 (95% CI 0.61 to 0.67) and for CIMT 0.61 (95% CI 0.59 to 0.64). The higher diagnostic accuracy of carotid plaque remained significant after adjusting for covariates in multivariate meta-regression. Negative predictive values of carotid plaque for future myocardial infarction over 10 years was also higher (96.0%, 95% CI 95.3 to 96.4) than for CIMT (95.2%, 95% CI 94.5 to 96.0). The annual event rates of myocardial infarction after negative results were 0.40% (95% CI 0.36 to 0.47) for carotid plaque and 0.47% (95% CI 0.42 to 0.55) for CIMT.

Diagnostic cohort studies: Ultrasound assessment of carotid plaque had a higher diagnostic accuracy (AUC 0.76, 95% CI 0.73–0.80) for the prediction of coronary artery disease than that of CIMT (AUC 0.74, 95% CI 0.72–0.76); the difference did not remain significant after adjusting for covariates in multivariate meta-regression. Pre-specified subgroup analyses showed CIMT measured in both the carotid bulb and internal carotid artery (AUC 0.79, 95% CI 0.77–0.81) had a higher diagnostic accuracy than when CIMT was measured only in the carotid artery (AUC 0.6, 95% CI 0.65–0.71).

Results of post hoc sensitivity analyses (details given) did not substantially differ from the main analysis.

Publication bias was not observed in the population-based studies, but this may have been present for the diagnostic cohort studies; it was estimated that six studies needed to be imputed to make the plot symmetrical.

Authors’ conclusions
Ultrasound assessment of carotid plaque had a higher diagnostic accuracy when compared with that of CIMT for the prediction of future coronary artery disease events.

CRD commentary
The review question was clear, supported by well-defined inclusion criteria. Relevant sources were searched without language restrictions, and some attempts were made to identify unpublished studies. Data extraction was conducted in duplicate, but it was unclear whether similar methods to reduce error and bias were employed during study selection. Appropriate criteria were used to assess the methodological quality of the included studies and results of the assessment were considered in the analysis.

The SROC model used was the Moses-Shapiro-Littenberg model; summary estimates of sensitivity and specificity being produced using standard meta-analytical methods, despite heterogeneity across studies. More robust SROC models were available to produce summary estimates of sensitivity and specificity. In addition, many of the analyses conducted were not planned a priori. Although the diagnostic accuracy of assessing carotid plaque was generally greater than that of assessing CIMT, the differences between the two was generally small and non-significant, and the AUCs were relatively low for both types of assessment. This, along with the limitations of the review and the methodological
limitations of some of the included studies, means the authors' conclusions and strong recommendations for practice should be treated with caution.

**Implications of the review for practice and research**

**Practice**: The authors recommended that CIMT assessment should always be supplemented by a thorough scan of the extracranial carotid arteries for carotid plaque assessment to increase the diagnostic performance of carotid ultrasound.

**Research**: The authors did not state implications for research.

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