Meta-analysis: retinal vessel caliber and risk for coronary heart disease

CRD summary
This independent patient data review investigated the association between retinal vessel calibre and risk for coronary heart disease. The authors concluded that there was an association between retinal vessel calibre changes and increased risk for coronary heart disease events in women but not men. These conclusions are likely to be reliable, although there is some uncertainty about the precise risk.

Authors’ objectives
To determine the association between retinal vessel calibre and risk for coronary heart disease.

Searching
MEDLINE and EMBASE were searched for the period 1950 to 4 June 2009. Search terms were provided.

Study selection
Studies of general population groups, that measured retinal vessel calibre from film or digital photographs using computer-assisted methods and recorded coronary heart disease events, were eligible for inclusion.

Measurement of retinal vessel calibre was similar across the included studies, though there were some variations. There was also some variation between trials in the extent of the clinical examination at baseline, recording of systolic blood pressure, measurement of cholesterol levels and how nonfatal coronary heart disease events were elicited.

The outcomes of interest were fatal and nonfatal (myocardial infarction, coronary artery bypass graft or coronary angioplasty) coronary heart disease events. Participants were free of coronary heart disease. Length of follow-up ranged from five to 14 years.

The authors did not state how the papers were selected for review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state the processes for checking the accuracy of the data.

Data extraction
The authors of eligible studies were contacted and invited to participate by providing the original individual patient data. All authors agreed to provide data. One relevant study was not included as insufficient outcome data were available at the time of the analysis.

The Parr-Hubbard formula was used to calculate the mean retinal vessel calibres from each study. The hazard ratio and 95% confidence interval for coronary heart disease events associated with each 20-micrometre (μm) decrease in arteriolar and increase in venular calibre were estimated for each study. These were adjusted for the other retinal vessel calibre, Framingham Risk Score variables and other risk factors associated with coronary heart disease and retinal calibre.

Methods of synthesis
Where no heterogeneity was present fixed-effect meta-analyses were undertaken, for men and women separately, to obtain pooled hazard ratios and 95% confidence intervals, adjusted for multiple standard coronary heart disease risk factors. The presence of heterogeneity was assessed by producing a stratified (by study) proportional hazards model that tested whether there was an interaction between study hazard ratio, retinal vessel calibre characteristics, sex or coronary heart disease risk factors. Sensitivity analyses using a standardised retinal vessel calibre measurement and a random-effects meta-analysis were also conducted.
Results of the review

Six cohort studies (n=22,159 participants) were included. The stratified model indicated that there was no evidence of heterogeneity between studies in the association between coronary heart disease events and retinal vessel calibre, or in Framingham risk variables (except for age and serum and high density lipoprotein cholesterol levels amongst women).

There were 2,219 coronary heart disease events (10%). For women there was an association between coronary heart disease events and wider venules (hazard ratio 1.16 per 20-μm increase in venular calibre, 95% confidence interval (CI): 1.06 to 1.26); and narrower arterioles (hazard ratio 1.17 per 20-μm decrease in arteriolar calibre, 95% CI: 1.07 to 1.28); but not for men (hazard ratio 1.02, 95% CI: 0.94 to 1.10 for venules and hazard ratio 1.02, 95% CI: 0.95 to 1.10 for arterioles). Hazard ratios were highest amongst women without hypertension or diabetes. Similar findings were obtained in the sensitivity analyses.

Authors’ conclusions

There was an independent association between retinal vessel calibre changes and increased risk for coronary heart disease events in women.

CRD commentary

This individual patient data analysis had clearly stated inclusion criteria. Two relevant databases were searched but specific attempts were not made to locate unpublished studies. Arguably, it is unlikely that there is a high risk of missed studies, as this is a small research field, and the authors were able to include data not yet published. The authors did not report whether they used standard methods to reduce error and bias in study selection. They also did not report what methods were used to ensure the quality of the individual patient data. However, they did report key differences in the methods used by studies. The analysis seemed appropriate. Several potentially important sources of heterogeneity were investigated using individual patient data rather than summary data, which was an important strength of the study. A key limitation identified by the authors was that the analysis did not take into account error in the measurement of retinal vessel calibre and Framingham variables, which may have led to an overestimate or underestimate of risk. Overall, the authors’ conclusions were appropriate and are likely to be reliable, although there is some uncertainty about the precision of the estimates.

Implications of the review for practice and research

Practice: The authors stated that the findings suggest the need to evaluate the microvasculature in women, who have no visible obstructions, when assessed by coronary angiography. However, the extent to which quantitative evaluation of retinal vessel calibre from retinal photographs by physicians adds to coronary heart disease risk prediction in women is unclear. It is not yet recommended for clinical practice.

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

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