MICROVASCULAR PROCESSES, such as narrowing of small coronary arteries, and macrovascular processes, such as atherosclerosis of large coronary arteries, are believed to contribute to the risk of coronary heart disease (CHD), a major public health problem with respect to morbidity and mortality in the United States and elsewhere. The cardiology literature suggests that microvascular disease may play a more prominent role than macrovascular disease in CHD in women1 and may explain observations such as women having poorer outcomes than men after coronary artery bypass graft surgery.2 To explore this hypothesis, one planned analysis of the Atherosclerosis Risk in Communities (ARIC) Study examined the association between retinal arteriolar narrowing, a marker of microvascular damage from hypertension and inflammation, and incident CHD in healthy middle-aged women and men.

Retinal Arteriolar Narrowing and Risk of Coronary Heart Disease

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Context: Microvascular processes have been hypothesized to play a greater role in the development of coronary heart disease in women than in men; however, prospective clinical data are limited.

Objective: To examine the association between retinal arteriolar narrowing, a marker of microvascular damage from hypertension and inflammation, and incident CHD in healthy middle-aged women and men.

Design, Setting, and Participants: The Atherosclerosis Risk in Communities Study, an ongoing prospective, population-based cohort study in 4 US communities initiated in 1987-1989. Retinal photographs were taken in 9648 women and men aged 51 to 72 years without CHD at the third examination (1993-1995). To quantify retinal arteriolar narrowing, the photographs were digitized, individual arteriolar and venular diameters were measured, and a summary arteriole-to-venule ratio (AVR) was calculated.

Main Outcome Measure: Risk of CHD associated with retinal arteriolar narrowing.

Results: During an average 3.5 years of follow-up, 84 women and 187 men experienced incident CHD events. In women, after controlling for mean arterial blood pressure averaged over the previous 6 years, diabetes, cigarette smoking, plasma lipid levels, and other risk factors, each SD decrease in the AVR was associated with an increased risk of any incident CHD (relative risk [RR], 1.37; 95% confidence interval [CI], 1.08-1.72) and of acute myocardial infarction (RR, 1.50; 95% CI, 1.10-2.04). In contrast, AVR was unrelated to any incident CHD in men (RR, 1.00; 95% CI, 0.84-1.18) or to acute myocardial infarction (RR, 1.08; 95% CI, 0.85-1.38).

Conclusion: Retinal arteriolar narrowing is related to risk of CHD in women but not in men, supporting a more prominent microvascular role in the development of CHD in women than in men. Future work is needed to confirm these findings.
Retinal Arteriolar Narrowing and Risk of CHD: What Did the ARIC Study Find?

In a prospective, population-based cohort study in 4 communities in the United States, retinal photographs were taken in 9648 men and women aged 51 to 72 years who did not have CHD at the time of examination between 1993 and 1995. The photographs were digitized, and the diameters of individual arterioles and venules coursing through a zone located one-half to 1 disc diameter from the optic disc margin were measured and summarized as an arteriole-venule ratio. During an average follow-up of 3 1/2 years, 84 women and 187 men had an incident CHD event. After controlling for other known risk factors for CHD, each 1-SD decrease in the arteriole-to-venule ratio was associated with an increased risk of any incident CHD (relative risk, 1.37; 95% confidence interval, 1.08-1.72) and of acute myocardial infarction (relative risk, 1.50; 95% confidence interval, 1.10-2.04) in women but not in men.

How Might These ARIC Study Results Impact on Ophthalmologists?

Do these results imply that routine care of patients by ophthalmologists should now include evaluating retinal arteriole-to-venule ratio (in women but not in men) and refer those patients for evaluation of CHD? Not yet. As the authors of the ARIC Study of retinal arteriolar narrowing and risk of CHD conclude, these results support “... a more prominent microvascular role in the development of CHD in women than in men. Future work is needed to confirm these findings.” These associations offer insights that support the hypothesis that microvascular disease may play a more prominent role in the development of myocardial ischemia and CHD in women. The study is limited from making a more definitive conclusion since the retinal microvasculature, not the coronary microcirculation, was assessed directly. Furthermore, these associations do not necessarily imply a cause (decreased retinal arteriole-to-venule ratio) and effect (incident CHD) relationship. Other unmeasured factors associated with a decreased retinal arteriole-to-venule ratio might have been the true cause of the incident CHD. Also, it is unclear why the association of a decreased retinal arteriole-to-venule ratio was not associated with incident CHD in men; the inconsistency suggests that additional confirmatory investigations are needed to be more sure about the association.

Why should ophthalmologists not refer people with low arteriole-to-venule ratios for further cardiac evaluations in case the association is real? After all, ophthalmologists are more likely than their primary care physician counterparts to identify such a finding on ophthalmoscopy as part of an annual eye examination in people older than 50 years. If the association is not truly a cause-and-effect relationship, then people referred for investigations or management of CHD on the basis of retinal arteriole-to-venule ratio findings may have unnecessary tests or treatments (and their associated risks) for CHD. Ophthalmologists should look at the solid investigations reported by the ARIC Study authors as providing support to the hypothesis that microvascular disease plays a more prominent role in the development of myocardial ischemia and CHD in women, but not as providing support to refer patients with low retinal arteriole-to-venule ratios for care beyond the current standard care for cardiovascular disease.

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REFERENCES