AMD Linked to Stroke Risk

The evidence linking AMD and stroke comes from cross-sectional studies.

REVIEWED BY TIEN YIN WONG, MD, MPH, PHD

Patients who are middle aged and have early signs of age-related macular degeneration (AMD) have a higher risk for stroke, independent of traditional stroke risk factors, according to research reported in the *Annals of Internal Medicine.*

"This cohort study increases the likelihood that AMD is a risk factor for stroke," wrote Tien Yin Wong, MD, MPH, PhD, and colleagues. "Stroke and AMD were relatively infrequent in this middle-aged cohort," the authors cautioned, however, only one retinal photograph was taken through nondilated pupils. Dr. Wong is from the Centre for Eye Research Australia, University of Melbourne in Victoria.

BACKGROUND

AMD affects 7 million people aged ≥ 40 years in the United States, according to the report. Risk factors for the disease are similar to that of stroke, therefore, the authors sought to determine if any relationship exists between AMD and incidental clinical stroke.

This prospective cohort investigation was part of the Atherosclerosis Risk in Communities (ARIC) study, a population-based study that included 15,792 men and women aged 45 to 64 years at recruitment in 1987. These patients returned for follow-up at intervals of 3 years. The current study included 10,405 patients who had returned for their third follow-up exam between 1993 and 1995, when retinal photography was performed, Dr. Wong and colleagues wrote. Investigators used a standardized protocol to evaluate the photographs for the presence of drusen and other signs of AMD; incident stroke was identified by a validated review of case records.

RESULTS

The investigators identified 498 cases of early-stage AMD and 10 cases of late-stage AMD (n=508). During a 10-year follow-up, 241 patients had an incident stroke event. The authors adjusted for age, sex, ethnicity and study site, and they found that patients with early-stage AMD had a higher cumulative incidence of stroke than those without AMD (4.08% vs 2.14%). Dr. Wong and colleagues wrote that the presence of early-stage AMD was associated with a higher adjusted risk for stroke (hazard ratio [HR], 1.87 {95% CI, 1.21-2.88}) (Table 1).

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When the investigators further adjusted the data for systolic blood pressure, diabetes, cigarette smoking and the use of antihypertensive agents, the association was not substantially altered (HR, 1.85 [95% CI, 1.19-2.87]). This is the first study to show a clear link between stroke and AMD, Dr. Wong said.

"For many years, there has been an underlying belief that there's an association between AMD and cardiovascular disease [CVD], mainly because they share many of the same risk factors, such as cigarette smoking and hypertension," Dr. Wong said in an interview with Medscape. The literature also reveals that carotid artery disease — a well-established stroke risk factor — and AMD are linked.

The association between early-stage AMD and stroke varied by study site and patient ethnicity. For example, in white patients in Minnesota and Maryland, the multivariable-adjusted HRs were 3.15 and 1.07, respectively, 3.77 in a sample of black patients in Mississippi and 0.33 in a mostly white sample (91%) in North Carolina.

TABLE 1. ADJUSTED RISK FOR INCIDENT STROKE ASSOCIATED WITH EARLY-STAGE AMD		
Cumulative adjusted 10-year incidence (%)	**HR**	**95% CI**
4.08	1.87	1.21-2.88

Unfortunately, no site included sufficient numbers of both black and white patients to determine whether ethnicity contributed to the observed differences at the study sites.

SHORTCOMINGS

The authors noted that their study was limited by the small number of cases of late-stage AMD, while the "cohort assembly method prohibited full understanding of variation by ethnicity and site."

Nonetheless, the study showed that middle-aged patients with signs of AMD had a higher stroke risk, regardless of traditional risk factors. "Based on these results, we believe individuals with AMD should also be monitored for stroke risk, because ophthalmologists in particular, and physicians in general, think of AMD only as an eye disease," Dr. Wong said in the interview with Medscape. "But this study indicates that physicians need to start thinking about whether patients with AMD might benefit from a more comprehensive assessment of cardiovascular risk."

IMPLICATIONS FOR RESEARCH

Dr. Wong said that the discovery of new genetic associations such as complement factor H that related to inflammation are now also thought to be key mechanisms in the development of both AMD and CVD.

More research is needed, however. Dr. Wong said that one example of a potential research avenue is that the Age-Related Eye Disease Study (AREDS) found high-dose antioxidant supplements plus zinc could significantly reduce the risk of AMD. It might be worthwhile, then, to study the same agents in stroke prevention. Statins may also be a potential area of research for AMD, he said.

There is a need to understand in more detail the relationship between AMD and systemic vascular disease, Dr. Wong said. "Simply focusing on AMD as an eye disease is not sufficient." ■

Tien Yin Wong, MD, MPH, PhD, is from the Centre for Eye Research Australia at the University of Melbourne. He may be reached at twong@unimelb.edu.au.

Wong TY, Klein R, Sun C, et al. Age-related macular degeneration and risk for stroke. *Ann Int Med.* 2006;145:98-106.