

So, what have we learnt from this study? Although limited by its retrospective and non-randomised nature, it reminds us of the importance of proper microbiological

work-up for patients with suspected CRBSI, the risk of recurrent bacteraemia following catheter retention and how the catheter type matters.<sup>4,5</sup>

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# Age-related macular degeneration is linked to cardiovascular disease

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**TITLE** Age-related macular degeneration and risk of coronary heart disease and stroke: the Cardiovascular Health Study

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## SUMMARY

Age-related macular degeneration (AMD) is a leading cause of irreversible vision loss in elderly persons in the UK and many other countries.<sup>1</sup> Although the aetiology of AMD remains poorly understood, there is increasing evidence that AMD shares similar risk factors (e.g. smoking and hypertension) and common pathogenic mechanisms (e.g. inflammation and genetic factors) with cardiovascular diseases.<sup>2</sup> However, there have been limited studies that have investigated whether AMD is a risk factor for cardiovascular disease, with somewhat inconsistent results to date.<sup>3–5</sup>

The current study examines the association of AMD with the incidence of coronary heart disease (CHD) and stroke events using data from the Cardiovascular Health Study, a population-based cohort study of cardiovascular disease in adults 65 years of age and older, living in four

communities in the USA. The baseline examination started in 1989, but the study population is derived from participants who were seen in 1997–98, when they had retinal photography to document the presence of AMD. Incident CHD and stroke events up to 2004 were ascertained using standardised methods.

Of the 1,786 persons free of CHD at the time of retinal photography, 303 developed incident CHD events over seven years. Participants with signs of early AMD (n=277) had a higher cumulative incidence of CHD than those without early AMD (25.8% vs 18.9%, p=0.001). After controlling for age, gender, race, systolic and diastolic blood pressure, hypertension status, fasting glucose, triglyceride, low density lipoprotein cholesterol, cigarette smoking, pack years of smoking and C-reactive protein, the presence of early AMD was associated with an increased risk of incident CHD (hazard ratio [HR] 1.57, 95% confidence intervals [CI] 1.17–2.22). Late

AMD signs were infrequent (n=25) and not associated with incident CHD (HR 0.78, 95% CI 0.25–2.48). Among 2,228 persons free of stroke at the time of retinal photography, 198 developed incident stroke; neither early nor late AMD were associated with incident stroke.

This study suggests that older persons with early AMD signs are more likely to develop CHD, although not stroke. This provides further support for asserting that AMD is associated with underlying systemic vascular disease, and may have broader implications for cardiovascular safety in the many thousands of patients with AMD who are treated with new AMD therapy.

## OPINION

Until recently, AMD was believed to be largely untreatable, but the introduction of therapies blocking vascular endothelial growth factor (VEGF), a major pathogenic factor for AMD, represents a landmark in the management of this disease.<sup>6</sup> It is now routine practice for ophthalmologists to offer intra-ocular injections of anti-VEGF agents (e.g. ranibizumab or bevacizumab) as the first-line treatment for neovascular AMD.<sup>7,8</sup> However, a major concern regarding anti-VEGF treatment is the potential increased risk of cardiovascular disease.<sup>2</sup> It is therefore important to re-examine carefully the relationship between AMD and cardiovascular disease in the context of anti-VEGF therapies for AMD.

Many epidemiological studies conducted in the past two decades have indicated that, with the possible exception of diabetes, all of the traditional cardiovascular risk factors, such as cigarette smoking, hypertension, elevated cholesterol levels and higher body mass index, are associated with a risk of AMD.

Emerging data now indicate that the presence of AMD also signals an increased risk of cardiovascular disease,

independent of the effects of age and shared risk factors. The Atherosclerosis Risk in Communities Study in the US showed that middle-aged persons with early AMD had double the risk of incident stroke, while those with late AMD had triple the risk of incident CHD. The Blue Mountains Eye Study in Australia reported a two-fold higher risk of CHD deaths in persons with early AMD.<sup>9</sup> The current analysis from the Cardiovascular Health Study, showing that patients with early AMD are at higher risk of CHD, is consistent with these findings. Taken in totality, these new data suggest that patients with AMD signs may be at increased risk of CVD.

A related question is whether anti-VEGF therapy increases the risk of CVD further in patients with age-related macular degeneration. It is well known that VEGF is essential for new vessel growth, such as the formation of collaterals in the myocardium and in other tissues. In theory, intra-ocular injections of anti-VEGF agents for the treatment of AMD appear to be safe, as they are given in small doses and into the vitreous cavity. In the major clinical trials to date, monthly intravitreal injections of anti-VEGF agents were not associated with an increased risk of cardiovascular events.<sup>6</sup> However, it should be noted that these clinical trials were not powered to detect small risk differences in cardiovascular disease, and because anti-VEGF treatment for AMD is given on a monthly to six-weekly basis, likely for many years, adverse cardiovascular effects due to long-term VEGF suppression will not be immediately apparent.

In summary, general physicians should be aware that AMD and cardiovascular disease are closely inter-related, and the presence of one condition is associated with an increased risk of developing the other. As the use of anti-VEGF agents for AMD becomes more widespread among the elderly population, it is equally important for physicians to know that these agents may potentially increase cardiovascular risk.

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