



# Long-term Management Considerations for Retinal Artery Occlusion and Cardiovascular and Cerebrovascular Mortality

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In this issue of *JAMA Network Open*, Hwang et al<sup>1</sup> report a population-based, retrospective, cohort study using the Korean National Health Insurance Service claims database to determine the incidence of retinal artery occlusion (RAO), and its associated rate (and cause) of death compared with the general population. RAO has 2 main subtypes, central RAO (CRAO) and noncentral RAO, depending on the location of the occlusion. CRAO is uncommon, is akin to acute ischemic stroke in the brain, and causes severe monocular loss of vision in the majority of cases.

Hwang et al<sup>1</sup> found that within the South Korean cohort between the years 2002 and 2018, 51 326 patients had RAO, of which 15 684 (30.6%) had CRAO and the remaining 35 642 (69.4%) had noncentral RAO. The incidence rate for all RAO was 7.38 (95% CI, 7.32-7.44) per 100 000 person-years, while the incidence of noncentral RAO (5.12 [95% CI, 5.07-5.18] per 100 000 person-years) was more than double that of CRAO (2.25 [95% CI, 2.22-2.29] per 100 000 person-years). Increasing exponentially with age, incidence rates were highest in the group aged 70 to 74 years for all RAO cases and in the age group aged 80 to 84 years for CRAO cases.

Death was significantly higher in patients with RAO compared with the general population, primarily as a result of cardiovascular or cerebrovascular disease. Importantly, the leading cause of death among patients with RAO was diseases of the circulatory system, including acute myocardial infarction (18.6%) and cerebral infarction (15.9%). In contrast, the cause of death in the general population was most commonly neoplasms.

The study by Hwang et al<sup>1</sup> adds to the growing literature surrounding associations between retinal vascular occlusion, clinical outcomes, and risk factors. Considering the inherent weaknesses from using an administrative data source, the strength of the study lies in its large sample size, providing a novel insight into the rate and causes of death in patients with RAO. However, the study did not account for competing risk of death, which may overestimate the projected risks of RAO. The study is also, to my knowledge, the first nationwide study to examine the incidence of noncentral RAO, which was comparable with that reported in other smaller studies conducted in Western countries.<sup>1,2</sup>

The study highlights the association between RAO and elevated cardiovascular risks, which other studies have demonstrated.<sup>3,4</sup> The association between RAO and increased risk of developing a subsequent stroke or acute coronary syndrome has previously been reported.<sup>1</sup> Studies using the Danish nationwide database have shown that risk factors connected with atherosclerosis, such as hypertension, ischemic heart disease, peripheral arterial disease, ischemic stroke, diabetes, and kidney disease, are all associated with RAO,<sup>3-5</sup> as well as glaucoma and cataracts. Moreover, atrial fibrillation (AF) was less prevalent in patients with RAO (being found in 8%), compared with the prevalence of AF in patients with stroke (13%).<sup>3</sup> This suggests that cardiogenic emboli (as opposed to embolism from atherosclerotic plaques in the carotid artery) are perhaps not one of the main causes of RAO.<sup>3</sup>

The Danish studies<sup>3-5</sup> suggest differences in pathophysiology between RAO and other retinal vascular occlusion or ischemic stroke. In RAO, both the presence of atherosclerosis and changes in intraocular perfusion pressure (IOP) (associated with glaucoma and cataracts) may predispose to the development of RAO. Although the predominant pathophysiological process leading to development

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of RAO is thought to be atherosclerosis, atherosclerosis may itself have a role to play in elevating IOP, thereby increasing the risk of RAO.<sup>4,5</sup>

The study by Hwang et al<sup>1</sup> found that hypertension, valvular heart disease, ischemic stroke, and chronic kidney disease were more common in patients with CRAO. Ischaemic heart disease and dyslipidemia were more common in patients with noncentral RAO. Given the strong presence of atherosclerosis as a risk factor underlying RAO, it is therefore essential to aggressively pursue preventive therapies and manage modifiable risk factors.

There remains a paucity of randomized clinical trial data supporting any form of commonly used, effective, and safe therapeutic strategy for managing acute RAO or determining the optimal time window for treatment. Furthermore, one systematic review concluded that conservative measures were no more effective than placebo.<sup>6</sup> Against this background, an understanding of the pathophysiology of RAO—and associated risk factors and risk of subsequent cardiovascular and cerebrovascular events and death—is essential to enable targeted preventive strategies to be developed. Multidisciplinary teamwork between ophthalmologists and other specialists, including cardiologists and stroke physicians, are expected to become important, and integrated care approaches may be developed in this field.

## ARTICLE INFORMATION

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