Ten-Year Evolution of Retinopathy Lesions in an Older Nondiabetic Population

Retinopathy lesions are common in generally healthy adults without diabetes (6%-13%)\(^1\)\(^2\) and/or hypertension.\(^3\) In the Beaver Dam Eye Study, the 15-year incidence of retinopathy was 14.2% among nondiabetic participants aged 43 to 86 years at baseline;\(^4\) in the Hoorn Study, the 9-year incidence was 7.3% in persons with normal glucose levels aged 50 to 74 years at baseline.\(^5\) We report the 10-year incidence, regression, associated risk factors, and prognosis of retinopathy lesions among Blue Mountains Eye Study participants.

Methods. Of 3654 baseline participants aged 49 years and older at the 5-year follow-up, 543 (14.9%) had died, 383 (10.5%) had moved, and 393 (10.8%) refused to participate, leaving 2335 (75.1% of survivors) who attended 5-year visits. At the 10-year follow-up, 1103 (30.2%) had died, 375 (10.3%) had moved, and 224 (6.1%) refused to participate, leaving 1952 (53.4% of the original cohort, 76.6% of survivors) who attended 10-year visits. All examinations were approved by the Human Research Ethics Committees of the Western Sydney Area Health Service and the University of Sydney. Signed informed consent was obtained from participants at each visit.

Photographs were obtained for at least 1 eye in 98.1% of the baseline participants, 98.8% of the 5-year follow-up participants, and 86.5% of the 10-year follow-up participants. Masked assessment of retinopathy lesions used the modified Early Treatment Diabetic Retinopathy Study classification of diabetic retinopathy. Retinopathy was diagnosed if the following lesions were detected: microaneurysms, blot- or flame-shaped hemorrhages outside the optic disc area including 0.5 disc diameter away from the disc margin, hard exudates, or cotton-wool spots. Mild retinopathy was defined as a single microaneurysm or hemorrhage in 1 or both eyes, and moderate retinopathy was defined as at least 2 microaneurysms/hemorrhages or hard exudates/cotton-wool spots in either eye.

Incidence of retinopathy was defined as lesions detected at follow-up in persons without lesions in either eye at baseline. Progression of retinopathy was defined as an increase in the number of lesions in subjects with retinopathy at baseline. Disappearance of retinopathy was assessed in subjects with retinopathy lesions at baseline and defined as the lesion(s) having completely disappeared at follow-up. Person-specific cumulative incidence was calculated using Kaplan-Meier methods. Discrete logistic regression models were used to assess risk factors associated with retinopathy incidence or persistence, adjusting for age and sex. Assessed risk factors are shown in the Table.

Results. In 1678 participants without diabetes who attended at least 1 follow-up visit, the cumulative 10-year incidence of retinopathy was 19.4% (95% CI, 17.4%-21.6%). Apart from age, no significant associations were found for incident mild retinopathy. Persons with hypertension or obesity were more likely to develop moderate retinopathy (Table).
Of the 291 nondiabetic participants with retinopathy at baseline, 121 (41.6%) died. Of the 170 survivors, 46 (27.1%) were lost to follow-up, 7 developed diabetes, and 2 developed retinal vein occlusion during the 10-year period. Among the remaining 115 persons, the retinopathy lesions disappeared in 64.3%. Current smoking was significantly associated with retinopathy persistence compared with disappearance (odds ratio = 3.52; 95% CI, 1.29-9.62).

For persons with and without retinopathy at baseline, the 10-year incidences of diabetes were similar (9.5% [95% CI, 8.1%-11.0%] vs 8.4% [95% CI, 5.0%-14.1%], respectively; P = .42), as were the 10-year incidences of stage 2 hypertension (47.2% [95% CI, 44.3%-50.3%] vs 51.9% [95% CI, 42.0%-62.4%], respectively; P = .58).

Comment. One in 5 persons without diabetes developed isolated retinopathy lesions during a 10-year period. Among those with retinopathy lesions at baseline, two-thirds had lesions that disappeared over time. Age, blood pressure, and obesity were 3 risk factors that predicted moderate retinopathy. Retinopathy lesions in people without diabetes are common but transient, and they are likely heterogeneous conditions as suggested by different prognoses.

Author Affiliations: Centre for Vision Research, Department of Ophthalmology and Westmead Millennium Institute, University of Sydney, Sydney (Drs Wang, Kaushik, Kifley, Cugati, and Mitchell and Ms Rochtchina), and Centre for Eye Research Australia, University of Melbourne, Melbourne (Drs Wang and Wong), Australia; and Singapore Eye Research Institute, National University of Singapore, Singapore (Dr Wong).

Correspondence: Dr Wang, Centre for Vision Research, Westmead Millennium Institute, Westmead Hospital, Hawkesbury Road, Westmead, New South Wales 2145, Australia (jiejin.wang@sydney.edu.au).

Financial Disclosure: None reported.

Funding/Support: This work was supported by grants 974159, 211069, and 302068 from the National Health and Medical Research Council and by the Centre for Clinical Research Excellence in Translational Clinical Research in Eye Diseases.