Ten-Year Incidence of Retinal Emboli in an Older Population

Sudha Cugati, MS; Jie Jin Wang, MMed, PhD; Elena Rochtchina, MApplStat; Paul Mitchell, MD, PhD

Background and Purpose—To assess 10-year incidence of retinal emboli and its predictors in an older population.

Methods—Survivors of 3654 Blue Mountains Eye Study participants ≥49 years of age were re-examined 5 and 10 years later. Incident emboli were assessed from retinal photographs.

Results—Cumulative 10-year incidence was 2.9% (95% CI, 2.1% to 3.6%) among 2361 at risk. Age was associated with incident emboli (P trend=0.0001). After multivariate adjustment, hypertension (odds ratio [OR], 1.8; CI, 1.0 to 3.1), hypercholesterolemia (OR, 1.3; CI, 1.0 to 1.6), overweight (OR, 3.3; CI, 1.6 to 6.9), current smoking (OR, 2.5; CI, 1.1 to 5.9), increasing fibrinogen level (OR per mg/dL, 1.1; CI, 1.0 to 1.2), and retinal vascular signs (arteriovenous nicking OR, 2.0; CI, 1.2 to 3.6; arteriolar wall opacification OR, 2.3; CI, 1.1 to 5.0; retinal vein occlusion OR, 3.2; CI, 1.0 to 9.9) were significantly associated with incident emboli.

Conclusions—The 3% incidence of retinal arteriolar emboli found in this older population is likely to be an underestimate attributable to the transient nature of emboli and differential loss to follow-up. Most cardiovascular risk factors predict retinal embolism. (Stroke. 2006;37:908-910.)

Key Words: cohort study ■ embolism ■ epidemiology ■ incidence

Amaurosis fugax, described by Fisher,1 is now considered symptomatic transient central retinal artery embolism.2 Most visible emboli are associated with internal carotid artery stenosis/occlusion,3,4 although some can also arise from aortic arch atheroma or cardiac chambers.5,6 Although frequently asymptomatic, retinal embolism is associated with increased mortality risk.7,8

A few population-based studies reported retinal embolus prevalence and associated factors.8–11 Only the Beaver Dam Eye Study (BDES) has reported 5- and 10-year incidence from a population-based sample.8,12 We previously reported a 1.4% prevalence of retinal emboli in an older Australian population9 and now aim to assess 10-year incidence and predictors of retinal emboli in the same population.

Materials and Methods

The Blue Mountains Eye Study (BMES), a population-based cohort study of older Australians ≥49 years of age, was approved by the Western Sydney area human ethics committee and conducted according to the Helsinki Declaration recommendations. Participants (n=3654; 82.4% of eligible) were examined at baseline (1992 to 1994),13 5 and 10 years later.

Stereoscopic retinal photographs (30°; Zeiss FF3) of Diabetic Retinopathy Study fields 1–6 were taken.13 Photographs were assessed for embolus type (cholesterol, fibrin-plaletlet, calcific), number, location and size,9 and retinal vascular signs (focal arteriolar narrowing, arteriogenous [AV] nicking, opacification of the arteriolar wall), and presence of retinopathy lesions.14

At baseline, we measured blood pressure (BP) and defined mean arterial BP (MABP) as one third systolic BP (SBP) plus two thirds diastolic BP (DBP), severe hypertension if SBP ≥160 mm Hg/DBP ≥100 mm Hg or use of antihypertensive medications, and overweight if body mass index ≥25. Current smokers included those who had stopped smoking <1 year before examination. Heavy drinkers included those who consumed ≥4 drinks per day. Participants with fasting blood samples (88.1%) had hematological and biochemical parameters assessed. We defined diabetes from medical history or fasting blood glucose (≥7.0 mmol/L).

Cumulative incidence rates were calculated using Kaplan–Meier methods, Statistical Analysis System (version 9). Multivariate-adjusted discrete logistic model15 was used to assess factors associated with incident retinal emboli. Eye-specific data (ocular factors) were analyzed using generalized estimating equation models.

Results

Of 3654 baseline participants, 2335 (75.1% of survivors) returned to the 5-year and 1952 (75.6% of survivors) to the 10-year examinations. Surviving participants who did not return to the 10-year examination were older (P=0.0001) and more likely to be current smokers at baseline (P=0.016).

Of 2564 participants we followed at either or both examinations, 31 with emboli at baseline and 172 without gradable photographs were excluded, leaving 2361 at risk. New emboli were detected in 57 persons (cumulative incidence, 2.9%; 95% CI, 2.1% to 3.6%). Two persons developed emboli bilaterally and 5 had emboli at both 5- and 10-year examinations, of whom 4 had different episodes (different types at
different locations), and 1 had the same embolus persisting from the 5- to 10-year visit.

In 1 of 31 participants with retinal emboli at baseline, the embolus persisted to the 10-year examinations. In 90.3% of baseline cases, the embolus disappeared at the next visit. One person had new episodes in the same and fellow eye at 5 years. Another had a second episode at 10 years. Overall, 66 eyes in 59 persons with incident episodes of embolism were found in 2392 (2361/H1100131) participants.

Of these 66 eyes, single embolus was present in 49, 2 in 8, and ≥3 in 9 eyes. Cholesterol accounted for 45.5%, followed by fibrin-platelet (31.7%), calcific (12.2%), and unknown (6.1%), with ≥2 types in 4.5%. Calcific embolus persisted at subsequent visits in 2 participants. Most emboli were either ≤63 µm (42%) or 64 to 125 µm (46.8%) in diameter. Embolism occurred along the arteriolar course (60.6%), at a bifurcation (30.3%) or arteriovenous crossing (1.5%), and at ≥1 location in 7.6%.

Increasing age was significantly associated with incident emboli (P = 0.0001). No significant gender difference was found (3.2% women versus 2.5% men; age-adjusted P = 0.31). After adjusting for age, sex, and all significant factors, SBP, MABP or hypertension, current smoking, overweight, high cholesterol and fibrinogen levels, and retinal vascular signs and retinal vein occlusion were predictors of incident embolism (Table). Hypertensive subjects who were current smokers had a 4-fold risk of embolism over nonsmokers (age-sex adjusted OR, 4.4; CI, 2.0 to 9.7).

Past histories of angina, stroke, myocardial infarction, and regular aspirin use were not significantly associated with retinal embolism. Men who had coronary artery bypass graft before baseline had a 3.9-fold increased risk (CI, 1.1 to 13.5) of incident embolism. We had insufficient number in women to assess this association.

### Discussion

In this older Australian population, the 10-year cumulative incidence of retinal emboli (2.9%) was nearly double that found in the BDES (1.5%). Our higher incidence could be explained by older age (49 to 97 years in BMES versus 43 to 86 years in BDES) and higher prevalence of hypertension in our population (age–sex-standardized prevalence among those ≥55 years of age: 48.7% in BMES versus 43.6% in BDES; P = 0.01).

The age-related increase in emboli incidence is consistent with BDES findings. We found no significant gender difference in embolus incidence, contrasting with previous reports. Our data confirm previous reported associations between retinal emboli and traditional cardiovascular risk factors, including hypertension, smoking, hypercholesterolemia, and plasma fibrinogen. In hypertensive subjects who smoked, a 4.4-fold risk of emboli over nonsmokers

### Systemic and Ocular Factors Associated With 10-Year Incidence of Retinal Emboli

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
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<tbody>
<tr>
<td></td>
<td>Age-Sex Adjusted</td>
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<tr>
<td></td>
<td>Model 1</td>
</tr>
<tr>
<td><strong>Systemic factors</strong></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.07 (1.03–1.11)</td>
</tr>
<tr>
<td>Sex</td>
<td>1.38 (0.64–2.03)</td>
</tr>
<tr>
<td>SBP (per 10 mm Hg)</td>
<td>1.19 (1.06–1.33)</td>
</tr>
<tr>
<td>DBP (per 10 mm Hg)</td>
<td>1.20 (0.93–1.37)</td>
</tr>
<tr>
<td>MABP (per 10 mm Hg)</td>
<td>1.29 (0.96–1.55)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2.39 (1.35–4.22)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.42 (0.56–3.61)</td>
</tr>
<tr>
<td>Fasting blood glucose (mmol/L)</td>
<td>1.11 (0.97–1.28)</td>
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<tr>
<td>Body mass index (kg/m²)</td>
<td>1.09 (1.03–1.14)</td>
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<tr>
<td>Overweight (body mass index ≥25)</td>
<td>2.64 (1.41–4.95)</td>
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<tr>
<td>Serum cholesterol (mmol/L)</td>
<td>1.34 (1.05–1.71)</td>
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<tr>
<td>Fibrinogen (mg/dL)</td>
<td>1.13 (1.02–1.24)</td>
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<tr>
<td>Current smoking</td>
<td>2.14 (1.05–4.35)</td>
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<tr>
<td><strong>Ocular factors‡</strong></td>
<td></td>
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<tr>
<td>Focal arteriolar narrowing</td>
<td>2.26 (0.98–5.22)</td>
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<tr>
<td>Arteriovenous nicking</td>
<td>2.26 (1.32–3.86)</td>
</tr>
<tr>
<td>Occlusion of arteriolar wall</td>
<td>4.08 (1.95–8.53)</td>
</tr>
<tr>
<td>Retinal vein occlusion</td>
<td>6.79 (2.35–19.62)</td>
</tr>
<tr>
<td>Vascular retinopathy§</td>
<td>2.69 (1.31–5.55)</td>
</tr>
</tbody>
</table>

Model 1*: Adjusting for all factors listed in the column; model 2†: adjusting for all significant systemic factors listed in model 1 and each ocular factor separately. ‡Using generalized estimating equation models; §assessed in persons without diabetes.
in 10 years was similar to the 4.7-fold risk found in BDES smokers.12

Our finding that retinal vessel wall signs predicted incident embolism is consistent with an earlier cross-sectional report11 but not with BDES.12 Our study is the first documenting the longitudinal associations between retinal vein occlusion and retinal embolism.

Because of selective survival and differential loss to follow-up in older cohorts, plus the transient nature of retinal emboli, we could have underestimated not only the incidence but also associations between cardiovascular risk factors and incident embolism. Strengths of this study include its population-based sample and reliable assessment of retinal emboli from 6-field retinal photographs. Clinical implications of our findings are in stroke prevention because retinal emboli are a marker of incident stroke and vascular death.

Acknowledgments
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References
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