Editorial Commentary

Retinal Vasculature
A Window on the Brain

J. David Spence, J. Alexander Fraser

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Ong et al. studied 2907 participants in the Atherosclerosis Risk in Communities Study, who were free of diabetes mellitus, stroke, or coronary artery disease at baseline, and were followed for 13 years. Using retinal photographs and a simplified classification of hypertensive retinopathy, they found that even among patients who were well-controlled on antihypertensive medication, moderate/severe retinopathy carried a nearly 3-fold increase in the risk of stroke.

Retinal signs of vascular pathology include an increased light reflex of the retinal arterioles (copper wiring or silver wiring, thought to occur as a result of atherosclerotic vessel wall thickening) and other arteriolar changes, including focal arteriolar narrowing, arteriovenous nicking, and microaneurysms. Retinal cotton-wool spots and exudates are the visible manifestations of small retinal infarctions and retinal hemorrhages, respectively, and represent the retinal consequences of the underlying arteriolar disease. All these findings predict an increased risk of vascular disease, and in particular, the risk of stroke, but the kind of stroke predicted differs with the underlying arteriolar disease. All these findings predict an increased risk of vascular disease, and in particular, the risk of stroke, but the kind of stroke predicted differs with the retinal findings as follows: copper wiring and silver wiring predict atherosclerotic cerebral infarction, whereas signs of hypertensive arteriolar disease predict lacunar infarction and probably also predict deep intracerebral hemorrhages because of hyaline degeneration or fibrinoid necrosis. Although in the past most of the focus was on retinal arterioles, it is now apparent that retinal venous caliber is also important, particularly for risk of intracerebral hemorrhage. In the Rotterdam study, wider venular caliber was associated with lobar hemorrhage and anticoagulant-associated hemorrhage. Increasingly sophisticated methods for analyzing retinal vascular geometry have shown in recent years that the fractal geometry of retinal arteriolar branching differs by small vessel disease subtype, increased complexity of retinal branching is associated with lacunar infarction, and age-related rarefaction of retinal arterioles with deep white matter intensities on MRI.

The classification by Ong et al. of retinopathy into none, mild, moderate, or severe is a simplified approach compared with historical classifications, such as the Keith–Wagener classification, but is helpful to clinicians. Also helpful was their pointing out that retinal photographs are readily available, even in optical shops in the community, and therefore, assessment of retinopathy is available even to clinicians not skilled in ophthalmoscopy.

One diagnostic trap is worth mentioning: as discussed by Matas, simple obscuration of the venular wall behind a thickened retinal arteriole is a result of atherosclerotic wall thickening and should not be mistaken for arteriovenous nicking. In arteriovenous nicking, the venule tapers in diameter behind the arteriole as it is strangled by its common sheath. These differences are illustrated in the Figure.

That retinopathy predicted the risk of stroke was not surprising; retinopathy is more common in patients with stroke or TIA, and retinopathy also predicted risk in the Multi-Ethnic Study of Atherosclerosis; however, the finding of Ong et al. that the increased risk of stroke was independent of blood pressure was unexpected. Possible reasons include masked hypertension, inadequate data to assess blood pressure control over the 13 years of follow-up, and perhaps individual susceptibility of some participants to hypertensive small vessel disease.

Such susceptibility might include structural factors affecting the resistance of the arteriole to pressure, such as abnormalities of collagen or elastin. An interesting hint of such possibilities comes from mutations of COL4A1, which encodes procollagen type IV α1. Some mutations of this gene are associated with tortuosity of retinal arterioles in addition to cerebral aneurysms and abnormalities of basement membranes in skin and kidneys.

Although we encourage our medical students to examine the fundi in every patient they see until they are skilled at this technique and have a good understanding of the range of normality, we acknowledge that many practicing physicians’ aptitudes have waned since medical school. Although ophthalmoscopy is a skill that takes time, practice, and perseverance to master, proficiency pays dividends in the hypertension clinic and the stroke prevention clinic, as this study and others clearly show. The retina is the one place in the body where the physician can actually directly inspect the body’s microvasculature, the tissue most directly at risk from hypertension. Like measurement of carotid plaque burden, which predicts cardiovascular risk much more strongly than a score based on risk factors, ophthalmoscopy is another approach to actually assessing the disease of interest. It is a skill that can be relearned (when lost), particularly when retinal photographs are available for comparison with one’s own ophthalmoscopic examination.
Disclosures

References
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