Patients with ischemic stroke have a high prevalence of hypertension and diabetes, which are risk factors for potentially blinding retinal diseases including diabetic retinopathy, retinal arteriolar emboli, and age-related macular degeneration (AMD). Recent studies also show that patients with diabetic retinopathy, retinal arteriolar emboli, and AMD may have a higher risk of ischemic stroke, suggesting that a retinal examination may be useful for stroke risk stratification. However, the prevalence and types of retinal diseases in patients with acute ischemic stroke are unknown.

In this study, we describe the prevalence of retinal abnormalities and the proportion requiring referral for an ophthalmology evaluation in patients with acute ischemic stroke.

**Materials and Methods**

We prospectively studied consecutive patients with acute ischemic stroke admitted to the Singapore General Hospital, a 1400-bed tertiary hospital in Singapore. This study was conducted as a clinical audit that was approved by the Singapore General Hospital’s Institutional Review Board.

For each patient, we used standardized forms to collect data on patients’ demographics, medical history, and clinical details. Retinal photography was offered routinely to all patients as part of a standard stroke pathway. After written informed consent, mydriatic eyedrops were instilled (one drop of 1% tropicamide to each eye) if there were no contraindications. We obtained retinal photographs of 4 fields (optic disc, macula, superior arcade, and inferior arcade) of each eye using a digital retinal camera (Canon NMR 45; Canon Inc).

The photographs were analyzed at the University of Melbourne for a list of prespecified retinal abnormalities and diseases (e.g., microaneurysm, hemorrhage, hard exudates, neovascularization, early and late AMD, retinal artery and vein occlusion, and glaucoma) according to a protocol used in other studies. This was performed initially by a trained retinal grader and subsequently confirmed by a retinal specialist (WTY), who were both masked to patients’ characteristics.

The ophthalmologist advised on the need for ophthalmology referral based on the retinal findings. Patients were informed by telephone and letter if ophthalmology evaluation was advised. They were subsequently contacted by telephone to determine if they heeded the advice.

Acute ischemic stroke was diagnosed by a neurologist based on clinical presentation and brain imaging and defined as onset within 7 days. Hypertension was defined as prior diagnosis by a physician, present use of antihypertensives, or by blood pressure criteria. Diabetes was defined as prior diagnosis by a physician or present treatment with oral hypoglycemic or insulin. Stroke was subtype by the Oxfordshire Community Stroke Project classification.

Standard statistical tests (chi-squared and t test) were used to examine associations.
Table. Comparison of Patients With Ischemic Stroke With and Without Retinal Abnormalities

<table>
<thead>
<tr>
<th>Retinal Abnormality Present (n=170)</th>
<th>No Retinal Abnormality (n=116)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 65 years</td>
<td>64 years</td>
<td>0.577</td>
</tr>
<tr>
<td>Male 62%</td>
<td>38%</td>
<td>0.247</td>
</tr>
<tr>
<td>Female 56%</td>
<td>44%</td>
<td></td>
</tr>
<tr>
<td>Hypertension 60%</td>
<td>40%</td>
<td>0.698</td>
</tr>
<tr>
<td>No hypertension 58%</td>
<td>42%</td>
<td></td>
</tr>
<tr>
<td>Diabetes 79%</td>
<td>21%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No diabetes 51%</td>
<td>49%</td>
<td></td>
</tr>
<tr>
<td>Hypertension and/or diabetes 62%</td>
<td>38%</td>
<td>0.158</td>
</tr>
<tr>
<td>No hypertension or diabetes 53%</td>
<td>47%</td>
<td></td>
</tr>
</tbody>
</table>

Results

From May to November 2006, we recruited 300 patients with acute ischemic stroke, which comprised 71% (300 of 432) of all patients with ischemic stroke admitted during this 6-month period. Reasons for nonparticipation were critical medical condition (n=63), declined participation (n=36), and logistical reasons (n=24).

The median age of the study sample was 65 years (range, 20 to 91 years), 58% were men, 69% were hypertensive, and 58% had diabetes. The median duration from symptom onset to retinal photography was 3 days with a range of 1 to 7 days. Stroke subtype distribution was 2% with total anterior circulation infarction, 15% partial anterior circulation infarction, 12% posterior circulation infarction, and 71% lacunar infarction.

Retinal photographs were gradable in 286 (95%) patients. The prevalence of any prespecified retinal abnormalities was 59%; 30% (n=87) had early or late AMD, 27% (n=76) had retinal hemorrhages, 13% (n=37) had microaneurysms, 11% (n=30) cotton wool spots, 7% (n=20) hard exudates, 1% (n=4) neovascularization, 1% (n=4) branch retinal vein occlusion, and 0.5% (n=1) branch retinal artery occlusion. Retinal abnormalities were significantly associated with diabetes but not age, gender, or hypertension (Table).

Ninety (31%) patients were determined to require an ophthalmology evaluation; 3% (9) on an urgent and 28% (81) nonurgent basis. Indications for urgent ophthalmology referral were severe diabetic retinopathy (5 patients), late AMD (2 patients), branch retinal artery occlusion (one patient), and glaucoma (one patient). Nonurgent ophthalmology evaluation was required for mild or moderate diabetic retinopathy (90 patients) and a case of AMD, which did not warrant treatment (one patient). Ophthalmology referral was higher for persons with than without diabetes (53% versus 22%, P<0.001) and hypertension (35% versus 23%, P=0.045). Among patients without either condition, however, 16% (12) still required an ophthalmology referral.

Of the 9 patients advised for urgent referral, 8 consulted an ophthalmologist and were prescribed treatment (6 laser therapy, 2 prescribed eyedrops) and all had active follow-up. Of the 81 patients advised for nonurgent referral, 62 consulted an ophthalmologist and 14 had treatment (10 laser therapy, 4 prescribed eyedrops) and all had active follow-up.

Discussion

This report documents a high frequency of retinal abnormalities (59%), including potentially blinding diseases, in patients with acute ischemic stroke. There are no present guidelines on the usefulness for a retinal examination in patients with stroke, although previous studies suggest that many retinal diseases, including hypertensive retinopathy, diabetic retinopathy, and AMD, are risk markers of stroke.

Our study now suggests that a retinal examination using high-quality retinal photography may also be useful to screen for significant retinal diseases, including proliferative diabetic retinopathy and AMD, in patients with ischemic stroke. The advice for ophthalmology referral was validated by the fact that the majority required treatment and were then on active ophthalmology follow-up. Although the prevalence of these conditions was higher among persons with diabetes and hypertension, 53% of patients with neither condition had some retinal abnormality and 16% required a referral. Thus, a retinal examination need not be confined to patients with hypertension or diabetes only.

There are limitations in this study. First, the advice for ophthalmology review was made by a retinal specialist masked to patients’ particulars. There may be tendency to refer patients without knowledge of a patient’s medical history. However, the need for follow-up was validated in the majority of cases. Second, retinal examination was performed using a digital retinal camera, and our results may not be directly translated to clinical ophthalmoscopy in detecting retinal abnormalities. It is likely that clinical ophthalmoscopy may be less sensitive to detect minor retinal abnormalities. Third, we performed photography after pupil dilation. In clinical practice, this may not be feasible on all patients. Future studies examining whether photography in undilated pupils provides the same level of information may be useful. Finally, critically ill patients were excluded and the prevalence of lacunar stroke higher than expected in the Singapore population. Also, hemorrhagic strokes were not included. Therefore, the study sample may not be fully representative of all patients with acute stroke. However, detection and treatment of retinal diseases may not be relevant among these critically ill patients.

Summary

A high proportion of patients with acute ischemic stroke had retinal abnormalities, with 3% requiring an urgent and 28% a nonurgent ophthalmology review. These findings suggest that a routine retinal examination should be performed among patients with acute ischemic stroke to identify vision-threatening retinal diseases.

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Disclosures
None.

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