South Asian Patients With Ischemic Stroke
Intracranial Large Arteries Are the Predominant Site of Disease

Deidre A. De Silva, MRCP; Fung-Peng Woon, MSc; Moi-Pin Lee, RBT; Christopher P.L.H. Chen, FRCP; Hui-Meng Chang, MBBS, FAMS; Meng-Cheong Wong, MBBS, FRCP

Background and Purpose—South Asians are the most prevalent ethnic group in the world. Intracranial disease is the most common vascular lesion worldwide.

Methods—We prospectively studied 200 consecutive ethnic South Asian patients with acute ischemic stroke in Singapore.

Results—Intracranial large-artery disease was prevalent among 54% of all stroke subtypes and was independently associated with hypertension and higher serum erythrocyte sedimentation rate.

Conclusions—Among ethnic South Asian patients with ischemic stroke, intracranial large arteries are the predominant site of disease. (Stroke. 2007;38:000-000.)

Key Words: hypertension ■ inflammation ■ intracranial ■ ischemic stroke ■ South Asian

South Asians originate from India, Sri Lanka, Bangladesh, Pakistan, Nepal, Bhutan, and the Maldives and are the most prevalent ethnic group in the world, numbering more than one billion.1 Intracranial large-artery disease (ICLAD) is the most common vascular lesion in stroke worldwide, varies in prevalence between ethnic groups, and carries a poor prognosis.2 There is emerging evidence for dual antiplatelet therapy and revascularization in ICLAD.2 Previous studies found that ICLAD was prevalent among 69% to 84% of ethnic South Asians with large-artery stroke.3,4 ICLAD and its associations among ethnic South Asians with ischemic stroke of all subtypes has not been reported. Singapore is a newly industrialized nation. Ethnic South Asians make up 8% of the population.

Materials and Methods
We prospectively and consecutively recruited ethnic South Asian patients with acute ischemic stroke admitted to the Singapore General Hospital, a 1400-bed tertiary hospital. Inclusion criteria were ischemic stroke within 7 days of onset, South Asian ethnicity (both parents of South Asian origin), and permanent Singapore residence. The study was approved by our hospital’s ethic committee. Informed consent was obtained.

Extracranial carotid artery assessment was performed with ultrasonography with B-mode imaging. Severe stenosis was defined as 70% to 99% using European Carotid Surgery Trialists’ (ECST) Collaborative Group criteria. Transcranial color-coded Doppler (TCCD) was performed on day 2 to 4 of hospital presentation. ICLAD definition was elevated peak systolic velocity of internal carotid artery ≥120 cm/s at 60 to 68 mm, middle cerebral artery ≥140 cm/s at 52 to 64 mm, anterior cerebral artery ≥120 cm/s at 68 to 72 mm, posterior cerebral artery ≥100 cm/s at 56 to 64 mm, and/or vertebrobasilar arteries ≥100 cm/s at 56 to 106 mm, or occlusion of middle cerebral artery if all other basal arteries were detectable or asymmetry middle cerebral artery index ≤21% compared with the contralateral middle cerebral artery.5 If there were poor TCCD windows, we used magnetic resonance angiography to assess ICLAD, defined as >50% luminal narrowing with or without loss of signal at the stenotic region involving internal carotid artery, middle cerebral artery, anterior cerebral artery, vertebrobasilar arteries, and/or posterior cerebral artery.6

Using the TOAST classification,7 large-vessel stroke definition was clinical and imaging findings consistent with >50% stenosis/occlusion of major/branch cortical artery, infarct ≥15 mm diameter, and appropriate intracranial or extracranial artery stenosis >50%. Cardioembolic stroke definition was clinical and imaging findings similar to large-vessel stroke, a cardioembolic source, and no large atherosclerotic thromboembolic source. Small-vessel stroke was defined as a traditional lacunar syndrome without cerebral cortical dysfunction, infarct ≥15 mm diameter, and no ipsilateral extracranial large-artery stenosis >50%. Stroke of other etiology was defined as attributable to rare causes like hypercoagulability or hematologic disorders. Stroke of undetermined etiology was defined as likely etiology despite extensive evaluation or ≥2 competing causes.

Hypertension, diabetes, and hyperlipidemia were defined as prior diagnosis, current use of appropriate medications, or by the Joint National Committee (JNC) VI, World Health Organization, and National Cholesterol Education Program III criteria, respectively. A patient was considered a smoker if there was a history of smoking in the prior 3 years. Serum erythrocyte sedimentation rate (ESR) was measured from the first blood sample taken after hospital admission.

Univariate analyses were performed using the χ2 test for categorical variables and the t test for continuous variables. Multivariate regression analysis was performed to look for independent associations of intracranial large-artery disease.

Received February 5, 2007; accepted March 1, 2007.
From the National Neuroscience Institute (D.A.D., H.M.C., M.C.W.), Singapore General Hospital Campus, Singapore; the National Heart Centre (F.P.W.), Singapore; Singapore General Hospital (M.P.L.), Singapore; and the National University of Singapore (C.P.L.H.C.), Singapore.
Correspondence to D.A. De Silva, MRCP, Department of Neurology, Singapore General Hospital, Outram Road, Singapore 169608. E-mail gnrdsl@sgh.com.sg
© 2007 American Heart Association, Inc.
Stroke is available at http://stroke.ahajournals.org DOI: 10.1161/STROKEAHA.107.484584
Results
From November 2003 to July 2006, we studied 200 consecutive ethnic South Asian patients. Every eligible ethnic South Asian was recruited. Over the 33-month period, ethnic South Asians formed 8% of 2692 patients with ischemic stroke admitted to the Singapore General Hospital. Mean age was 64 years and 70% were male. Prevalence of hypertension was 78%, diabetes 61%, hyperlipidemia 75%, and smoking 35%. Mean National Institutes of Health Stroke Scale score was 4.8 (range, 0 to 26). Mean ESR was 23.8 mm/h (range, 1 to 138 mm/h).

All patients had electrocardiography, 28% transthoracic echocardiography, 100% brain CT, 99% TCCD studies, and 40% magnetic resonance angiography. None had transesophageal echocardiography. TOAST subtype distribution was 41% large-vessel stroke, 35% small-vessel stroke, 10% cardioembolic stroke, 3% stroke of other etiology, and 11% stroke of undetermined etiology. Of 198 patients with extracranial carotid ultrasound, 10% had severe stenosis/occlusion.

Fifty-four percent (102 of 188) of patients with adequate intracranial vessel assessment had ICLAD. Of 198 patients with TCCD studies, 166 had adequate windows (87 had ICLAD, 79 did not) and 32 inadequate windows (15 had ICLAD on magnetic resonance angiography, 7 did not, 10 had no magnetic resonance angiography). Two patients did not have either TCCD or magnetic resonance angiography studies.

The burden of ICLAD was 76% for large-vessel stroke, 27% for small-vessel stroke, 45% for cardioembolic stroke, 50% for stroke of other etiology, and 68% for stroke of undetermined etiology. Among patients with extracranial carotid artery stenosis/occlusion, 80% (16 of 20) had ICLAD.

The Table shows the associations of ICLAD. In multivariate regression analysis using hypertension, gender, National Institutes of Health Stroke Scale score, extracranial carotid artery status, and ESR as variables, hypertension ($P = 0.013$) and higher ESR ($P = 0.003$) were independently associated with ICLAD, but gender ($P = 0.367$), National Institutes of Health Stroke Scale score ($P = 0.126$), and extracranial carotid artery status ($P = 0.337$) were not.

### Table: Associations of Intracranial Large-Artery Disease Among Ethnic South Asian Patients With Ischemic Stroke

<table>
<thead>
<tr>
<th></th>
<th>Intracranial Large-Artery Disease (n=102)</th>
<th>No Intracranial Large-Artery Disease (n=86)</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y</td>
<td>64</td>
<td>62</td>
<td>0.274</td>
</tr>
<tr>
<td>Male</td>
<td>66 (65%)</td>
<td>69 (80%)</td>
<td>0.031</td>
</tr>
<tr>
<td>Hypertension</td>
<td>91 (89%)</td>
<td>59 (69%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>68 (67%)</td>
<td>49 (57%)</td>
<td>0.172</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>75 (74%)</td>
<td>66 (77%)</td>
<td>0.610</td>
</tr>
<tr>
<td>Smoker</td>
<td>35 (34%)</td>
<td>35 (41%)</td>
<td>0.361</td>
</tr>
<tr>
<td>Mean National Institutes of Health Stroke Scale score</td>
<td>5.6</td>
<td>4.0</td>
<td>0.047</td>
</tr>
<tr>
<td>Severe extracranial carotid artery stenosis/occlusion</td>
<td>16 (17%)</td>
<td>4 (5%)</td>
<td>0.008</td>
</tr>
<tr>
<td>Mean ESR (mm/h)</td>
<td>31</td>
<td>17</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Discussion
The high burden of ICLAD found among ethnic South Asians adds to the evidence that ICLAD is the most common vascular lesion in stroke worldwide. Although ICLAD was most prevalent in large-vessel stroke, it was also common among other stroke subtypes. ICLAD as a potential large atherosclerotic thromboembolic source excludes classification of cardioembolic stroke and stroke of other etiology. We postulate ICLAD in these stroke subtypes was asymptomatic. Although ipsilateral extracranial large-artery stenosis excludes small-vessel stroke, ipsilateral ICLAD does not. Therefore, ICLAD was either asymptomatic or concurrent with small-vessel stroke.

The independent association of hypertension with ICLAD concurs with previous literature, which showed that hypertension was a powerful risk factor for ICLAD but not extracranial carotid disease. Inflammation is believed to be involved in atherosclerosis pathogenesis, explaining our novel association of higher ESR and ICLAD.

Presentation bias is likely minimal because Singapore is small and the public ambulance service sends patients to allocated hospitals by geographical zones. TCCD studies were not repeated with potential inability to distinguish in situ thrombosis from embolism. However, TCCD studies were performed more than 48 hours after stroke onset for most patients (85%), and spontaneous recanalization in embolic stroke occurs in 72% by 48 hours. We acknowledge that most ethnic South Asians live in South Asia and this study population are migrant ethnic South Asians. Because Singapore is a newly developed urban nation, these data may be extrapolated to ethnic South Asians in urban regions of South Asia and large migrant ethnic South Asian populations living in developed countries such as the United Kingdom and the United States.

Summary
This prospective study highlights that intracranial large arteries are the predominant site of disease among ethnic South Asian patients with ischemic stroke.

Disclosures
None.
References

South Asian Patients With Ischemic Stroke. Intracranial Large Arteries Are the Predominant Site of Disease
Deidre A. De Silva, Fung-Peng Woon, Moi-Pin Lee, Christopher P.L.H. Chen, Hui-Meng Chang and Meng-Cheong Wong

Stroke. published online July 26, 2007;
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2007 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/early/2007/07/26/STROKEAHA.107.484584.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org/subscriptions/