Correlation of Large Artery Intracranial Occlusive Disease With Carotid Intima-Media Thickness and Presence of Carotid Plaque

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Background and Purpose—Large artery intracranial occlusive disease (LAICOD) is a predominant cause of ischemic stroke in China. Carotid intima-media thickness (CIMT) and presence of carotid plaque are also related to subsequent ischemic stroke. However, the correlation between these and LAICOD is less clear.

Methods—This was a community-based cross-sectional study. All subjects underwent carotid duplex ultrasonography and transcranial Doppler. Mean CIMT value of bilateral common carotid arteries was used. Plaque was defined as a focal CIMT of >1.5 mm. LAICOD in transcranial Doppler was defined by peak systolic velocity and age, and presence of turbulence or musical sound was also considered.

Results—for the 537 subjects studied (mean age, 54.7±10.1 years; 46.9% males), mean CIMT was 0.74±0.12 mm, with the 75th percentile of 0.80 mm. CIMT ≥1.0 mm was identified in 13 subjects (2.4%). Plaques were detected in 79 subjects (14.7%). Compared with those without LAICOD, the 48 subjects (8.9%) with LAICOD had greater CIMTs (0.77±0.09 versus 0.73±0.12 mm; P=0.044), more with CIMT of higher quartiles (P=0.007), and more with carotid plaques (25.0% versus 13.7%; P=0.035). However, after adjusting for confounding factors, CIMT and presence of carotid plaque were not significantly associated with LAICOD.

Conclusions—The results suggest that CIMT and presence of carotid plaque probably are not independently correlated with LAICOD in Chinese community residents, which supported the existence of pathologic and pathophysiologic differences in atherogenesis of intra- and extracranial arteries. (Stroke. 2013;44:68-72.)

Key Words: carotid intima-media thickness ■ carotid plaque ■ intracranial occlusive disease

Stroke is the second most common cause of death and a leading cause of adult disability worldwide,1 with ischemic stroke being a predominant subtype.2,3 In Asian populations, large artery intracranial occlusive disease (LAICOD) is the most common cause of ischemic stroke.4,5 Carotid intima-media thickness (CIMT) and presence of carotid plaque have also been found to relate to subsequent ischemic stroke in several large cohort studies mostly performed in whites,6 for instance, the Atherosclerosis Risk in Communities study7 and the Northern Manhattan Study.8

Although LAICOD, increased CIMT, and presence of carotid plaque are common in clinical practice and all closely relate to ischemic stroke, the associations between them are less clear. Thus, we conducted this study to examine whether CIMT and presence of carotid plaque were correlated with LAICOD, as well as to briefly overview the distribution of CIMT and the prevalence of carotid plaque and LAICOD, in community-dwelling subjects.

Methods

The Hong Kong Cardiovascular Risk Factor Prevalence Study (CRISPS) was a community-based prospective cohort study of cardiovascular risk factors in Hong Kong Chinese.9,10 Community-dwelling subjects of CRISPS-3 (2005–2008) recruited between April 2007 and September 2008 who underwent both carotid duplex ultrasonography (CD) and transcranial Doppler (TCD) were enrolled into the present cross-sectional study. Institutional review board approval had been obtained from the institutional review board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster. All subjects provided written informed consent before participation. All subjects were asked information about smoking and drinking...
habits, histories of common diseases, and medications. Histories of hypercholesterolemia, hypertension, diabetes mellitus, ischemic heart disease, and stroke were defined as previously diagnosed diseases or receiving corresponding medications. All subjects underwent measurements of body weight, height, waist and hip circumferences, and resting blood pressure. Waist-to-hip ratio and body mass index were calculated. All subjects were required to be fasting overnight before visits, and blood was taken for analysis of fasting blood glucose, total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, urea, and uric acid.

**CD Protocol**

CD was performed using Terson t3000 Ultrasound System (Terson, Burlington, VT) equipped with a 7-MHz high-resolution linear array transducer. An experienced technician examined all subjects in the supine position. Three scanning angles (anterior-oblique, lateral, and posterior-oblique) were used, focusing on the posterior wall of carotid arteries. Longitudinal B mode images from the angle showing the greatest distance between the lumen-intima interface and the media-adventitia interface were stored directly from the system for subsequent offline analysis by another technician unaware of patients’ clinical data, using a semiautomated computerized edge-detection and measurement software MATH (version 3.0, METRIS Co, Argenteuil, France). CIMT was measured at the far wall of the common carotid artery (CCA) proximal to the bifurcation, along a plaque-free segment of ≥10 mm long at each side,11 with a quality index of ≥0.60. Then CIMTs of bilateral CCA s were averaged to get a mean CIMT of a single subject. CIMTs were measured twice in a small sample by the same technician, for subsequent assessment of intrarater reproducibility. Carotid plaques were detected in bilateral CCAs, bifurcations, and extracranial portion of the internal carotid arteries. It was defined as the presence of focal wall thickening that is ≥50% greater than that of the surrounding vessel wall, or as a focal CIMT >1.5 mm protruding into the lumen.11

**TCD Protocol**

We performed TCD using an EME TC2000 ultrasonography system with a 2-MHz pulsed wave transducer, based on a standardized protocol previously described.12 We investigated intracranial arteries through corresponding windows and depths as follows: middle cerebral artery (MCA; temporal window, 56–64 mm), siphon internal carotid artery (ICA; temporal window, 68–72 mm), posterior cerebral artery (PCA; temporal window, 56–64 mm), siphon internal carotid artery (orbital window, 60–68 mm), and vertebrobasilar artery (occipital window, 56–106 mm). Because technically it was difficult to separate vertebral arteries from basilar artery by TCD, they were considered as 1 segment. Similarly, we also regarded terminal internal carotid arteries and MCA as 1 segment. Subjects were classified as having LAICOD if ≥1 of the arteries studied met the criteria defined by peak systolic velocity: ≥140 cm/s for MCA, ≥120 cm/s for ACA and siphon internal carotid arteries, and ≥100 cm/s for PCA and vertebrobasilar arteries.12 In addition, age, presence of turbulence, or musical sound, and whether the abnormal velocity was segmental, were also taken into account. In the case of poor or absent temporal windows, MCAs, ACAs, and PCAs were considered nonocclusive.

**Statistical Analysis**

Pearson correlation coefficient and mean absolute and relative differences were calculated in a small sample between replicate readings by the same technician, to evaluate intrarater reproducibility of CIMT measurement, where relative difference (%) between replicate readings of CIMT for 1 subject was defined as the ratio of absolute difference (mm) and CIMT value of the first measurement (mm). All subjects recruited were divided into 2 subgroups for analysis, LAICOD (+) or LAICOD (−). Demographic characteristics, vascular risk factors, and CD findings were compared between the 2 subgroups in univariate analysis, using Pearson χ² test, trend test, or independent samples t test. Both quartiles and a cut point of 1.0 mm were used in categorical analyses of CIMT. CD findings significantly different between the 2 subgroups were then put into logistic regression models, to calculate both crude and adjusted odds ratios (ORs) for LAICOD. ORs were adjusted for age and other confounding factors, which were most significantly different between the 2 subgroups in univariate analysis. All statistical analyses were performed in PASW Statistics (version 18.0, IBM SPSS Statistics, Chicago, IL). Two-sided P values of <0.05 were considered statistically significant.

**Results**

A total of 537 community-dwelling subjects were recruited. An overview of demographic characteristics, classic vascular risk factors, and ultrasound findings of all subjects is shown in Table 1. The mean age was 54.2±10.1 years; 312 subjects (46.9%) were male, of which 71 (13.2%) and 85 (15.8%) subjects were current and former smokers, respectively. A total of 171 (31.8%), 146 (27.2%), 40 (7.5%), 25 (4.7%), and 14 (2.6%) subjects had histories of hypercholesterolemia, hypertension, diabetes mellitus, ischemic heart disease, and stroke, respectively. Mean systolic blood pressure and diastolic blood pressure were 124.5±18.7 and 77.8±10.1 mm Hg, respectively. CIMT of left and right CCAs were 0.75±0.14 and 0.73±0.13 mm, respectively (P<0.001). Overall mean CIMT of bilateral CCA s was 0.74±0.12 mm, with the 75th percentile of 0.80 mm. Mean CIMT of bilateral CCA s ≥1.0 mm was identified in 13 subjects (2.4%). In a small sample of 31 subjects, Pearson correlation coefficient between replicate readings of mean CIMT was 0.99, and mean absolute and relative differences of replicate measurements were 0.01 mm and 1.2%, respectively. Carotid plaques were detected in 79 subjects (14.7%), among whom only 4 (0.7% of 537) had stenotic plaques.

LAICOD was detected in 48 subjects (8.9%). The comparison of baseline information between the subgroups of LAICOD (+) and LAICOD (−) is also shown in Table 1. The 77 individuals (14.3%) with poor or absent temporal windows were considered nonocclusive of MCAs, ACAs, or PCAs. Compared with those in the subgroup of LAICOD (−), those with LAICOD were older (62.6±8.8 versus 53.9±9.9 years; P<0.001) and had slightly lower diastolic blood pressure (74.8±11.1 versus 78.0±10.0 mm Hg; P=0.037) but higher high-density lipoprotein cholesterol (1.40±0.47 versus 1.25±0.43 mmol/L; P=0.031). In addition, more of them had histories of hypertension (39.6% versus 26.0%; P=0.043) and ischemic heart disease (14.6% versus 3.7%; P=0.004). Subjects with LAICOD also had greater CIMT values (0.77±0.09 versus 0.73±0.12 mm; P=0.044), and more of them had carotid plaques (25.0% versus 13.7%; P=0.035) and CIMT within higher quartiles (P=0.007). However, percentages of CIMT ≥1.0 mm were not significantly different between the 2 subgroups (0% versus 2.7%; P=0.618). Coexistence of carotid plaque and CIMT ≥75th percentile (12.5% versus 7.6%; P=0.233), was not significantly different between the 2 subgroups either.

Crude ORs of CIMT ≥75th percentile (versus CIMT <25th percentile) and presence of carotid plaque for LAICOD were 2.92 (95% CI, 1.02–8.35; P=0.046) and 2.10 (95% CI, 1.04–4.24; P=0.038), respectively. However, these associations attenuated after adjusting for age, with ORs of 0.79 (95% CI, 0.24–2.61; P=0.700) and 1.00 (95% CI, 0.46–2.16; P=0.990), respectively (Table 2). After combining other confounding factors, CIMT in quartiles (OR for quartile 4 versus quartile
Discussion
In the present study, we evaluated atherosclerosis of intra- and extracranial arteries among 537 community-dwelling subjects in Hong Kong by using TCD and CD. We found a much higher prevalence of LAICOD than that of carotid artery stenosis, and there were no significant correlations among CIMT, presence of carotid plaque, and LAICOD. The findings provided further evidence for the existence of pathologic and pathophysiologic differences between intra- and extracranial atherosclerosis in Asian populations.

We used mean CIMT values of left and right CCAs in the current study, in accordance with recommendations of Mannheim carotid intima-media thickness consensus 2004–2006 and a consensus statement from the American Society of Echocardiography, although we observed side differences between bilateral CIMT values. This trend was also observed in several other cohorts, the reasons for which are not clear. Luo et al argued that this asymmetry might be associated with different anatomical origins of bilateral CCAs, after finding that risk factors affecting bilateral CIMTs differed after adjusting for age, with right CIMT primarily correlated with hemodynamic parameters and left CIMT better correlated with blood biochemical indices.
Stenotic and nonstenotic carotid plaques were regarded as markers of advanced and early stages of arterial injury and atherosclerosis, respectively. In this study, we found carotid plaques in 79 subjects (14.7%), among whom only 4 had stenotic plaques. This was comparable to a study on stroke risk of asymptomatic adults in Japan, in which study carotid plaques (defined as a focal CIMT of >1.0 mm) and carotid arterial stenoses were observed in 435 (16%) and 40 (1.4%) of 2924 subjects, respectively.

LAICOD could be considered as an advanced course of intracranial arterial atherosclerosis. In this community-based study, the prevalence of LAICOD (8.9%) was much higher than that of carotid artery stenosis (0.7%). It indicated that atherosclerosis might start earlier in intracranial arteries and that extracranial arterial stenosis might represent more advanced systemic atherosclerosis in the Chinese population. This was in accordance with the fact that, unlike white people, Asians have relatively higher prevalence of LAICOD than extracranial arterial stenosis, as reported in white people, Asians have relatively higher prevalence of LAICOD in community-dwelling adults in Hong Kong Special Administrative Region, China, which further supported the existence of pathologic and pathophysiologic differences among CIMT, presence of carotid plaque, and LAICOD in community-dwelling adults in Hong Kong Special Administrative Region, China, which further supported the existence of pathologic and pathophysiologic differences in atherogenesis of intra- and extracranial arteries.

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### Table 2. Crude and Adjusted ORs of CIMT and Presence of Carotid Plaque for LAICOD

<table>
<thead>
<tr>
<th>CD Findings</th>
<th>No. of Events/No. at Risk</th>
<th>Unadjusted</th>
<th>Adjusted for Age</th>
<th>Adjusted for Age and Other Confounding Factors*</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIMT in quartiles</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quartile 1 (≤0.66 mm)</td>
<td>5/130</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Quartile 2 (0.66–0.71 mm)</td>
<td>7/128</td>
<td>1.45 (0.45–4.68)</td>
<td>0.538</td>
<td>0.86 (0.25–2.90)</td>
</tr>
<tr>
<td>Quartile 3 (0.72–0.79 mm)</td>
<td>22/145</td>
<td>4.47 (1.64–12.18)</td>
<td>0.003</td>
<td>2.09 (0.72–6.07)</td>
</tr>
<tr>
<td>Quartile 4 (≥0.80 mm)</td>
<td>14/134</td>
<td>2.92 (1.02–8.35)</td>
<td>0.046</td>
<td>0.79 (0.24–2.61)</td>
</tr>
<tr>
<td>Presence of carotid plaque</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No plaque</td>
<td>36/458</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>≥1 plaque</td>
<td>12/79</td>
<td>2.10 (1.04–4.24)</td>
<td>0.038</td>
<td>1.00 (0.46–2.16)</td>
</tr>
</tbody>
</table>

*OR indicates odds ratios; CIMT, carotid intima-media thickness; LAICOD, large artery intracranial occlusive disease; and CD, carotid duplex ultrasonography.

*Other confounding factors included history of ischemic heart disease, diastolic blood pressure, and fasting blood high-density lipoprotein cholesterol, which were the 3 variables most significantly different between the 2 subgroups in univariate analysis.

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Disclosures

None.

References

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