Population-Based Study of Cerebral Microbleeds in Stroke-Free Older Adults Living in Rural Ecuador

The Atahualpa Project

Victor J. Del Brutto, MD; Mauricio Zambrano, BS; Robertino M. Mera, MD, PhD; Oscar H. Del Brutto, MD

Background and Purpose—Prevalence of cerebral microbleeds (CMB) in white and Asian populations range from 4% to 15%. However, there is no information from indigenous Latin American people. We aimed to assess prevalence and cerebrovascular correlates of CMB in stroke-free older adults living in rural Ecuador.

Methods—Of 311 Atahualpa residents aged ≥60 years identified during a door-to-door survey, 258 (83%) underwent brain magnetic resonance imaging. Twenty-one were further excluded for a diagnosis of overt stroke. Using multivariate logistic regression models, adjusted for demographics and cardiovascular risk factors, we evaluated whether CMB were independently associated with silent strokes, white matter hyperintensities, and global cortical atrophy.

Results—Twenty-six (11%) of 237 participants had CMB, which were single in 54% of cases. CMB were deep in 11 patients, cortical in 9, and located both deep and cortical in 6. In univariate analyses, CMB were associated with age, systolic blood pressure, moderate-to-severe white matter hyperintensities, silent lacunar infarcts, and cortical atrophy. Mean (±SD) values for systolic blood pressure were 155±27 mm Hg in patients who had CMB versus 142±26 mm Hg in those who did not (P=0.017). In the adjusted models, moderate-to-severe white matter hyperintensities (P=0.009), silent lacunar infarcts (P=0.003), and global cortical atrophy (P=0.04) were independently associated with CMB.

Conclusions—Prevalence of CMB in stroke-free older adults living in Atahualpa is comparable with those reported from other ethnic groups. There is a strong relationship between CMB and increased age, high systolic blood pressure, silent markers of cerebral small vessel disease, and cortical atrophy. (Stroke. 2015;46:1984-1986. DOI: 10.1161/STROKEAHA.115.009594.)

Key Words: cerebral small vessel disease ■ Ecuador ■ ethnic groups ■ microbleed

Cerebral microbleeds (CMB) represent foci of hemosiderin-laden macrophages resulting from extravasation of blood components that have been related to fibrohyalinosis of small penetrating vessels, amyloid angiopathy, and other vasculopathies.1 CMB are associated with imaging markers of cerebral small vessel disease and with cognitive decline, stroke recurrence, and vascular mortality.2 Therefore, recognition of CMB is important for the prompt implementation of preventive strategies. The prevalence of CMB in apparently healthy community dwellers range from 4% to 15% and is markedly influenced by age.3-6 These studies have been conducted in white and Asian populations, but there is no information from indigenous inhabitants of Latin America. We aimed to assess prevalence and correlates of CMB in stroke-free older adults living in rural Ecuador.

Methods

The Atahualpa Project is a population-based cohort study designed to reduce the increasing burden of stroke in rural Ecuador. The village was selected because it is representative of the region. More than 95% of the population belong to the Native/Mestizo ethnic group, and their living characteristics are homogeneous, as detailed elsewhere.2 The neuroimaging substudy enrolled all Atahualpa residents aged ≥60 years with no contraindications for magnetic resonance imaging (MRI) who signed the informed consent.4 The Institutional Review Board of Hospital-Clínica Kennedy, Guayaquil (FWA 00006687), approved the study.

MRIs were performed with a Philips Intera 1.5T machine (Philips Medical Systems, Best, the Netherlands) at Hospital-Clínica Kennedy, Guayaquil, after a well-defined protocol detailed elsewhere.4 In brief, MRI included 2-dimensional multislice turbo spin echo T1-weighted, fluid attenuated inversion recovery, T2-weighted, and gradient-echo sequences in the axial plane, as well as a T1-weighted sequence oriented in the sagittal plane. We used the pre-established brain imaging package delivered by the manufacturer to homogenize applicability by technicians; slice thickness was 5 mm with 1-mm gap between slices.

Two readers, blinded to clinical data, independently reviewed all neuroimaging studies after the standards for research into small vessel disease proposed by Wardlaw et al.9 In particular, CMB were identified and rated according to the Microbleed Anatomical Rating...
Cerebral Microbleeds in Rural Ecuador

Del Brutto et al

Results

MRIs were performed in 258 (83%) of 311 Atahualpa residents aged ≥60 years identified during a door-to-door survey. Reasons for not obtaining MRI included refusal to participate (n=26), severe disability (n=11), claustrophobia (n=8), and implanted pacemaker (n=1); 7 additional patients had died or emigrated between the survey and the invitation. Twenty-one of the 258 participants were further excluded because of a diagnosis of overt stroke. Mean age of the 237 individuals enrolled in this study was 70±8 years, and 140 (59%) were women. Twenty-six (11%) individuals had CMB, which were single in 54% of cases; CMB were deep in 11 cases, cortical in 9, and located both deep and cortical in 6. Moderate-to-severe WMH were noticed in 52 (22%) patients, silent lacunar infarcts in 28 (12%), and moderate-to-severe global cortical atrophy in 120 (51%).

Kappa coefficients for inter-rater agreements of MRI lesions of interest were 0.90 for WMH, 0.76 for deep and 0.53 for cortical CMB, 0.90 for lacunar infarcts, and 0.82 for cortical atrophy. The modest agreement rate for cortical CMB was related to the endemicity of calcified neurocysticercosis in the village because both lesions may appear identical on MRI. As previously described by our group, inter-rater discrepancies were resolved by consensus and by reviewing CT findings and, for the present study, we only included lesions that were definitive cortical CMB.

Table 1 summarizes clinical and imaging characteristics of participants and across the categories of CMB. In univariate analyses, CMB were associated with age, systolic blood pressure, moderate-to-severe WMH, silent lacunar infarcts, and cortical atrophy. In multivariate adjusted models, moderate-to-severe WMH, silent lacunar infarcts, and global cortical atrophy were independently associated with CMB (Table 2).

Discussion

Prevalence of MB in stroke-free older adults living in Atahualpa (11%) is within the range of that reported from industrialized nations. Our results provide robust evidence for an association between CMB and age, high systolic blood pressure, silent markers of cerebral small vessel disease, and cortical atrophy. Population-based studies conducted in developed countries have presented conflicting results about the association of CMB with cardiovascular risk factors or with markers of small vessel disease in individuals without history of cerebrovascular disease.

To our knowledge, no population-based study from Latin America has addressed the prevalence and cerebrovascular correlates of CMB in patients not consulting for a vascular disorder. A potential limitation of the present study is the small sample size, which is counterbalanced by its population-based design and the unbiased selection of participants. Additional studies in other regional communities or in Latin American immigrants to the United States (Hispanics) are needed to confirm our findings, and longitudinal studies would be of value to address the consequences of CMB in this ethnic group.

Table 1. Characteristics of Stroke-Free Atahualpa Residents Aged ≥60 Years According to the Presence of Cerebral Microbleeds

<table>
<thead>
<tr>
<th></th>
<th>Total Series (n=237)</th>
<th>Microbleeds (n=26)</th>
<th>No Microbleeds (n=211)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, mean±SD</td>
<td>70±8</td>
<td>75±9</td>
<td>69±8</td>
<td>0.0001</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>140 (59)</td>
<td>14 (54)</td>
<td>126 (60)</td>
<td>0.718</td>
</tr>
<tr>
<td>Current smokers, n (%)</td>
<td>2 (1)</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Poor physical activity, n (%)</td>
<td>16 (7)</td>
<td>4 (15)</td>
<td>12 (6)</td>
<td>0.082</td>
</tr>
<tr>
<td>BMI, kg/m² (mean±SD)</td>
<td>27±5</td>
<td>26±5</td>
<td>27±5</td>
<td>0.337</td>
</tr>
<tr>
<td>Systolic BP, mmHg, mean±SD</td>
<td>143±26</td>
<td>155±27</td>
<td>142±26</td>
<td>0.017</td>
</tr>
<tr>
<td>Diastolic BP, mmHg, mean±SD</td>
<td>72±11</td>
<td>74±10</td>
<td>72±11</td>
<td>0.378</td>
</tr>
<tr>
<td>Fasting glucose, mg/dL, mean±SD</td>
<td>102±40</td>
<td>110±49</td>
<td>101±39</td>
<td>0.282</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL, mean±SD</td>
<td>212±40</td>
<td>214±40</td>
<td>212±40</td>
<td>0.810</td>
</tr>
<tr>
<td>Moderate-to-severe cortical atrophy, n (%)</td>
<td>120 (51)</td>
<td>19 (73)</td>
<td>101 (48)</td>
<td>0.027</td>
</tr>
<tr>
<td>Moderate-to-severe WMH, n (%)</td>
<td>52 (22)</td>
<td>14 (54)</td>
<td>38 (18)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Silent lacunar infarcts, n (%)</td>
<td>28 (12)</td>
<td>10 (38)</td>
<td>18 (9)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

BMI indicates body mass index; BP, blood pressure; and WMH, white matter hyperintensities.
Table 2. Association of Cerebral Microbleeds With Moderate-to-Severe White Matter Hyperintensities of Presumed Vascular Origin, Silent Lacunar Infarctions, and Moderate-to-Severe Global Cortical Atrophy in Multivariate Logistic Regression Models Adjusted for Demographics and Cardiovascular Risk Factors

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silent lacunar infarction</td>
<td>11.82</td>
<td>2.3–60.3</td>
<td>0.003</td>
</tr>
<tr>
<td>White matter hyperintensities</td>
<td>5.67</td>
<td>1.6–20.7</td>
<td>0.009</td>
</tr>
<tr>
<td>Silent lacunar infarction + white matter hyperintensities</td>
<td>11.35</td>
<td>2.51–51.5</td>
<td>0.002</td>
</tr>
<tr>
<td>Global cortical atrophy</td>
<td>2.61</td>
<td>1.04–6.57</td>
<td>0.042</td>
</tr>
</tbody>
</table>

CI indicates confidence interval.

Sources of Funding

This study was partially supported by Universidad Espíritu Santo—Ecuador, Guayaquil, Ecuador.

Disclosures

Dr Mera has stock interests in GlaxoSmithKline. The other authors report no conflicts.

References

Population-Based Study of Cerebral Microbleeds in Stroke-Free Older Adults Living in Rural Ecuador: The Atahualpa Project
Victor J. Del Brutto, Mauricio Zambrano, Robertino M. Mera and Oscar H. Del Brutto

Stroke. 2015;46:1984-1986; originally published online May 28, 2015;
doi: 10.1161/STROKEAHA.115.009594

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/46/7/1984

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/