Basilar Artery Dolichoectasia: Prevalence and Correlates With Markers of Cerebral Small Vessel Disease in Community-Dwelling Older Adults

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Background: Basilar artery (BA) dolichoectasia has been associated with cerebral small vessel disease (SVD). However, studies have focused on stroke patients, and results cannot be extrapolated to the population at large. In this study, we aimed to assess prevalence of BA dolichoectasia and its association with SVD in community-dwelling older adults living in rural Ecuador. *Methods:* Atahualpa residents aged ≥60 years underwent brain magnetic resonance imaging and magnetic resonance angiography of intracranial vessels. Following Smoker's criteria, the mean BA diameter plus 2 standard deviation defined ectasia. In addition, a location lateral to the lateral margin of the clivus of dorsum sellae or a bifurcation at the third ventricle floor or higher defined dolichosis. Associations between BA abnormalities and imaging markers of SVD were assessed by the use of regression models adjusted for demographics and cardiovascular risk factors. *Results:* Of 346 participants, 11 (3.2%) had ectasia, 40 (11.6%) had dolichosis, and 47 (13.6%) had dolichoectasia (ectasia, dolichosis, or both). BA diameter was only associated with severity of white matter hyperintensities ($P = .038$). Dolichosis was associated with deep cerebral microbleeds ($P = .002$) but not with white matter hyperintensities. Dolichoectasia was associated with both white matter hyperintensities ($P = .031$) and cerebral microbleeds ($P = .001$). There were no associations with lacunar infarcts or enlarged perivascular spaces in any model. *Conclusions:* Prevalence of BA dolichoectasia in this rural setting is similar to that reported in other populations. Associations with imaging markers of SVD differ according to whether the subject has ectasia or dolichosis. **Key Words:** Basilar artery dolichoectasia—small vessel disease—white matter hyperintensities—cerebral microbleeds—lacunar infarcts—enlarged perivascular spaces.

Introduction

Intracranial dilated arteriopathy, one form of nonatherosclerotic disease, has received substantial attention during the past years because of its increasingly recognized association with stroke and other neurologic conditions.[1-3] The most commonly accepted name for this arteriopathy is dolichoectasia, reflecting the abnormal elongation (dolichosis) and dilation (ectasia) of the involved arteries.[3] This condition particularly affects the posterior circulation, that is, the basilar artery (BA), and has been related to arterial wall thinning caused by degeneration of the internal elastic lamina and smooth muscular atrophy.[4] Despite these advances, pathogenetic

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mechanisms involved in the occurrence of dolichoectasia are still elusive, and its actual burden in the population has not been elucidated. Major caveats for accurate prevalence assessment have been discrepancies of definition and the fact that almost all studies have focused on patients with stroke. In some of these studies, the prevalence of the different neuroimaging signatures of small vessel disease (SVD) has been found to be significantly higher among patients with dolichoectasia than in those without.[5-7] However, the few studies assessing prevalence of intracranial dolichoectasia in unbiased samples of apparently healthy individuals have not attempted to correlate its occurrence with the aforementioned imaging markers.[8-10]

The Atahualpa Project is an ongoing population-based cohort study designed to reduce the increasing burden of stroke and other non-communicable neurologic disorders in rural Ecuador and similar populations of Latin America.[11] In this study, we aimed to assess the prevalence of BA dolichoectasia and its association with imaging markers of SVD in community-dwelling older adults.

Methods

Study Population

Atahualpa is a rural village located in Coastal Ecuador. More than 95% of the population belongs to the Ecuadorian native/Mestizo ethnic group. As previously described, living characteristics and socioeconomic status of villagers are homogeneous.[12] Methodology of the Atahualpa Project neuroimaging substudy has also been detailed elsewhere.[13] In brief, all Atahualpa residents aged ≥60 years identified during door-to-door surveys and prospectively enrolled in the Atahualpa Project were invited to undergo brain magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) of intracranial vessels, and those who signed the informed consent and had no contraindications for the practice of these imaging studies were registered. The protocol was approved by the Institutional Review Board of Hospital-Clínica Kennedy, Guayaquil, Ecuador (FWA 00006867).

Neuroimaging Protocol

Studies were performed with a Philips Intera 1.5T (Philips Medical Systems, Heindhoven, the Netherlands) at Hospital-Clínica Kennedy. MRIs included two-dimensional multislice turbo spin echo T1-weighted, fluid-attenuated inversion recovery (FLAIR), T2-weighted, and gradient-echo sequences in the axial plane, as well as a FLAIR sequence oriented on the sagittal plane. In about 80% of cases, an additional T1-weighted inversion recovery sequence oriented on the coronal plane and perpendicular to the long axis of the temporal bone was obtained. 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, with the exception of the T1-weighted inversion recovery sequence, in which slice thickness was 4 mm with no gap. MRAs were performed using a three-dimensional time-of-flight sequence; slice thickness was interpolated down at 1 mm.

SVD Assessment

MRIs were reviewed following research standards for cerebral SVD proposed by Wardlaw et al.[14] In particular, white matter hyperintensities (WMH) of presumed vascular origin were defined as lesions appearing hyperintense on T2-weighted images that remained bright on FLAIR (without cavitation) and graded in none, mild, moderate, and severe, according to the modified Fazekas scale.[15] Cerebral microbleeds (CMB) were identified and rated according to the microbleed anatomical rating scale[16]; for this study, only CMB located deep in the brain (including the subcortical white matter, basal ganglia, thalamus, brainstem, or cerebellum) were considered. Lacunar infarcts (LI) were defined as fluid-filled cavities measuring 3-15 mm located in the territory of a perforating arteriole,[14] and enlarged perivascular spaces (EPVS) were defined as small (<3 mm) structures of cerebrospinal fluid (CSF) intensity located in the basal ganglia or centrum semiovale that followed the orientation of perforating arteries; EPVS were rated as abnormal if >10 of these lesions were present.[17] Two readers independently reviewed all MRIs, and discrepancies were resolved by consensus. As previously described, kappa coefficients for interrater agreement were high for the neuroimaging signatures of interest.[13,18]

BA Assessment

Source MRA digital images were viewed on the Osirix Medical Imaging software (Pixmeo, Geneva, Switzerland) for measurement of BA diameter (Fig 1). The diameter was measured at several points along the vertical course of the BA by 2 independent readers, and a mean value of the maximal diameter obtained by each reader was calculated for analyses. When measurements from the 2 readers differed by .5 mm or more, images were sent to another reader for consensus. According to Smoker et al,[8] the mean BA diameter in our population plus 2 standard deviations was used to define ectasia. In addition, the continuous BA diameter (in millimeters) was used for analyses.

Laterality and height of bifurcation of the BA were assessed on digital images by the use of criteria proposed by Smoker et al[8] (Fig 2). BAs located in the midline or medial to the lateral margin of the clivus of dorsum sellae were considered normal, and those located (at any point of their course) lateral to the lateral margin or the clivus or dorsum sellae or at the cerebellopontine angle were considered to represent dolichosis. Likewise, the height of bifurcation of the BA was considered normal if located