Vertebrobasilar Ectasia in Patients with Lacunar Stroke: The Secondary Prevention of Small Subcortical Strokes Trial

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Background: The clinical implications of vertebrobasilar ectasia (VBE) in patients with cerebral small-artery disease are not well defined. We investigated whether VBE is associated with recurrent stroke, major hemorrhage, and death in a large cohort of patients with recent lacunar stroke. *Methods:* Maximum diameters of the vertebral and basilar arteries were measured by magnetic resonance angiography and computed tomographic angiography in 2621 participants in the Secondary Prevention of Small Subcortical Strokes trial. VBE was defined a priori as basilar artery greater than 4.5 mm and/or vertebral artery greater than 4.0 mm. Patient characteristics and risks of stroke recurrence and mortality during follow-up (median, 3.5 years) were compared between patients with and without VBE. *Results:* VBE affecting 1 or more arteries was present in 200 (7.6%) patients. Patient features independently associated with VBE were increasing age, male sex, white race ethnicity, hypertension, and higher baseline diastolic blood pressure. Baseline systolic blood pressure was inversely associated with VBE. After adjustment for other risk factors, VBE was not predictive of recurrent stroke (hazard ratio [HR], 1.3; 95% confidence interval [CI], .85-1.9) or major hemorrhage (HR, 1.5; CI, .94-2.6), but was of death (HR, 1.7; CI, 1.1-2.7). *Conclusions:* In this large well-characterized cohort of patients with recent lacunar stroke, VBE was predictive of death but not of recurrent stroke or major hemorrhage. In these exploratory analyses, the frequency of VBE was directly related to diastolic blood pressure but inversely related to systolic blood pressure. **Key Words:** Lacunar stroke—prognosis—recurrent stroke—death—arterial diameter—vertebrobasilar ectasia.

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Intracranial arterial dolichoectasia is characterized by increased dilatation and tortuosity of the arteries compared with expected values.[1-5] Because the basilar artery and vertebral artery are preferentially involved, the term "vertebrobasilar (dolicho) ectasia (VBE)" is commonly used. Reports of the prevalence of VBE range from .06%-6% among healthy individuals[6-10] to 1%-11% in stroke patients,[11-17] with variability of rates partially because of differences in radiologic definitions, patient populations, and stroke subtypes across studies.

Currently, there is insufficient evidence regarding prognosis of lacunar stroke patients with VBE.[4,5,7,8,10,13,18-25] Several small case series and observational studies have reported an unfavorable prognosis in patients with VBE.[7,8,10,13,18-25] In addition, a few studies have also reported a relationship between VBE and small-vessel disease including lacunar stroke.[9,11,13-15,25]

The aim of this study was to investigate the prevalence and prognostic implications of VBE in patients with recent lacunar stroke because of cerebral small-artery disease.

Materials and Methods

Subjects

Participants were from the Secondary Prevention of Small Subcortical Strokes (SPS3) trial. Details about the study rationale, design, patient characteristics, and main results have been previously reported.[26-29] Briefly, patients with a recent (>2 weeks, <6 months) small symptomatic subcortical stroke documented on magnetic resonance imaging (MRI) were randomized simultaneously in a 2 × 2 factorial design to an antiplatelet therapy (double-blind, aspirin + placebo versus aspirin + clopidogrel) and a target level of systolic blood pressure (130-149 mm Hg versus <130 mm Hg). Corresponding lesion of the lacunar syndrome was verified on MRI. MRI scans were submitted for central interpretation by a neuroradiologist (C.B.). The baseline MRI had to demonstrate a qualifying lesion meeting at least one of the following 4 specific criteria: (1) diffusion-weighted imaging lesion of 20 mm or less in size at the largest dimension (including rostrocaudal extent); (2) well-delineated focal hyperintensity of 20 mm or less in size at largest dimension on fluid-attenuated inversion recovery (FLAIR) or T2 and clearly corresponding to the clinical syndrome; (3) multiple hypointense lesions of size 3-15 mm in size at the largest dimension in the cerebral hemispheres on FLAIR or T1 in patients whose qualifying event is clinically hemispheric; and (4) well-delineated hypointense lesion of 15 mm or less in size at the largest dimension on FLAIR or T1 corresponding to the clinical syndrome with the MRI carried out at least 1 month after the qualifying stroke.

Old subcortical infarcts, remotely symptomatic or asymptomatic, were defined as hypointense lesions on FLAIR and/or T1 measuring 3 mm or greater but no more than 15 mm in maximum dimension. Lesions at the level of the anterior commissure, convexity, or midbrain were interpreted as enlarged perivascular spaces and not classified as infarcts, unless the lesion was surrounded by a hyperintense halo on FLAIR.[1] Patients were required to have vascular imaging of the intracranial arteries to qualify for study entry. Magnetic resonance angiography (MRA), computed tomography angiography (CTA), or angiogram images were submitted to the Coordinating Center.

Baseline systolic and diastolic blood pressures were determined by the average of 2 blood pressure measurements taken at least 1 week apart and at least 2 weeks after the qualifying stroke. Each measurement was the average of 3 blood pressure readings separated by at least 2 minutes in the seated position. History of hypertension pertained before the qualifying stroke and was based on physician review of the patient's medical records or participant use of at least 1 antihypertensive medication at study entry.

Dilatation of Arteries and Intracranial Arterial Dolichoectasia

All available MRA and CTA were reviewed by a neurologist (M.N.) blinded to clinical information. MRA/CTAs with no scale and those visualizing only 4 or less of the 7 intracranial arteries within the image were not included. To measure arterial diameters, reconstructed maximum intensity projection images were used for MRA and source images were used for CTA. Maximum diameters at any point along the course of each of the basilar artery, intracranial internal carotid arteries, M1 segment of the middle cerebral arteries, and V4 portion of the vertebral artery were measured. MRA and CTA were assessed on digital (n = 2505) or film images (n = 289) as submitted to the Coordinating Center from each study site. Arterial diameters on digital images were measured manually using a DICOM viewer software available online (http://www.radiantviewer.com), and those on film images were measured using a graduated lens with scales (Fig S1 in Appendix).[14]

Intrarater reliability (correlation coefficient) was assessed for each of the 7 intracranial artery measurements on a random sample of images for 50 patients re-read more than 6 months after initial reading. Readings for the intracranial internal carotid arteries and M1 segment of the middle cerebral arteries were not sufficiently reproducible (correlation coefficients ≤.70) such that we did not include those results further in these analyses. Patients included in these analyses have a measurement for the basilar artery and at least 1 vertebral artery. Correlation coefficients for the first and second readings of the basilar and vertebral artery measurements ranged from .84 to .89. The random sample was also read by a second