Low Ankle-Brachial Index is a Simple Physical Exam Sign Predicting Intracranial Atherosclerotic Stenosis in Ischemic Stroke Patients

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Background: The investigation of ischemic stroke etiology is commonly limited to the heart and extracranial vessels. Nevertheless, the diagnosis of intracranial stenosis may carry important therapeutic implications. The aims of this study were to determine the prevalence and clinical predictors of intracranial atherosclerotic stenosis (ICAS) in a sample of patients with ischemic stroke. *Methods:* Consecutive patients admitted to a university-based outpatient stroke clinic underwent CT angiography of the intracranial and extracranial brain vessels. Clinical, demographic, and laboratory characteristics were compared between patients with increasing levels of stenosis. Ankle-brachial index (ABI) was measured to quantify peripheral arterial disease, defined as an ABI less than or equal to .9. Multivariable ordinal logistic regression was constructed to predict increasing stenosis grades (none, 1%-49%—mild, 50%-69%—moderate, 70%-100%—severe). *Results:* We studied 106 subjects, mean age 62 ± 15 years, 54% female. ICAS was present in 38 (36%) patients: 19 (50%) mild, 7 (18%) moderate, and 12 (32%) severe. Of 74 patients where ABI was measured, low ABI was found more frequently with increasing ICAS severity (26%, 42%, 67%, and 89% of patients with none, mild, moderate, and severe ICAS, respectively). In univariable analysis, higher age, presence of diabetes, abdominal obesity, and low ABI correlated with increasing stenosis grades. In multivariable analysis, only low ABI remained independently associated with increasing stenosis grades. *Conclusions:* The ABI is independently associated with increasing severity of ICAS, making it a potentially useful triaging tool for more invasive test selection. **Key Words:** Ischemic stroke—ankle-brachial index—intracranial arterial stenosis—extracranial arterial stenosis—CT angiography.

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Introduction

In patients with ischemic stroke (IS), etiological investigation plays an important role in defining management strategies and preventing future events. Nevertheless, examination is frequently limited to heart conditions and extracranial artery atherosclerosis. Intracranial atherosclerotic stenosis (ICAS), which usually affects carotid siphon, middle cerebral artery (MCA), and basilar artery (BA), is frequently overlooked, although it may be responsible for over 10% of stroke events.[1-4]

Defining which populations are at high risk for ICAS is important for diagnostic test selection and potentially for planning therapeutic strategies. However, predictive models based on cerebrovascular risk factors have shown low discriminatory capability.[5-7] Simple noninvasive physical exam signs such as abdominal circumference and ankle-brachial index (ABI) may add predictive ability to these classical risk factors, but have not been previously investigated. Thus, our objective was to determine the predictors of ICAS in a sample of patients with IS, with a particular emphasis on noninvasive physical exam signs as potential predictors.

Materials and Methods

This is a cross-sectional study that included consecutive patients with the diagnosis of IS admitted to a university-based outpatient stroke clinic in Bahia, Brazil. We excluded patients with contraindications for CT angiography (CTA), such as renal failure (blood urea nitrogen >50 mg/dL or creatinine >1.5 mg/dL) and allergy to iodine. The study was approved by the local ethics committee and all patients signed informed consent.

Clinical, demographic, and laboratory characteristics were collected upon recruitment through structured interviews and previous exam data available in patient records. Patients underwent 64-channel CTA of the intracranial and extracranial brain vessels to analyze the presence and degree of intracranial and extracranial stenoses. All CTA analyses were performed by 1 radiologist (A.D.M.B.) blinded to patient characteristics. ICAS status was classified by the following severity grades: (1) none, (2) 1%-49% stenosis (mild), (3) 50%-69% stenosis (moderate), and (4) 70%-100% stenosis (severe).

Measurement of the ABI was added to routine clinical evaluation after February 2009. In order to calculate the ABI, measurement of systolic blood pressure (SBP) of the 4 limbs was performed. ABI was obtained through the ratio of lowest lower limb SBP by the highest upper limb SBP, as previously described.[8,9] Peripheral arterial disease (PAD) was defined as an ABI of less than or equal to .9. Abdominal obesity was defined as a waist circumference greater than 102 cm in men and greater than 88 cm in women. Hypertension was defined as an SBP greater than or equal to 140 mmHg and/or diastolic blood pressure greater than or equal to 90 mmHg on at least 2 outpatient visits or by previous use of antihypertensive medications.

Statistical Analysis

To establish an association between specific variables and increasing stenosis grades, Spearman's correlation was used for continuous variables and trend test was used for categorical variables. Variables with possible association with increasing stenosis grades on univariable analyses ($P < .20$) were independent variables in a multivariable ordinal logistic regression model where stenosis grades were the dependent variable. Significant independent associations were considered for P values <.05. To account for missing data, a sensitivity analysis was performed using multiple imputations with the same model. Statistical analysis was performed using the *Statistical Package for the Social Sciences* version 17.0 software (SPSS Inc. Chicago, IL, USA, 2008).

Results

One-hundred and seventy-nine patients were screened between September 2008 and July 2013, and 73 were excluded because of abnormal renal function tests (n = 15) or missed scheduled CTA or withdrawal consent (n = 58). The final sample consisted of 106 patients, mean age 63 ± 15 years, 55 (52%) female. Most patients (64%) had no ICAS, whereas 18% had 1%-49% stenosis, 7% had between 50% and 69% stenosis, and 11% had greater than or equal to 70% stenosis. Location of ICAS was distributed as follows: 5 (10.6%) at the site of the internal carotid artery (ICA), 6 (12.7%) at the anterior cerebral artery (ACA), 10 (21.3%) at the MCA, 13 (27.7%) at the posterior cerebral artery (PCA), 7 (14.9%) at the vertebral artery (VA), and 6 (12.7%) at the BA. When considering only ICAS with greater than or equal to 50% stenosis, 2 (6.5%) were at the ICA, 3 (9.7%) at the ACA, 7 (22.6%) at the MCA, 10 (32.3%) at the PCA, 4 (12.9%) at the VA, and 5 (16.1%) at the BA. Considering ICAS with greater than or equal to 70% stenosis, 1 (6.7%) was located at the ICA, 1 (6.7%) at the MCA, 7 (46.7%) at the PCA, 3 (20.0%) at the VA, and 3 (20.0%) at the BA. Other clinical variables are shown in Table 1. Of the 74 patients with available ABI measurements, 38% presented with ABI less than or equal to .9. There were no significant differences between patients who underwent intracranial vascular imaging or those who were screened but did not undergo imaging.

Table 2 shows the univariable associations with increasing ICAS grades ($P < .05$): presence of diabetes mellitus, abdominal obesity, and PAD. Increasing age showed a trend for an association with increasing ICAS grades (P = .087) and was included in the multivariable model. PAD predicted severe (>70%) ICAS with 89%