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Clinical Study

Relationship between augmentation index and acute ischemic stroke subtype

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ABSTRACT

The aim of the present study was to explore the relationship between augmentation index (AIx) and vascular risk factors according to stroke subtypes. Patients were eligible for this study if they experienced their first ischemic stroke within the preceding 7 days and were 45 years of age or older. AIx was measured by applanation tonometry (SphygmoCor, AtCor Medical, Sydney, Australia) and ischemic stroke was classified according to the Trial of Org 10172 in the Acute Stroke Treatment (TOAST) classification system. A total of 189 patients were enrolled. The most frequent stroke subtype was lacune (76, 40.2%), followed by stroke of undetermined etiology, negative work-up (SUDn) (59, 31.2%), large artery atherosclerosis (LAA) (31, 16.4%), and cardioembolism (23, 12.2%). While there were no significant differences among the groups for hemodynamic indices, AIx at 75 beats per minute (AIx@75) was higher in lacune subtype (29.6%) than SUDn (28.4%), LAA (26.6%), and cardioembolism (24.8%) ($p = 0.064$). The AIx@75 was significantly related to age ($r = 0.189$), sex ($r = 0.252$), peripheral systolic blood pressure (SBP) ($r = 0.189$), peripheral diastolic blood pressure (DBP) ($r = 0.191$), and peripheral mean arterial pressure (MAP) ($r = 0.327$). Multiple linear regression analysis revealed that age, sex, peripheral SBP, peripheral DBP and peripheral MAP were significant ($p < 0.002$). This study showed that arterial stiffness is increased in acute lacunar infarction. Considering the pathogenesis of lacunar infarction and the potential interconnected causes of arterial stiffness, our findings indicate that increased arterial stiffness in acute lacunar infarction may be related to the pathogenesis of lacunar infarction.

1. Introduction

Arterial walls stiffen with age, but this is not necessarily normal. Aging, environmental, and genetic factors are responsible for the structural and functional changes of the arterial wall, leading to decreased elasticity and increased stiffness [1]. Accelerated arterial stiffness occurs in the presence of diabetes mellitus (DM), hypercholesterolemia, hypertension, and metabolic syndromes. Arterial stiffness is an independent predictor of all-cause and cardiovascular (CV) mortality, fatal and non-fatal coronary events, and symptomatic strokes [2,3]. Arterial stiffness has also been associated with cognitive impairment, the presence of a lacunar infarction, white matter hyperintensity, and cerebral microbleeds [2,4]. Arterial stiffness may be an independent predictor of functional outcome in patients with acute ischemic stroke [5]. There are several arguments regarding the relationship between arterial stiffness and ischemic stroke subtypes. Although some researchers have suggested that lacunar infarction is associated with increased arterial stiffness, currently it is not proven which stroke subtype or subtypes are associated with increased arterial stiffness [6].

In this context, we investigated arterial stiffness by measurement of the augmentation index (AIx) in patients with acute ischemic stroke. The aim of the present study was to explore the relationship between AIx and vascular risk factors according to stroke subtype.

2. Material and methods

2.1. Patient selection

We enrolled all consecutive patients with a diagnosis of acute ischemic stroke or transient ischemic attack (TIA) admitted to the Neurology Department at the Sanggye Paik Hospital between November 2010 and November 2011. The diagnosis required brain CT scan and/or MRI to exclude hemorrhages and other causes of symptoms. A patient required at least one vascular imaging study, including conventional angiography, magnetic resonance angiography (MRA), or CT angiography (CTA). Standard systemic investigations were performed in every patient, which included 12-lead

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electrocardiography (ECG), chest radiograph, and blood tests. Transcranial Doppler, carotid duplex sonography, transthoracic echocardiography (TTE), transesophageal echocardiography (TEE), and 24-hour Holter ECG monitoring were performed in selected patients. AIx was a part of the standard evaluation, except in patients with poor systemic condition. The demographics, vascular risk factors, and neurologic examination, including the National Institutes of Health Stroke Scale (NIHSS) score, were collected at baseline.

Patients were eligible for the study if they had experienced their first ischemic stroke within the preceding 7 days and were 45 years of age or older. Hypertension was defined as a systolic blood pressure (BP) of at least 140 mmHg or a diastolic BP of at least 90 mmHg. DM was defined as present if the participant was receiving hypoglycemic treatment or their fasting serum glucose level was 126 mg/dL or higher [7]. Hypercholesterolemia was defined as present if the participant was receiving treatment for the condition or if their total serum cholesterol level was 230 mg/dL or higher. Patients who smoked regularly during the previous year or had stopped during the previous year were classified as smokers.

All subjects signed an informed consent form and this study was approved by the local Ethical Committee.

2.2. Stroke classification

The type of acute ischemic stroke was classified according the Trial of Org 10172 in the Acute Stroke Treatment (TOAST) classification system, and the criteria were strictly applied [8].

2.3. Pulse wave analysis

At Day 7 (±2) after stroke onset, AIx was measured by applanation tonometry (SphygmoCor, AtCor Medical, Sydney, Australia). Applanation tonometry was used to record the radial artery pressure waveform continuously, and mean values of the two screens of pulse waves of good quality were used for analysis. On the basis of the collected data, an averaged radial pressure waveform was generated and a corresponding aortic pressure waveform and BP were calculated by the validated transfer function (SphygmoCor version 7.1). The aortic pressure waveform was used to calculate the AIx. In addition, since AIx is influenced by heart rate, an index normalized for heart rate of 75 beats per minute (AIx@75) was used [9]. Only high-quality recordings, defined as an in-device quality index $\geqslant$80% (derived from an algorithm including average pulse height, pulse height variation, diastolic variation, and the maximum rate of rise of the peripheral waveform), and acceptable curves on visual inspection, were included in the analysis.

2.4. Statistical analysis

Data are expressed as the mean ± standard deviation or n (%). The baseline characteristics were compared among the groups using a one-way analysis of variance. Pearson's correlation coefficients were calculated to evaluate the correlations of AIx with vascular risk factors in relation to TOAST subtype classification. A two-sided p value of <0.05 was considered statistically significant. The Statistical Package for the Social Sciences (SPSS Inc., Chicago IL, USA) version 12.0 was used for statistical analysis.

3. Results

A total of 257 patients who had experienced acute cerebral infarction or TIA within 7 days of the onset of symptoms were reviewed for the study. The mean age was 67.1 and 40.1% were women. The subtypes of ischemic stroke were classified in 234 patients and the most frequent stroke subtype was lacune (85, 33.1%), followed by stroke of undetermined etiology (SUD) (83, 32.3%; 67 with negative work up [SUDn], 15 with more than two causes identified, and one with incomplete evaluation), large-artery atherosclerosis (LAA) (36, 14%), cardioembolism (CE) (29, 11.3%), and stroke of other determined etiology (one, 0.4%). AIx was performed in 231 patients (90%) and the proportions of test implementation were comparable among the stroke subtypes ($p > 0.281$). For this study, patients with TIA (23, 8.9%) and/or age <45 years (19, 7.4%) were excluded. Table 1 shows the baseline characteristics of the enrolled patients. Of the 189 patients, 59.3% had a history of hypertension, 30.2% of diabetes, 12.7% of dyslipidemia, and 30.7% of current smoking. A brain CT scan was performed in 83.1% of patients. Brain MRI and diffusion-weighted imaging was performed in 96.3% of patients. All patients had at least one vascular imaging study (MRA in 96.3%, CTA in 2.6%, and cerebral angiography in 2.6%). Echocardiographic studies were performed in 97.9% of patients (TTE in 97.9% and TEE in 9.5%).

The most frequent stroke subtype was lacune (76, 40.2%), followed by SUDn (59, 31.2%), LAA (31, 16.4%), and CE (23, 12.2%). The baseline characteristics were well balanced among the groups, and there were no statistically significant differences in these characteristics except serum triglyceride (TG) level and baseline NIHSS score (Table 1). Lacunar subtype patients had a higher serum TG level than CE ($p < 0.039$) and baseline NIHSS score was higher in the LAA subtype than lacunar and SUDn ($p < 0.006$). Hemodynamic indices of the enrolled patients are shown in Table 2. While there

Table 1
Baseline characteristics of the study population

	Total (n = 189)	LAA (n = 31)	CE (n = 23)	Lacune (n = 76)	SUDn (n = 59)	p value
Age, years	67.47 [10.42]	68.65 [8.18]	70.87 [11.84]	67.51 [10.28]	65.47 [10.87]	0.171
Female	73 (38.6%)	8 (25.8%)	12 (52.2%)	30 (39.5%)	23 (40%)	0.266
BMI, kg/m^2	23.94 [3.50]	24.14 [3.47]	24.25 [2.76]	24.09 [3.77]	23.51 [3.46]	0.728
Hypertension	112 (59.3%)	18 (58.1%)	15 (65.2%)	47 (61.8%)	32 (54.2%)	0.757
Diabetes mellitus	57 (30.2%)	7 (22.6%)	7 (30.4%)	24 (31.6%)	19 (32.2%)	0.793
Hypercholesterolemia	24 (12.7%)	3 (9.7%)	1 (4.3%)	9 (11.8%)	11 (18.6%)	0.304
Smoking	58 (30.7%)	11 (35.5%)	6 (26.1%)	21 (27.6%)	20 (33.9%)	0.757
Fasting plasma glucose, mg/dL	121.62 [52.91]	129.74 [64.42]	125.22 [36.43]	123.11 [57.13]	114.05 [45.95]	0.555
Total cholesterol, mg/dL	176.32 [35.42]	179.23 [30.20]	174.04 [36.96]	173.41 [33.76]	179.44 [39.70]	0.738
LDL cholesterol, mg/dL	113.74 [30.27]	114.84 [28.48]	108.96 [31.91]	111.61 [28.01]	117.76 [33.42]	0.568
HDL cholesterol, mg/dL	43.83 [11.19]	45.00 [16.46]	47.13 [6.88]	42.71 [10.39]	43.36 [10.05]	0.363
Triglyceride, mg/dL	118.58 [55.43]	118.52 [41.29]	91.48 [31.24]	128.89 [62.52]	115.88 [56.69]	**0.039**
Baseline NIHSS score	3.13 [3.46]	5.29 [4.76]	3.57 [4.93]	2.34 [1.66]	2.83 [3.28]	**0.001**

Data are presented as mean [standard deviation] or n (%).
Significant p values are in bold.
BMI = body mass index, CE = cardioembolism, HDL = high-density lipoprotein, LAA = large artery atherosclerosis, LDL = low-density lipoprotein, NIHSS = National Institutes of Health Stroke Scale, SUDn = stroke of undetermined etiology, negative work-up.