Atherosclerosis 236 (2014) 150–153

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Increased augmentation index is paradoxically associated with lower in-hospital mortality in patients with acute ischemic stroke

Konstantinos Tziomalos*, Stella D. Bouziana, Marianna Spanou, Vasilios Giampatzis, Maria Papadopoulou, Pavlina Kazantzidou, Stavroula Kostaki, Vasiliki Dourliou, Christos Savopoulos, Apostolos I. Hatzitolios

First Propedeutic Department of Internal Medicine, Medical School, Aristotle University of Thessaloniki, AHEPA Hospital, Thessaloniki, Greece

A R T I C L E I N F O

Article history:
Received 10 February 2014
Received in revised form
17 May 2014
Accepted 30 June 2014
Available online 11 July 2014

Keywords:
Arterial stiffness
Stroke
Pulse wave velocity
Augmentation index
Central blood pressure

A B S T R A C T

Objective: To evaluate the association between arterial stiffness and stroke severity and in-hospital outcome in patients admitted with acute ischemic stroke.
Methods: We prospectively studied 415 consecutive patients who were admitted with acute ischemic stroke (39.5% males, age 78.8 ± 6.6 years). On the third day of hospitalization, the following markers of arterial stiffness were recorded: central systolic blood pressure (cSBP), diastolic BP (cDBP), mean pressure (cMP), pulse pressure (cPP), augmentation index (AIx) and pulse wave velocity (PWV). The severity of stroke was assessed on admission with the National Institutes of Health Stroke Scale (NIHSS) score. The outcome was evaluated with rates of dependency at discharge (modified Rankin scale score between 2 and 5) and in-hospital mortality.
Results: None of the markers of arterial stiffness showed significant correlation with the NIHSS score on admission. However, there was a trend for an inverse correlation with AIx ($r = -0.142$, $p = 0.064$) and for a positive correlation with PWV ($r = 0.235$, $p = 0.054$). None of the markers of arterial stiffness differed between patients who were dependent at discharge and those who were independent. Patients who died during hospitalization had higher cDBP and cMP but lower cPP and AIx than patients who were discharged. In binary logistic regression analysis, independent predictors of in-hospital mortality were NIHSS score on admission (relative risk (RR) 1.16, 95% confidence interval (CI) 1.08–1.25, $p < 0.001$), presence of atrial fibrillation (RR 6.41, 95% CI 1.37–29.93, $p = 0.018$) and AIx (RR 0.94, 95% CI 0.89–0.99, $p = 0.030$).
Conclusions: Increased AIx appears to be associated with lower in-hospital mortality rates in elderly patients with acute ischemic stroke. Other markers of arterial stiffness do not appear to be associated with short-term outcome in this population.

1. Introduction

Stroke currently represents a leading cause of death and long-term disability worldwide [1,2]. Since the outcome of acute stroke varies widely, risk stratification in these patients is essential to tailor treatment and plan rehabilitation [3]. Accordingly, both multivariable models incorporating clinical parameters as well as an array of serum markers have been evaluated for predicting the outcome of acute stroke [4–6]. However, their predictive ability appears to be limited, stressing the need for developing novel prognostic markers [4–6].

In the last decade, several prospective studies showed that increased arterial stiffness is independently associated with greater risk for cardiovascular events, including stroke [8]. Several markers of arterial stiffness have been proposed, including pulse wave velocity (PWV), augmentation index (AIx), central systolic blood pressure (cSBP) and central pulse pressure (cPP), and all appear to be associated with increased cardiovascular risk [7,8]. Moreover, arterial stiffness can be simply, safely and accurately evaluated with non-invasive, reproducible and well-validated techniques [9,10]. However, very few and small studies evaluated the predictive ability of markers of arterial stiffness in acute stroke [11–13]. Increased PWV was associated with worse functional outcome in 2 reports from the same group [11,12]. Higher AIx also predicted

* Corresponding author. First Propedeutic Department of Internal Medicine, AHEPA Hospital, 1 Stilponos Kyriakidi Street, Thessaloniki 54636, Greece. Tel.: +30 2310 994621; fax: +30 2310 994773.
E-mail address: ktziomalos@yahoo.com (K. Tziomalos).

http://dx.doi.org/10.1016/j.atherosclerosis.2014.06.028
0021-9150/

better in-hospital outcome in one study [13] but had no predictive value in the 2 above-mentioned reports [11,12].

The aim of the present study was to evaluate the association between different markers of arterial stiffness and stroke severity and in-hospital outcome in patients admitted with acute ischemic stroke.

2. Patients and methods

We prospectively studied all patients who were admitted in our Department with acute ischemic stroke between September 2010 and February 2013 ($n = 415$; 39.5% males, age 78.8 ± 6.6 years).

On admission, demographic data (age, sex), history of cardiovascular risk factors [hypertension, type 2 diabetes mellitus (T2DM), atrial fibrillation, smoking, alcohol consumption, family history of premature cardiovascular disease (CVD), chronic kidney disease (CKD)], history of concomitant CVD (coronary heart disease, previous stroke, congestive heart failure) and pharmacological treatment were recorded. Anthropometric parameters (weight, height) and systolic and diastolic blood pressure (SBP and DBP) were also measured. The severity of stroke was assessed with the National Institutes of Health Stroke Scale (NIHSS) score. On admission, stroke was rated as mild, moderate severe, moderate severe/severe and severe in 39.3, 38.3, 6.7 and 15.7% of the patients, respectively (i.e. NIHSS score between 1–4, 5–15, 16–20 and 21–42, respectively).

Routine laboratory investigations were performed on the first day after admission after overnight fasting, and included serum levels of glucose, total cholesterol, high-density lipoprotein cholesterol, triglycerides, creatinine and uric acid. Low-density lipoprotein cholesterol levels were calculated using Friedewald's formula [14]. Glomerular filtration rate (GFR) was estimated using the Modification of Diet in Renal Disease equation [15]. CKD was defined as estimated GFR <60 ml/min/1.73 m^2. All patients underwent brain computed tomography on admission and a second brain computed tomography was performed if clinically indicated. No patient underwent thrombolysis or any surgical intervention.

On the third day of hospitalization, the following markers of arterial stiffness were recorded with the Sphygmocor device (Atcor Medical, Sydney, Australia): cSBP, central DBP (cDBP), cPP, central mean pressure (cMP), AIx and PWV. Measurements were performed in the morning, in supine position, after at least 10 min of rest, and after fasting for at least 4 h [10]. Measurements were performed at the right side except in patients with right hemiparesis, in whom the left side was used. Two measurements were performed and the mean was recorded. If the 2 measurements differed by >0.5 m/s in PWV or by >5% in AIx, a third measurement was performed and the median was recorded. Markers of arterial stiffness were evaluated in all patients, including those with severe stroke.

At discharge, the modified Rankin scale (mRS) score was recorded. Dependency at discharge was defined as mRS score between 2 and 5. In-hospital mortality rates were also recorded.

3. Statistical analysis

All data were analyzed using the statistical package SPSS (version 17.0; SPSS, Chicago, IL, USA). Data are presented as percentages for categorical variables and as mean and standard deviation for continuous variables. Differences in categorical and continuous variables between groups were assessed with the chi-square test and independent samples t-test, respectively. Correlations between parameters were assessed with Pearson's correlation. Binary logistic regression analysis was used to identify independent predictors of dependency at discharge and in-hospital mortality. In all cases, a two-tailed $p < 0.05$ was considered significant.

Table 1
Correlations between markers of arterial stiffness and National Institutes of Health Stroke Scale score on admission.

Marker of arterial stiffness	r	p
Central systolic blood pressure	0.113	0.144
Central diastolic blood pressure	0.115	0.136
Central mean pressure	0.126	0.101
Central pulse pressure	0.122	0.114
Augmentation index	−0.142	0.064
Pulse wave velocity	0.235	0.054

4. Results

None of the markers of arterial stiffness showed significant correlation with the NIHSS score on admission (Table 1). However, there was a trend for an inverse correlation with AIx ($r = -0.142$, $p = 0.064$) and a trend for a positive correlation with PWV ($r = 0.235$, $p = 0.054$).

At discharge, 224 patients (53.9%) were dependent. Clinical and laboratory characteristics of patients who were dependent at discharge and of those who were independent at discharge are shown in Table 2. Patients who were dependent at discharge were older, more frequently current smokers and had higher prevalence of previous ischemic stroke, lower SBP, peripheral pulse pressure and serum triglyceride levels as well as higher NIHSS score on admission. Markers of arterial stiffness in patients who were dependent at discharge and in those who were independent at discharge are shown in Table 3. None of the measured markers of arterial stiffness differed between the 2 groups. In binary logistic regression analysis, independent predictors of dependency at

Table 2
Clinical and laboratory characteristics of the study population according to dependency at discharge.

	Dependent at discharge ($n = 224$)	Independent at discharge ($n = 191$)	p
Age (years)	79.7 ± 6.3	76.8 ± 6.2	<0.001
Males (%)	35.7	39.8	0.550
Peripheral systolic blood pressure (mmHg)	143 ± 24	149 ± 23	0.027
Peripheral diastolic blood pressure (mmHg)	80 ± 12	81 ± 12	0.330
Peripheral mean pressure (mmHg)	101 ± 14	104 ± 17	0.072
Peripheral pulse pressure (mmHg)	63 ± 20	68 ± 20	0.039
Hypertension (%)	80.3	86.9	0.151
Smoking (current/past)(%)	12.7/17.3	9.6/28.8	0.048
Type 2 diabetes mellitus (%)	35.7	29.8	0.338
Atrial fibrillation (%)	33.9	32.9	0.911
Body mass index (kg/m^2)	27.3 ± 5.3	27.8 ± 4.9	0.486
Overweight/obese (%)	41.4/24.2	38.3/28.0	0.813
Coronary heart disease (%)	27.2	30.9	0.553
Chronic kidney disease (%)	40.6	32.5	0.266
Previous ischemic stroke (%)	52.7	31.4	<0.001
National Institutes of Health Stroke Scale score on admission	10.3 ± 7.8	2.1 ± 2.6	<0.001
Glucose (mg/dl)	113 ± 45	107 ± 41	0.238
Low-density lipoprotein cholesterol (mg/dl)	109 ± 41	117 ± 42	0.138
High-density lipoprotein cholesterol (mg/dl)	45 ± 15	47 ± 14	0.342
Triglycerides (mg/dl)	111 ± 44	132 ± 58	0.002
Uric acid (mg/dl)	5.5 ± 1.8	5.8 ± 1.7	0.120
Estimated glomerular filtration rate (ml/min/1.73m^2)	66 ± 23	71 ± 24	0.094