Brachial-ankle Arterial Stiffness is Associated with Cerebral Small Vessel Disease in Patients with Acute Ischemic Stroke

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ABSTRACT

Background: Increased arterial stiffness develops alterations of the cerebral vasculature and is known predictor of cerebrovascular diseases. Vessel wall damage in relation to arterial stiffness develops more frequently in the small vessels of brain. The objective of this study was determined the association between arterial stiffness, as measured by brachial-ankle pulse wave velocity (baPWV) and MRI markers of cerebral small vessel disease (SVD) in acute ischemic stroke. **Methods:** We studied 88 subjects with acute cerebral infarction. All patients underwent baPWV and brain MRI. The number of microbleeds and lacunar infarcts were rated. The locations of microbleeds and lacunar infarcts were divided into infratentorial, lobar, and deep regions. The WMH were separated in deep and periventricular regions and the severity of WMH were assessed. **Results:** Increased baPWV was associated with lacunar infarcts and WMH ($p<0.05$). There was no association between microbleeds and baPWV. On multivariable analysis, the association of baPWV and lacunar infarcts in the deep regions was stronger than other imaging markers of SVD ($p<0.01$). **Conclusions**: Increased arterial stiffness was associated with the severity of cerebral SVD in acute ischemic stroke. Lacunar infarcts in deep regions are more related to arterial stiffness. These findings show that baPWV is a reliable surrogate marker of SVD.

METHODS

We retrospectively selected patients who had been admitted between March 2010 and July 2012 with acute cerebral infarction within seven days of symptom onset. Among them, we included patients who had undergone brain MRI and baPWV measurement. We excluded patients with high- or medium-risk potential cardiac embolic sources of embolism based on the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification. Eighty-eight patients were ultimately included for this study.

Arterial stiffness was examined as measured by baPWV using a volume-plethysmography device (VP-1000; Collin, Komaki, Japan) on both side. We used the average of both side. The baPWV is divided to tertile.

The number of CMBs were rated using gradient-echo T2*-weighted MRI. The number of LIs were rated using T1- and T2-weighted images. The locations of CMBs and LIs were divided into infratentorial, lobar and deep region using a modified microbleed anatomical rating scale devised by Gregoire et. al. (Fig.1). The WMLs were separated in deep and periventricular regions and the total grade of WMLs were scored: 1, minimal; 2, moderate, and 3, severe (Table 1). All calculations were done using SPSS version 12.0 and p values < 0.05 were considered statistically significant.

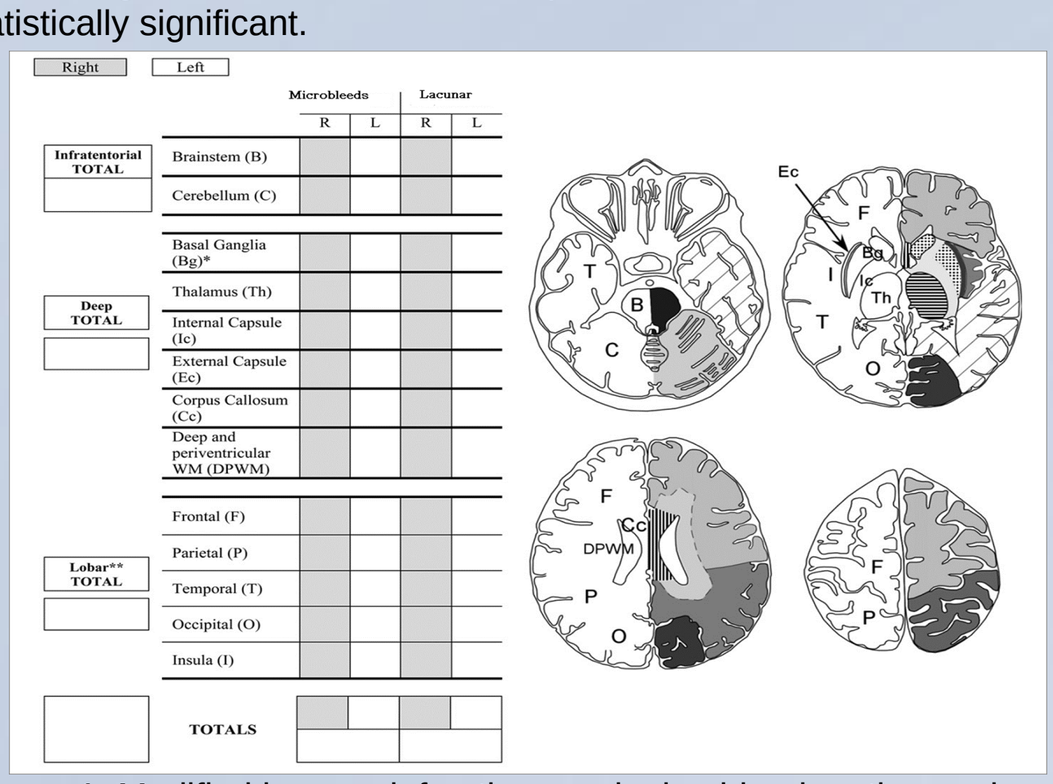

Figure. 1. Modified lacunar infarctions and microbleeds rating scale.

Table 1. Degree of white matter hyperintensity.

	D1 (<10mm)	D2 (10-24mm)	D3 (>24mm)
P1(5mm in capping and banding)	Minimal	Minimal	Moderate
P2(between P1 and P3)	Minimal	Moderate	Moderate
P3(>10mm in capping or banding)	Moderate	Moderate	Severe

RESULTS

Table 2. Baseline demographics and clinical characteristics of the acute ischemic stroke according to pulse wave velocity

	baPWV (<1699 cm/s) (n=29)	baPWV (1699-2023 cm/s) (n=30)	baPWV (>2023 cm/s) (n=29)	*p*-value
Sex (Male/Female)	23/6	21/9	14/15	0.038
Age (years)	58.8±10.2	70.6±9.7	70.6±8.5	<0.001
Hypertension, n (%)	13 (44.8)	14 (46.7)	15 (51.7)	0.601
Diabetes mellitus, n (%)	3 (10.3)	10 (33.3)	9 (31.0)	0.070
Hyperlipidemia, n (%)	5 (17.2)	4 (13.3)	4 (13.8)	0.713
Current Smocking, n (%)	11 (37.9)	9 (30.0)	6 (20.7)	0.152
Alcohol, n (%)	11 (37.9)	13 (43.3)	10 (34.5)	0.789
Prior stroke, n (%)	4(13.8)	3 (10.0)	5 (17.2)	0.704
Coronary artery disease, n (%)	2 (6.9)	2 (6.7)	2 (6.9)	0.971
Systolic BP (mmHg)	133.3±12.4	146.0±22.4	162.8±26.4	<0.001
Pulse pressure (mmHg)	51.9±9.3	62.1±13.4	66.9±15.5	<0.001
Diastolic BP (mmHg)	81.4±8.4	87.0±22.9	91.8±10.6	0.004
Heart rate (beats/min)	65.0±8.5	63.3±15.3	72.5±12.1	0.021
Hemoglobin (g/dL)	14.3±1.4	13.4±1.7	13.1±1.2	0.017
ESR (mm/hr)	13.3±9.4	20.8±21.7	28.2±24.6	0.017
Creatine (mg/dL)	0.8±0.2	1.0±1.1	1.01±0.7	0.510
GFR (mL/min)	101.8±23.7	98.5±23.3	80.8±37.2	0.015
Fasting blood sugar (mg/dl)	105.7±33.3	125.3±102.8	108.4±21.6	0.282
Total cholesterol (mg/dl)	193.0±45.4	174.1±63.1	192.5±42.0	0.412
Body mass index (kg/m^2)	23.6±2.0	23.9±2.7	22.9±2.8	0.645

Table 3. Imaging markers of small vessel disease according to tertiles between brachial-ankle pulse wave velocity

	baPWV (<1699 cm/s) (n=29)	baPWV (1699-2023 cm/s) (n=30)	baPWV (>2023 cm/s) (n=29)	*p*-value
Cerebral microbleeds				
Total	1.24±4.62	1.50±4.02	1.24±2.53	0.488
Infratentorial	0.14±0.58	0.23±0.57	0.28±0.92	0.531
Deep	0.69±2.97	1.00±3.64	0.69±1.56	0.463
Lobar	0.41±1.15	0.27±0.74	0.24±0.69	0.559
Lacunar infarctions				
Total	1.66±2.41	2.10±1.81	4.10±3.71	0.001
Infratentorial	0.17±0.76	0.33±0.61	0.41±0.87	0.106
Deep	1.03±1.80	1.50±1.68	3.03±2.96	0.001
Lobar	0.45±0.95	0.23±0.50	0.66±1.14	0.349
WM hyperintensities				
Periventricular WM	1.03±0.50	1.23±0.43	1.48±0.57	0.008
Deep WM	1.07±0.53	1.33±0.55	1.48±0.51	0.016
Total grade	1.07±0.47	1.17±0.38	1.38±0.56	0.042

Table 3. Multivariable analysis on relationship between brachial-ankle pulse wave velocity and cerebral small vessel disease load

	baPWV, Model 1		baPWV, Model 2	
	β	*p*-value	β	*p*-value
Cerebral microbleeds				
Total	0.005	0.957	-0.001	-0.990
Infratentorial	0.093	0.270	0.120	0.206
Deep	0.000	1.000	-0.006	0.947
Lobar	-0.055	0.515	-0.078	0.413
Lacunar infarcts				
Total	0.226	0.007	0.175	0.077
Infratentorial	-0.012	0.893	-0.017	0.856
Deep	0.265	0.001	0.304	0.001
Lobar	0.181	0.035	0.085	0.408
WM hyperintensities				
Periventricular WM	0.179	0.044	0.182	0.068
Deep WM	0.117	0.203	0.114	0.297
Total grade	0.128	0.150	0.099	0.332

CONCLUSIONS

We found that increased peripheral arterial stiffness is associated with the severity of cerebral SVD in acute non-cardioembolic ischemic stroke. These findings show that baPWV is a reliable surrogate marker of SVD.

Moreover, deep regions, such as basal ganglia and thalamus, are more related with arterial stiffness. Arterial stiffness was independently associated with lacunar infarcts in deep region but not microbleeds or WM hyperintensities. These findings suggest a pathophysiological association between arterial stiffness and lacunar infarcts in deep region.

There have been a few studies investigating the association between arterial stiffness and acute SVD which showed conflicting results. Arterial stiffness impairs compliance of the vessel walls, increases the pulse pressure and contributes to systemic hypertensive injury. In particular, small arteries of the brain are vulnerable to highly pulsatile systemic pressure since the brain has a low vascular resistance. Through these presumed mechanisms, arterial stiffness might contribute to the brain injury associated with SVD.

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