Original Article

N-terminal Pro-B-type Natriuretic Peptide is Associated with Arterial Stiffness as Measured According to the Brachial-ankle Pulse Wave Velocity in Patients with Takayasu Arteritis

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Aim: Takayasu arteritis (TA) is associated with increased cardiovascular morbidity and mortality, and the degree of arterial stiffness is an independent predictor of cardiovascular mortality in a variety of diseases. In addition, the levels of N-terminal pro-brain natriuretic peptide (NT-proBNP), a marker of ventricular dysfunction, have been found to be higher in patients with TA than in healthy controls. In this study, we aimed to investigate the relationship between the plasma NT-proBNP levels and arterial stiffness in patients with TA.

Methods: Seventy-two patients with TA were recruited in this study. The participants were analyzed with respect to the NT-proBNP levels, cardiovascular risk factors, TA-related variables and arterial stiffness assessed according to the brachial-ankle pulse wave velocity (baPWV). The patients were divided into two groups based on the mean baPWV, and the association between the NT-proBNP and baPWV values was tested using uni- and multivariate analyses.

Results: Twenty-four patients (33.3%) were classified into the high-baPWV group. The body mass index ($p=0.035$), systolic blood pressure ($p<0.001$), diastolic blood pressure ($p=0.001$), mean blood pressure ($p<0.001$), plasma NT-proBNP levels ($p=0.036$) and total cholesterol levels ($p=0.030$) were significantly higher in the high-baPWV group than in the low-baPWV group. A stepwise multiple linear regression analysis revealed the mean blood pressure ($p<0.001$), age ($p=0.002$), and NT-proBNP level ($p=0.002$) to be independent determinants of the ba-PWV after adjusting for other confounding factors.

Conclusions: The plasma NT-proBNP levels are independently associated with the degree of arterial stiffness measured according to the baPWV in patients with TA.

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Key words: N-terminal pro-brain natriuretic peptide, Arterial stiffness, Brachial-ankle pulse wave velocity, Takayasu arteritis

Introduction

Takayasu arteritis (TA) is a form of chronic vasculitis that predominantly affects the aorta and its

main branches, resulting in luminal stenosis, occlusion, dilation and/or aneurysm formation¹. This condition is associated with a significantly increased risk of cardiovascular diseases (CVD)²⁻⁴. Although the exact mechanisms linking the onset of TA to late CV events remain unclear, endothelial dysfunction and chronic vascular injury have been proposed to be main contributing factors³⁻⁵. As a reliable marker of vascular damage, increased arterial stiffness is associated with atherosclerosis and an independent risk factor for CV events in various clinical settings^{6,7}. Furthermore, the pulse wave velocity (PWV) is used as a standard

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indicator for indirectly estimating the extent of arterial stiffness in patients with rheumatic conditions⁸⁾.

N-terminal pro-brain natriuretic peptide (NT-proBNP), a diuretic peptide secreted from cardiomyocytes in response to ventricular wall stretching⁹⁾, is considered to be a useful marker for evaluating the risk of CVD¹⁰⁻¹²⁾. Recently, we reported that the NT-proBNP levels are higher in patients with TA than in healthy controls¹³⁾. TA is characterized by increased arterial stiffness in the central elastic arteries, which may in turn increase the NT-proBNP level^{14, 15)}. However, the relationship between NT-proBNP and arterial stiffness has not been fully elucidated. In the present study, we aimed to evaluate the clinical characteristics of TA patients with a high degree of arterial stiffness and assess the relationship between the plasma NT-proBNP levels and arterial stiffness measured according to the brachial-ankle PWV (baPWV) in patients with TA.

Methods

Patients

A total of 72 patients with TA treated at Fuwai Hospital between October 2010 and 2013 were studied. All patients fulfilled the American College of Rheumatology classification criteria for TA¹⁶⁾. Patients were excluded if they met any of the following criteria: lack of available data for the baPWV or NT-proBNP levels, heart failure, acute myocardial infarction, renal dysfunction (serum creatine > 1.5 mg/dL), other inflammatory diseases and an ankle brachial index (ABI) of <0.9 (**Fig. 1**). The study protocol was approved by the Institutional Ethics Committee of Fuwai Hospital and all participants provided their informed consent.

Classification Criteria

TA is classified into four types according to the criteria of Lupi-Herrera: Type I, arteritis affecting the aortic arch and its main branches; Type II, arteritis affecting the thoracic and abdominal aorta; Type III, arteritis affecting the whole aorta; and Type IV, arteritis affecting the pulmonary artery¹⁷⁾.

Disease Activity Assessment

Clinically active disease was diagnosed if the patient presented with the new onset or worsening of at least two of the following features: (1) systemic symptoms without infection; (2) characteristics of vascular ischemia or inflammation, such as claudication, vascular pain (carotidynia), bruit or asymmetry in pulses and/or blood pressure; (3) an increased erythrocyte sedimentation rate (ESR); and (4) typical angio-

Fig. 1. Flow diagram of the inclusion and exclusion of the participants.

BaPWV: brachial-ankle pulse wave velocity; NT-proBNP: N-terminal pro-brain natriuretic peptide; ABI: ankle-brachial pressure index; AMI: acute myocardial infarction; HF: heart failure; RD: renal dysfunction; RA: rheumatoid arthritis; AS: ankylosing spondylitis

graphic characteristics¹⁸⁾.

Measurement of baPWV

The baPWV was measured using a validated oscillometric device (BP-203RPE III [VP-1000], Omron, Japan), which simultaneously recorded blood pressure, ABI and electrocardiogram findings¹⁹⁾. The patients were examined in the supine position after five minutes of bed rest in a quiet, temperature-controlled room. In our analysis, we used the mean values for the bilateral baPWV and ABI and the higher value of the brachial blood pressure. The patients were divided into the high-baPWV group and low-baPWV group according to the mean baPWV value.

Laboratory Tests

Blood samples were collected from the participants after an overnight fast for measurement of the complete blood count, ESR, high-sensitivity C-reactive protein (hs-CRP) and NT-proBNP levels and other biochemical indexes. The ESR and hs-CRP values were determined according to the Westergren method and immunonephelometry, respectively. The NT-proBNP level was determined using specific NT-proBNP assay kits (Biomedica, Vienna, Austria). The intra- and inter-assay coefficients of variation were below 5% and 10%, respectively.

Table 1. Demographic and clinical characteristics of the 72 patients with TA

Age, years	34.5 ± 11.9	Uric acid, μmol/L	292.0 ± 74.2
Female, n (%)	62 (86.1%)	Triglyceride, mmol/L	1.1 (0.8-1.5)
Height, cm	162.7 ± 7.6	Total cholesterol, mmol/L	4.4 ± 1.2
Body weight, kg	61.8 ± 10.1	HDL-C, mmol/L	1.4 ± 0.4
BMI, kg/m ²	23.3 ± 3.4	LDL-C, mmol/L	2.6 ± 0.9
Disease duration, years	5.0 (1.0-10.8)	ESR, mm/h	10.0 (7.0-17.0)
Hypertension, n (%)	40 (55.6%)	Hs-CRP, mg/L	2.6 (0.9-8.5)
Diabetes mellitus, n (%)	4 (5.6%)	NT-proBNP, pmol/L	751.1 ± 326.5
Hyperlipidemia, n (%)	16 (22.2%)	BaPWV, cm/s	1424.1 ± 431.2
Systolic BP, mmHg	130.4 ± 24.4	ABI	1.1 ± 0.1
Diastolic BP, mmHg	71.0 ± 16.3	Clinical classification, n (%)	
Mean BP, mmHg	94.3 ± 18.8	Type I	30 (41.7%)
Pulse Pressure, mmHg	61.8 ± 16.1	Type II	18 (25.0%)
Heart rate, beats/min	77.9 ± 13.2	Type III	21 (29.2%)
WBC counts, × 10 ⁹ /L	8.3 ± 3.0	Type IV	3 (4.2%)
RBC counts, × 10 ¹² /L	4.4 ± 0.6	Medications at discharge, n (%)	
Hemoglobin, g/L	123.4 ± 21.4	Prednisone	60 (83.3%)
Platelet counts, × 10 ⁹ /L	255.6 ± 80.0	Aspirin	52 (72.2%)
Albumin, g/L	42.2 ± 3.4	ACEIs	9 (12.5%)
ALT, IU/L	17.9 ± 9.3	ARBs	10 (13.9%)
AST, IU/L	16.1 ± 5.6	β-Blockers	39 (54.2%)
Fasting glucose, mmol/L	4.7 ± 0.9	Calcium channel blockers	29 (40.3%)
Serum creatinine, mg/dL	0.7 ± 0.2	Diuretics	8 (11.1%)
Blood urea nitrogen, mmol/L	5.0 ± 1.3	Statins	19 (26.4%)

The data are presented as the mean ± SD or median (interquartile range) and number (percentage).

BMI: body mass index; BP: blood pressure; WBC: white blood cell; RBC: red blood cell; ALT: alanine aminotransferase; AST: aspartate aminotransferase; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; ESR: erythrocyte sedimentation rate; Hs-CRP: high-sensitivity C-reactive protein; NT-proBNP: N-terminal pro-brain natriuretic peptide; BaPWV: brachial-ankle pulse wave velocity; ABI: ankle-brachial pressure index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker

Statistical Analysis

The Kolmogorov-Smirnov test was used to evaluate the normality of the distribution of continuous data. Continuous variables are presented as the mean ± standard deviation or median (interquartile range), and categorical variables are expressed as the total number (percentage). Differences between the groups were assessed using the independent-*t* test or Mann-Whitney *U*-test for continuous data and the chi-square test or Fisher's exact test for categorical data. Correlations between the baPWV values and other variables were analyzed using Pearson or Spearman correlation coefficients. A stepwise multiple linear regression analysis was used to investigate independent determinants of the baPWV values in the patients with TA. A two-sided significance level of 0.05 was used in all analyses (SPSS 17.0; SPSS Inc., Chicago, Illinois, USA).

Results

Patient Characteristics

The demographic and clinical characteristics of the 72 patients with TA are shown in **Table 1**. The average age of the patients with TA was 34.5 ± 11.9 years and 86.1% were women. A total of 30 patients (41.7%) were in the active phase of the disease, and the median disease duration was 5.0 (1.0-10.8) years. Based on the classification criteria, Type I disease (41.7%) was most frequent in the patients with TA. Comorbidities included hypertension (55.6%), diabetes (5.6%) and hyperlipidemia (22.2%). Sixty patients (83.3%) were treated with prednisone at a mean daily dose of 18.4 ± 10.7 mg.

Comparison of the Patient Characteristics between the High-baPWV and Low-baPWV Groups

The demographic and clinical characteristics of the patients in the high-baPWV and low-baPWV groups are presented in **Table 2**. Twenty-four patients

Table 2. Comparisons of the patient characteristics between the high-baPWV and low-baPWV groups

	High baPWV group (<i>n</i> = 24)	Low baPWV group (<i>n</i> = 48)	<i>p</i> value
Age, years	36.6 ± 12.0	33.4 ± 11.9	0.284
Female, <i>n</i> (%)	23 (95.8%)	39 (81.3%)	0.149
Height, cm	161.2 ± 4.9	163.5 ± 8.6	0.155
Body weight, kg	63.7 ± 8.0	60.9 ± 11.0	0.269
BMI, kg/m ²	24.5 ± 3.0	22.7 ± 3.5	0.035
Disease duration, years	4.5 (0.9-14.3)	5.0 (1.0-10.0)	0.971
Hypertension, <i>n</i> (%)	19 (79.2%)	21 (43.8%)	0.004
Diabetes mellitus, <i>n</i> (%)	2 (8.3%)	2 (4.2%)	0.597
Hyperlipidemia, <i>n</i> (%)	9 (37.5%)	7 (14.6%)	0.027
Active disease, <i>n</i> (%)	15 (62.5%)	15 (31.3%)	0.011
Systolic BP, mmHg	146.0 ± 26.1	122.6 ± 19.6	<0.001
Diastolic BP, mmHg	81.4 ± 19.2	65.8 ± 11.8	0.001
Mean BP, mmHg	107.6 ± 22.0	87.6 ± 12.7	<0.001
Pulse Pressure, mmHg	66.5 ± 15.0	59.4 ± 16.3	0.081
Heart rate, beats/min	79.3 ± 14.5	77.3 ± 12.6	0.556
WBC counts, × 10 ⁹ /L	8.9 ± 3.6	8.0 ± 2.6	0.256
RBC counts, × 10 ¹² /L	4.4 ± 0.6	4.4 ± 0.5	0.667
Hemoglobin, g/L	124.0 ± 24.0	123.1 ± 20.2	0.862
Platelet counts, × 10 ⁹ /L	260.2 ± 79.3	253.3 ± 81.1	0.735
Albumin, g/L	42.2 ± 3.2	42.2 ± 3.5	0.967
ALT, IU/L	19.2 ± 8.0	17.3 ± 9.9	0.430
AST, IU/L	16.0 ± 4.7	16.2 ± 6.0	0.860
Fasting glucose, mmol/L	5.0 ± 1.2	4.5 ± 0.7	0.058
Serum creatinine, mg/dL	0.7 ± 0.1	0.7 ± 0.2	0.485
Blood urea nitrogen, mmol/L	4.8 ± 1.4	5.1 ± 1.3	0.382
Uric acid, μmol/L	296.0 ± 73.4	290.1 ± 75.2	0.752
Triglyceride, mmol/L	1.2 (0.8-1.6)	1.0 (0.8-1.4)	0.788
Total cholesterol, mmol/L	4.9 ± 1.5	4.2 ± 1.0	0.030
HDL-C, mmol/L	1.4 ± 0.4	1.4 ± 0.4	0.980
LDL-C, mmol/L	2.9 ± 1.1	2.4 ± 0.8	0.074
ESR, mm/h	12.5 (6.3-22.5)	10.0 (7.0-16.8)	0.409
Hs-CRP, mg/L	5.4 (1.0-11.7)	2.3 (0.9-5.4)	0.099
NT-proBNP, pmol/L	864.6 ± 381.3	694.4 ± 282.9	0.036
BaPWV, cm/s	1904.0 ± 408.4	1184.1 ± 151.0	<0.001
ABI	1.1 ± 0.2	1.1 ± 0.1	0.816

(33.3%) were classified into the high-baPWV group according to the mean baPWV value. Hypertension ($p=0.004$) and hyperlipidemia ($p=0.027$) were more frequent in the high-baPWV group than in the low-baPWV group. The body mass index ($p=0.035$), systolic blood pressure ($p<0.001$), diastolic blood pressure ($p=0.001$), mean blood pressure ($p<0.001$), plasma NT-proBNP levels ($p=0.036$) and total cholesterol levels ($p=0.030$) were significantly higher in the high-baPWV group than in the low-baPWV group. More patients were prescribed calcium channel blockers ($p=0.001$) and statins ($p=0.008$) in the high-baPWV

group than in the low-baPWV group.

Correlations between the baPWV Values and Other Variables

The correlations between the baPWV values and other clinical parameters are shown in **Table 3**. The baPWV values positively correlated with body mass index ($r=0.251$, $p=0.034$), systolic blood pressure ($r=0.422$, $p<0.001$), diastolic blood pressure ($r=0.373$, $p=0.001$), mean blood pressure ($r=0.474$, $p<0.001$) and the plasma NT-proBNP levels ($r=0.382$, $p=0.001$) in the patients with TA.

(Cont Table 2)

	High baPWV group (<i>n</i> = 24)	Low baPWV group (<i>n</i> = 48)	<i>p</i> value
Clinical classification, <i>n</i> (%)			0.249
Type I	9 (37.5%)	21 (43.8%)	
Type II	9 (37.5%)	9 (18.8%)	
Type III	6 (25.0%)	15 (31.3%)	
Type IV	0 (0%)	3 (6.3%)	
Medications at discharge, <i>n</i> (%)			
Prednisone	22 (91.7%)	38 (79.2%)	0.314
Aspirin	15 (62.5%)	37 (77.1%)	0.193
ACEIs	5 (20.8%)	4 (8.3%)	0.149
ARBs	6 (25.0%)	4 (8.3%)	0.074
β -Blockers	16 (66.7%)	23 (47.9%)	0.132
Calcium channel blockers	16 (66.7%)	13 (27.1%)	0.001
Diuretics	1 (4.2%)	7 (14.6%)	0.255
Statins	11 (45.8%)	8 (16.7%)	0.008

The data are presented as the mean $\pm$ SD or median (interquartile range) and number (percentage).

BMI: body mass index; BP: blood pressure; WBC: white blood cell; RBC: red blood cell; ALT: alanine aminotransferase; AST: aspartate aminotransferase; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; ESR: erythrocyte sedimentation rate; Hs-CRP: high-sensitivity C-reactive protein; NT-proBNP: N-terminal pro-brain natriuretic peptide; BaPWV: brachial-ankle pulse wave velocity; ABI: ankle-brachial pressure index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker

As for the disease activity, the baPWV values were significantly higher in the patients with active disease ($1,568.9 \pm 465.6$ cm/s) than in those in remission ($1,320.7 \pm 377.2$ cm/s, $p=0.015$). However, there were no significant correlations between the baPWV values and inflammatory markers, such as the ESR ($r=0.076$, $p=0.527$) and hs-CRP ($r=0.210$, $p=0.077$) levels.

Multivariate Regression Analysis of Determinants of baPWV

A stepwise multiple linear regression analysis showed that the mean blood pressure (standardized coefficient=0.515, $p<0.001$), age (standardized coefficient=0.345, $p=0.002$) and NT-proBNP levels (standardized coefficient=0.316, $p=0.002$) were independently associated with the baPWV values in the patients with TA after adjusting these parameters for the body mass index, total cholesterol level and use of calcium channel blockers and statins (Table 4).

Discussion

The present results showed the mean blood pressure, age and NT-proBNP level to be independent determinants of a high degree of arterial stiffness assessed according to the ba-PWV in patients with TA.

It is well established that TA is associated with accelerated atherosclerosis resulting in increased CV morbidity and mortality²⁻⁴. Therefore, detecting the early signs of CVD is important so that effective protective therapy against CV can be implemented⁸. As a composite index of deleterious effects on the vascular system, the PWV is a valuable tool for assessing early vascular dysfunction²⁰. It has previously been demonstrated that the degree of arterial stiffness measured based on the carotid-femoral PWV (cfPWV) is increased in TA patients with or without traditional CV risk factors^{14, 15}. Although the cfPWV is currently recognized to be the most prevalent index for assessing arterial stiffness, the procedure is not simple and specialized techniques are required. Recent studies have demonstrated that arterial stiffness can also be measured simply using the brachial-ankle PWV (baPWV), which has been shown to strongly correlate with the aortic PWV and can be used for CV risk stratification^{19, 21, 22}.

The NT-proBNP level is traditionally considered to be a useful cardiac biomarker for diagnosing and evaluating congestive heart failure^{23, 24}. Recent evidence suggests that inflammation also affects the NT-proBNP levels. For example, the NT-proBNP levels have been found to be increased in patients with systemic inflammatory diseases, such as rheumatoid arthritis.

tis, systemic lupus erythematosus and TA^{13, 25, 26}. Previous studies have shown that an increased plasma NT-proBNP level is accompanied by the deterioration of elastic properties in patients with hypertension²⁷ and coronary artery disease²⁸ as well as in healthy individuals²⁹. In the present study, we evaluated the relationship between the NT-proBNP level and arterial stiffness and found the NT-proBNP levels to be independently associated with the baPWV values in patients with TA. There are several possible factors accounting for this association. First, increased arterial stiffness results in the earlier arrival of reflected pulse waves and increased left ventricular afterload, thus stimulating NT-proBNP release²⁷. Second, an increase in the PWV shifts pressure wave reflections from diastole to systole, leading to increased systolic blood pressure and decreased diastolic blood pressure, which subsequently increases the level of myocardial oxygen and decreases coronary perfusion³⁰. Kingwell B.A. *et al.*³¹ reported that a high degree of artery stiffness is an important determinant of the myocardial ischemic threshold, independent of major risk factors and the severity of coronary stenosis. Recent studies have also demonstrated that myocardial perfusion abnormalities on 201Tl myocardial scintigraphy and late gadolinium enhancement on cardiac magnetic resonance imaging are frequently observed in patients with asymptomatic TA^{32, 33}. Consequently, subclinical myocardial ischemia may induce the production of NT-proBNP from the intima in human coronary arteries³⁴. Hence, the alterations related to increased arterial stiffness may stimulate the synthesis and release of NT-proBNP.

Endothelial cell dysfunction and elevated arterial stiffness are associated with many rheumatic diseases in addition to increased CV mortality³⁵⁻³⁷. The association between arterial stiffness and inflammation in the setting of these rheumatic disorders remains unclear. In patients with antineutrophil cytoplasmic antibody-associated systemic vasculitis, arterial stiffness is correlated with the degree of active inflammation³⁵. However, no associations between the degree of arterial stiffness and ESR or hs-CRP values were observed in our study patients, consistent with previous findings in patients with TA^{14, 15}. In contrast with the findings of these two studies, in which the PWV was not found to be associated with the disease activity in TA patients, in our study, the patients with active disease had significantly higher baPWV values than those in remission. One explanation for this observation is that the ESR and CRP levels may not be ideal markers of the disease activity in patients with TA. It has also been reported that the ESR is elevated in only 72% of patients with clinically active disease and remains high

Table 3. Correlations between the baPWV values and other variables

Parameters	BaPWV	
	<i>r</i>	<i>p</i>
Age, years	0.217	0.067
Height, cm	-0.086	0.473
Body weight, kg	0.167	0.161
BMI, kg/m ²	0.251	0.034
Disease duration, years	0.057	0.637
Systolic BP, mmHg	0.422	<0.001
Diastolic BP, mmHg	0.373	0.001
Mean BP, mmHg	0.474	<0.001
Pulse Pressure, mmHg	0.224	0.059
Heart rate, beats/min	0.056	0.641
WBC counts, × 10 ⁹ /L	0.185	0.120
RBC counts, × 10 ¹² /L	0.111	0.352
Hemoglobin, g/L	0.107	0.369
Platelet counts, × 10 ⁹ /L	-0.041	0.734
Albumin, g/L	-0.066	0.584
ALT, IU/L	0.200	0.092
AST, IU/L	0.029	0.807
Fasting glucose, mmol/L	0.113	0.345
Serum creatinine, mg/dL	0.143	0.232
Blood urea nitrogen, mmol/L	0.053	0.656
Uric acid, μmol/L	0.077	0.521
Triglyceride, mmol/L	0.105	0.379
Total cholesterol, mmol/L	0.232	0.050
HDL-C, mmol/L	-0.015	0.898
LDL-C, mmol/L	0.210	0.076
ESR, mm/h	0.076	0.527
Hs-CRP, mg/L	0.210	0.077
NT-proBNP, pmol/L	0.382	0.001
ABI	0.076	0.526

BMI: body mass index; BP: blood pressure; WBC: white blood cell; RBC: red blood cell; ALT: alanine aminotransferase; AST: aspartate aminotransferase; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; ESR: erythrocyte sedimentation rate; Hs-CRP: high-sensitivity C-reactive protein; NT-proBNP: N-terminal pro-brain natriuretic peptide; ABI: ankle-brachial pressure index

in 56% of patients in remission, according to the analysis of the National Institutes of Health study¹⁸. Similarly, another study found active disease to be present despite normal laboratory parameters in 23% of patients with TA³⁸. Another explanation for the above finding is that the sample size of both studies was relatively small^{14, 15}. Salles R.N.N. *et al.*¹⁵ examined arterial stiffness in women with TA and comparable controls in order to reduce the influence of confounding factors. However, the objective of our study was to better

Table 4. Stepwise multiple linear regression analysis of factors associated with baPWV

	B	SE	Standardized coefficient	<i>t</i>	<i>p</i>
Constant	-618.916	348.061		-1.778	0.080
Mean BP	11.776	2.485	0.515	4.740	<0.001
Age	12.494	3.786	0.345	3.300	0.002
NT-proBNP	0.418	0.131	0.316	3.183	0.002
BMI	9.954	13.521	0.079	0.736	0.464
TC	-3.898	36.027	-0.011	-0.108	0.914
CCBs	-68.893	92.861	-0.074	-0.742	0.461
Statins	-100.325	181.983	-0.054	-0.551	0.583

BP: blood pressure; NT-proBNP: N-terminal pro-brain natriuretic peptide; BMI: body mass index; TC: total cholesterol; CCB: calcium channel blocker

understand the relationship between the NT-proBNP level and arterial stiffness under “real-world” conditions, and patients with related risk factors were not excluded from our study population. We recently demonstrated that the NT-proBNP level is a useful marker of the disease activity in patients with TA¹³⁾. In the current study, the NT-proBNP levels were higher in the high-baPWV group than in the low-baPWV group, and the univariate and multivariate analyses showed the NT-proBNP levels to be independently associated with the baPWV values in the patients with TA. These results suggest that, compared with the conventional inflammatory indexes ESR and CRP, the NT-proBNP level may correlate better with the extent of arterial injury and aortic stiffness.

In this study, we found that age and mean blood pressure are also potential risk factors for arterial stiffness based on the baPWV measurements, in agreement with previous findings in TA patients¹⁵⁾. It is well known that aging and chronic elevation of BP are associated with structural and functional alterations in the elastic properties of the arterial wall that subsequently induce profound changes in the degree of arterial stiffness³⁹⁾. Several studies have also shown that arterial stiffness is increased in both older individuals and patients with hypertension^{39, 40)}.

Several limitations associated with this study should be noted. First, this study lacked a control group to explore whether the relationship between the NT-proBNP level and arterial stiffness is specific to patients with TA. Second, more patients were prescribed calcium channel blockers and statins in the high-baPWV group than in the low-baPWV group. However, since this study was cross-sectional, it is difficult to determine whether these medications have beneficial effects on the extent of arterial stiffness and the NT-proBNP level. Therefore, our findings should be confirmed in long-term prospective studies before

any causal relationships between the plasma NT-proBNP levels and arterial stiffness in patients with TA can be established.

In conclusion, the present findings indicate that an increased plasma NT-proBNP level is independently associated with increased arterial stiffness measured according to the baPWV in patients with TA.

Conflicts of Interest/Disclosures

The authors have no conflicts of interest to declare.

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