Association between increased arterial stiffness measured by brachial-ankle pulse wave velocity and cardiovascular events in patients with Takayasu's arteritis

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ABSTRACT

Objective. *This study aims to investigate the association between arterial stiffness measured by brachial-ankle pulse wave velocity (baPWV) and cardiovascular events (CVEs) in patients with Takayasu's arteritis (TAK).*

Methods. *A total of 240 TAK patients, who underwent baPWV measurement, were included in the study. The primary outcome was CVEs, which was defined as presently or previously diagnosed with myocardial infarction, unstable angina, congestive heart failure, aortic aneurysm/dissection, cerebral infarction/transient ischaemic attack (TIA), or cerebral haemorrhage.*

Results. *A total of 74 (30.8%) patients with CVEs were included in the present cohort. Compared with the patients without CVEs, those with CVEs had a higher prevalence of hyperlipidaemia (HL), smoking history, active stage, angiographic type V, renal dysfunction (RDF), higher baPWV and high sensitive C-reactive protein (hs-CRP) level (all, $p<0.05$). The multivariate logistic regression analysis showed that HL (OR: 2.465, 95%CI: 1.308–4.648, $p=0.005$), smoking history (OR: 4.764, 95%CI: 1.623–13.985, $p=0.004$), baPWV (OR: 1.132, 95%CI: 1.063–1.204, $p<0.001$), and hs-CRP (OR: 1.111, 95%CI: 1.040–1.188, $p=0.002$) were independently associated with the presence of CVEs. The multiple linear regression analysis revealed that age ($\beta=0.100$, $p=0.002$), mean blood pressure ($\beta=0.071$, $p<0.001$), angiographic type V ($\beta=3.681$, $p<0.001$) and RDF ($\beta=1.800$, $p=0.048$) were independently correlated with baPWV.*

Conclusion. *Increased baPWV was independently associated with CVEs in patients with TAK. Age, angiographic type V, mean blood pressure and RDF were the strongest determinants for baPWV in TAK. BaPWV may be a potential maker to predict CVEs in patients with TAK.*

Introduction

Takayasu's arteritis (TAK), a non-specific chronic vasculitis with unknown aetiology, mainly involves the aorta and its major branches. The inflammation in vessel walls leads to luminal stenosis, occlusion, dilation or aneurysm formation, and eventually results in high risk of cardiovascular morbidity and mortality. Alibaz-Oner *et al*. reported that TAK patients had a higher rate of cardiovascular risk factors, when compared to age- and gender-matched controls, and TAK patients experienced more cardiovascular events (CVEs) during the seven-year follow-up (1). A Korean nationwide study indicated that the mortality of TAK patients was three times higher than that in the general population, and the most common cause of death was cardiovascular disease (2). In TAK, it has been considered that inflammation and traditional risk factors co-participate in the pathogenesis of atherosclerosis (3). Studies have also well-established that compared with the general population, TAK patients are more prone to accelerated atherosclerosis, which manifests as dysfunction of the vascular endothelium, thickening of the carotid artery intima-media, formation of atherosclerotic plaques, aortic or coronary calcifications, and increased arterial stiffness (4-6).

Pulse wave velocity (PWV) is a reliable indicator of arterial stiffness, which reflects the velocity of arterial pulse moving along the vessel wall. Studies have demonstrated that PWV is a prognostic factor for CVEs in the general population and that its predictive value is especially higher in the patients with

high risk of CVEs (7). However, it remains unclear whether arterial stiffness is associated with CVEs in TAK patients. The present study aims to investigate the relationship between increased arterial stiffness measured through the brachial-ankle pulse wave velocity (baPWV) and CVEs in patients with TAK, and assess the determinants of baPWV.

Methods

Patients

Patients diagnosed with TAK between 2009 and 2016 in Fuwai Hospital have been included in our study. TAK classification was based on the 1990 American College of Rheumatology (ACR) criteria (8). Patients were excluded when their baPWV assessment was not performed or undetected, or their ankle brachial index (ABI) was less than 0.9. According to the Hata and Numano angiographic classification criteria, TAK is classified into five types: type I, affecting major branches of the aortic arch; type IIa, affecting the ascending aorta, aortic arch and its branches; type IIb, affecting the ascending aorta, aortic arch, and/or its branches and the thoracic descending aorta; type III, affecting the thoracic descending aorta, abdominal aorta, and/or the renal arteries; type IV, affecting the abdominal aorta and/or renal arteries; type V, the combined features of type IIb and type IV (9). Disease activity was evaluated by the US National Institutes of Health (NIH) criteria: (1) systemic symptoms without other causes identified; (2) elevated erythrocyte sedimentation rate (ESR); (3) features of vascular ischaemia or inflammation, such as claudication, diminished or absent pulse, bruits, vascular pain, and asymmetric blood pressure; (4) typical angiographic features. Patients who had new onset or worsening of two or more features were considered to have active disease (10).

Data on demographics, medical history, comorbidities and medications were obtained during the interview, and by reviewing documented medical records of the patients. Hypertension (HTN) was defined as brachial blood pressure (BP) ≥140/90 mmHg or popliteal BP ≥160/90 mmHg on repeated measurements or on anti-hypertensive medication prior to enrolment. Diabetes mellitus (DM) was defined as a history of DM, fasting blood glucose (FBG) ≥7.0 mmol/L, or the use of antidiabetic drugs. Hyperlipidaemia (HL) was defined as an abnormal lipid profile (triglycerides [TG] >2.26 mmol/L, total cholesterol [TC] >5.18 mmol/L, or low density lipoprotein cholesterol [LDL-C] >3.37 mmol/L), or on lipid-lowering therapy. Renal dysfunction (RDF) was defined as an estimated glomerular filtration rate (eGFR) of <90 ml/min/1.73 m^2. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was used to calculate the eGFR.

The presence of CVEs was defined as a previous history of myocardial infarction, unstable angina, congestive heart failure, aortic aneurysm/dissection, cerebral infarction/transient ischaemic attack (TIA) or cerebral haemorrhage, or newly diagnosed with these diseases on discharge. Myocardial infarction was defined as having elevated myocardial enzymes together with typical symptoms or dynamic changes of electrocardiogram or imaging evidence of myocardial ischaemia. Unstable angina was defined as patients admitted with typical chest pain that lasted for more than 10 minutes, but with negative biomarkers of necrosis. Congestive heart failure was defined as having a left ventricular ejection fraction of ≤40% or presenting with typical clinical symptoms. Cerebral infarction and haemorrhage was diagnosed as having a focal neurological deficit with a computed tomography or magnetic resonance, confirming an infarct or haemorrhage. Aneurysm was defined as a ≥50% dilation of the normal arterial diameter, and aortic dissection was defined as having an image indicating the separation of the lamellae in the aortic wall. A trained research physician reviewed all the medical records and interviewed all patients, confirming the above diagnosis. All patients were divided into two groups according to whether they had CVEs or not. The research conforms to the ethical guidelines of the 1975 Declaration of Helsinki. The study protocol was approved by the Ethics Committee of Fuwai Hospital.

Clinical data and laboratory tests

Patients fasted overnight and their blood samples were collected in the morning for the measurement of fasting plasma glucose (FBG), TC, TG, high-density lipoprotein cholesterol (HDL-C), LDL-C, serum creatinine, and high sensitive C-reactive protein (hs-CRP) by an auto analyser (HITACHI-7170, Hitachi, Tokyo). Erythrocyte sedimentation rate (ESR) was measured using the Westergren method.

BaPWV measurement

BaPWV was measured on the same day or the next day when the blood samples were collected. BaPWV, ABI, blood pressure of four limbs, and heart rate were simultaneously measured with an automated oscillometric analyser (BP-203RPEIII [VP-1000], Omron, Japan) according to manufacturer's instruction. Briefly, all patients were examined in the supine position after at least five minutes of rest in a quiet, temperature-controlled room. Cigarette, caffeine, alcohol and medications were prohibited for at least eight hours before the baPWV measurement. Blood pressure cuffs were wrapped around the right and left arms and ankles. Electrocardiogram electrodes were bilaterally placed on the wrists, and the microphone was placed on the left edge of the sternum, to detect the heart sounds. The brachial and ankle pulse-volume waveforms were recorded by the semiconductor pressure sensors, and the bilateral baPWV was automatically calculated. ABI, blood pressure and heart rate were recorded at the same time as the evaluation of the baPWV. The higher values of blood pressure on the bilateral upper limbs, as well as the mean value of the bilateral baPWV and ABI were taken into analysis.

Statistical analysis

Statistical analysis was made using the SPSS 21.0 statistical package for Windows. Figures were presented using GraphPad Prism version 6.01. Quantitative data were expressed as mean ± standard deviation (SD) for normal distribution or median (interquartile range, IQR) for non-normal distribution. The distribution of continuous variable was

Table I. Demographic and clinical characteristics of 240 TAK patients.

Variables	Total patients, n=240
Age, years	34 (24-44)
Females, n (%)	200 (83.3)
Disease duration, months	35 (6-120)
Hypertension, n (%)	160 (66.7)
Diabetes mellitus, n (%)	9 (3.8)
Hyperlipidaemia, n (%)	76 (31.7)
Cigarette smoking, n (%)	18 (7.5)
Family history of CVD, n (%)	59 (24.6)
Active stage, n(%)	64 (26.7)
BMI, kg/m^2	22.7±3.3
Angiographic classification, n I/IIa/IIb /III/IV/V	55/9/11/7/46/112
SBP, mmHg	127 (110-150)
DBP, mmHg	69 (60-85)
MBP, mmHg	88 (77-105)
ABI	1.11 (1.02-1.25)
Heart rate, bpm	78 (70-89)
baPWV, m/s	13.35 (11.31-16.43)
Haemoglobin, g/L	126.7±19.5
FBG, mmol/L	4.64 (4.29-5.05)
eGFR, ml/kg/1.73m^2	107.8 (91.9-120.3)
ESR, mm/H	10 (5-23)
hs-CRP, mg/L	2.16 (0.85-7.56)
TG, mmol/L	1.07 (0.83-1.50)
TC, mmol/L	4.27 (3.59-4.95)
HDL-C, mmol/L	1.26 (1.06-1.59)
LDL-C, mmol/L	2.43 (1.93-2.98)
Medicines pre-enrolment, n (%)	
Corticosteroids	65 (27.1)
Antiplatelet agents	63 (26.3)
Statins	27 (11.3)
CCB	77 (32.1)
β Blockers	64 (26.7)
ACEI/ARB	57 (23.8)
Diuretics	30 (12.5)

The data are presented as the mean±SD or median (IQR) and number (percentage).
TAK: Takayasu's arteritis; CVD: cardiovascular disease; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; MBP: mean blood pressure; ABI: ankle brachial index; baPWV: brachial ankle pulse wave velocity; FBG: fasting blood glucose; eGFR: estimated glomerular filtration rate; ESR: erythrocyte sedimentation rate; hsCRP: high sensitive C-reactive protein; TG: triglyceride; TC: total cholesterol; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; CCB: calcium channel blockers; ACEI: angiotensin converting enzyme inhibitors; ARB: angiotensin receptor blocker.

evaluated by the Kolmogorov-Smirnov test. Differences between two groups were compared by independent *t*-test or Mann-Whitney U-test, as appropriate. Categorical data were presented as a number (percentage). Differences between the two groups were compared by the chi-square or Fisher's exact test. The multivariate logistic regression, which included variables (HL, cigarette smoking, active stage, angiographic classification, baPWV, RDF, hs-CRP and medications) related to CVEs in the univariate analysis, was used to analyse the independent determinants of CVEs in TAK, and the odds ratio (OR) and 95% confidence interval (CI) were provided. Angiographic type V *vs*. non-angiographic type V was chosen for the angiographic type in the multivariate logistic regression. Spearman correlation coefficients and probability were conducted to analyse the relationship between baPWV and other variables. Multivariate linear regression was used to analyse the independent determinants of baPWV. Mean blood pressure was selected to represent blood pressure in the multivariate model. Variables with a significance of <0.05 in the univariate analysis were included in the multivariate analysis. The receiver-operating characteristic (ROC) curve analysis was performed to determine the optimal cut-off value of baPWV for predicting CVEs. A *p*-value with two-sides <0.05 was indicated to be statistically significant.

Results

Demographic and clinical characteristics of the 240 TAK patients

The demographic and clinical characteristics of all TAK patients are listed in Table I. A total of 240 TAK patients, with a mean age of 34 years (IQR 24-44), were included in the present study, and the median disease duration was 35 (IQR 6–120) months. The male-to-female ratio was 1:5. According to the angiographic classification, angiographic type V was the most common type (112, 46.7%), followed by type I (55, 22.9%), type IV (46, 19.2%), type IIb (11, 4.6%), type IIa (9, 3.8%), and type III (7, 2.9%). The median baPWV was 13.35 (IQR 11.31–16.43) m/s. A total of 74 (30.8%) patients had CVEs. Among these patients, 7 (9.5%) patients had myocardial infarction, 24 (32.4%) patients had unstable angina, 14 (18.9%) patients had aortic aneurysm or dissection, 18 (24.3%) patients had congestive heart failure, 23 (31.1%) patients had cerebral infarction/TIA, and 4 (5.4%) patients had cerebral haemorrhage.

Differences between patients with and without CVEs

The differences in demographic and clinical characteristics between patients with and without CVEs are presented in Table II. HL (45.9% *vs*. 25.3%, *p*=0.001), smoking history (14.9% *vs*. 4.2%, *p*=0.004), active disease at admission (36.5% *vs*. 22.3%, *p*=0.022), angiographic type V (59.5% *vs*. 41.0%, *p*=0.008), and RDF (33.8% *vs*. 17.5%, *p*=0.005) were more prevalent in patients with CVEs, when compared to patients without CVEs. The median baPWV (15.05[12.47-21.26] m/s *vs*. 12.75[11.12–14.69] m/s, *p*<0.001) and hs-CRP (4.09 [1.23–10.88] mg/L *vs*. 1.87 [0.75–5.55] mg/L, *p*=0.001) were also significantly higher in patients with CVEs than those without. In terms of medications, antiplatelet agents (44.6% *vs*. 18.1%, *p*<0.001), statins (29.7% *vs*. 3.0%, *p*<0.001), β-blockers (35.1% *vs*. 22.9%, *p*=0.048), and diuretics (18.9% *vs*. 9.6%, *p*=0.045) were more frequently prescribed in patients with CVEs, while no difference was observed in the prescription of corticosteroids (24.3% *vs*. 28.3%, *p*=0.521) between patients with CVEs and those without.

Multivariate logistic regression analysis of determinants for CVEs

The multivariate logistic regression analysis revealed that the presence of HL (OR: 2.465, 95%CI 1.308-4.648, *p*=0.005), smoking history (OR: 4.764, 95%CI 1.623–13.985, *p*=0.004), higher baPWV (OR: 1.132, 95%CI 1.063–1.204, *p*<0.001) and higher hs-CRP (OR: 1.111, 95%CI 1.040–1.188, *p*=0.002) were significantly associated with an increased risk of CVEs.

Cut off value for baPWV in prediction of CVEs

The ROC curve analysis showed that the optimal cut-off value of baPWV for CVEs was 16.26 m/s (area under the curve [AUC]: 0.672, 95% CI: 0.594–0.750, *p*<0.001; Fig. 1); sensitivity and specificity were 45.9% and 83.7%, respectively.

The correlation between baPWV and other variables

The univariate linear regression analy-

Table II. Comparisons of the characteristics of the TAK patients with and without CVEs.

Variables	TAK with CVEs n=74	TAK without CVEs n=166	*p*-value
Age, years	37 (26-45)	34 (24-44)	0.333
Females, n (%)	58 (78.4)	142 (85.5)	0.169
Disease duration, months	58 (6-144)	26 (6-117)	0.245
Hypertension, n (%)	49 (66.2)	111 (66.9)	0.921
Diabetes mellitus, n (%)	4 (5.4)	5 (3.0)	0.463
Hyperlipidaemia, n (%)	34 (45.9)	42 (25.3)	0.001
Cigarette smoking, n (%)	11 (14.9)	7 (4.2)	0.004
Family history of CVD, n (%)	17 (23.0)	42 (25.3)	0.699
Active stage, n (%)	27 (36.5)	37 (22.3)	0.022
BMI, kg/m^2	22.7 ± 3.2	22.6 ± 3.4	0.880
Angiographic classification, n (%)			
Type I	10 (13.5)	45 (27.1)	0.021
Type IIa	5 (6.8)	4 (2.4)	0.139
Type IIb	3 (4.1)	8 (4.8)	>0.999
Type III	1 (1.4)	6 (3.6)	0.442
Type IV	11 (14.9)	35 (21.1)	0.258
Type V	44 (59.5)	68 (41.0)	0.008
SBP, mmHg	123 (105-150)	128 (112-149)	0.425
DBP, mmHg	67 (57-89)	71 (61-85)	0.201
MBP, mmHg	87 (75-106)	90 (78-105)	0.387
ABI	1.12 (1.02-1.33)	1.11 (1.02-1.23)	0.353
Heart rate, bpm	80 (68-89)	77 (70-88)	0.507
baPWV, m/s	15.05 (12.47-21.26)	12.75 (11.12-14.69)	<0.001
Haemoglobin, g/L	126.3±20.0	126.8±19.3	0.829
FBG, mmol/L	4.59 (4.33-5.18)	4.66 (4.24-5.04)	0.565
eGFR, ml/kg/1.73m^2	102.6 (83.6-118.3)	110.3 (97.3-120.6)	0.010
RDF, n (%)	25 (33.8)	29 (17.5)	0.005
ESR, mm/H	13 (5-31)	9 (5-19)	0.116
Hs-CRP,mg/L	4.09 (1.23-10.88)	1.87 (0.75-5.55)	0.001
TG, mmol/L	1.07 (0.84-1.45)	1.07 (0.81-1.52)	0.827
TC, mmol/L	4.13 (3.26-4.78)	4.35 (3.70-4.97)	0.046
HDL-C, mmol/L	1.16 (0.97-1.36)	1.34 (1.10-1.62)	0.001
LDL-C, mmol/L	2.39 (1.82-3.11)	2.45 (1.98-2.97)	0.278
Medicines pre-admission, n (%)			
Corticosteroid	18 (24.3)	47 (28.3)	0.521
Antiplatelet agents	33 (44.6)	30 (18.1)	<0.001
Statins	22 (29.7)	5 (3.0)	<0.001
CCB	20 (27.0)	57 (34.3)	0.263
β Blockers	26 (35.1)	38 (22.9)	0.048
ACEI/ARB	15 (20.3)	42 (25.3)	0.398
Diuretics	14 (18.9)	16 (9.6)	0.045

The data are presented as the mean ± SD or median (IQR) and number (percentage).
TAK: Takayasu's arteritis; CVE: cardiovascular events; CVD: cardiovascular disease; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; MBP: mean blood pressure; ABI: ankle brachial index; baPWV: brachial-ankle pulse wave velocity; FBG: fasting blood glucose; eGFR: estimated glomerular filtration rate; RDF: renal dysfunction; ESR: erythrocyte sedimentation rate; hsCRP: high sensitive C reactive protein; TG: triglyceride; TC :total cholesterol; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; CCB: calcium channel blockers; ACEI: angiotensin converting enzyme inhibitors; ARB: angiotensin receptor blocker.

sis indicated that age, disease duration, HTN, HL, active disease, body mass index, angiographic type V, mean blood pressure, RDF and hs-CRP were associated with baPWV (all, $p<0.050$; Table III). The stepwise multiple regression analysis revealed that only age (β=0.100, $p=0.002$), mean blood pressure (β=0.071, $p<0.001$), angiographic type V (β=3.681, $p<0.001$) and RDF (β=1.800, $p=0.048$) were independently correlated with baPWV (Table III).

Discussion

To the best of our knowledge, the present study was the first and largest one to explore the relationship between increased arterial stiffness and CVEs in TAK patients. Our study identified that increased baPWV was an independent risk factor for CVEs in TAK patients. Age, blood pressure, angiographic type V, and RDF were the strongest determinants for arterial stiffness measured by baPWV in these patients.

TAK patients had a higher prevalence of cardiovascular risk factors, and dramatically experienced more CVEs, when compared to the general population (1, 11, 12). Inflammatory response contributes to platelet hyperactivity, increasing the risk of acute CVEs (13). Evidence has also implicated that the function of platelet and fibrinogen were enhanced in TAK, leading to a higher incidence of thrombosis events (14). Coronary artery disease has been reported to be present in 10–20% of TAK patients, and cerebrovascular disease could occur in 10% of TAK patients (1, 15, 16). In the present study, nearly 28.4% of patients presented with CVEs, and the most common types were unstable angina and cerebral infarction/TIA, followed by congestive heart failure, aortic aneurysm or dissection, myocardial infarction and cerebral haemorrhage. Cardiovascular complications predisposed TAK patients to a higher mortality (17-19). Early identifying patients who were at higher risk of CVEs would be beneficial to improve the prognosis in TAK.

Arterial stiffness has been recognised as an independent predictor for cardiovascular disease and all-cause mortality in the general population (20, 21). BaPWV was one of the most common methods to evaluate arterial stiffness in clinical practice. However, studies regarding PWV in TAK are limited. The first study on PWV in TAK was conducted by Ng *et al*., in which merely 10 TAK patients were enrolled (6). In their study, the carotid-femoral pulse wave velocity (cfPWV) and augmentation index increased in TAK patients. Our study included a larger number of patients, and confirmed that TAK patients had increased arterial stiffness, as measured by baPWV. The median value of baPWV was 13.35 m/s in the present study, which was higher than the age-matched reference values of baPWV (12.0 m/s) in an Asian population proposed by Yiming *et al*. (22). And the results of our research further revealed that increased arterial stiffness was independently associated with

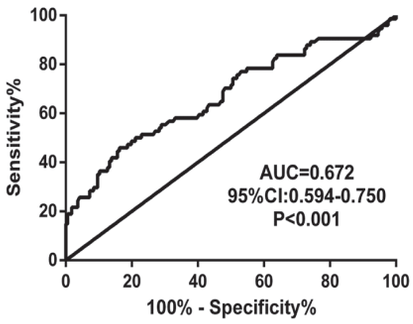

Fig. 1. ROC curve illustrating baPWV in the prediction of CVEs.
ROC: receiver-operator-characteristics; AUC: areas under the curve; CI: confidence intervals; baPWV: brachial-ankle pulse wave velocity; CVEs: cardiovascular events.

Table III. Uni- and multivariate linear analysis of correlations between clinical variables and baPWV in TAK patients.

Variables	Univariable analysis		Multivariable analysis	
	r	*p*	β	*p*
Age	0.272	<0.001	0.100	0.002
Females	-0.073	0.257		
Disease duration	0.192	0.003		
Hypertension	0.316	<0.001		
Diabetes mellitus	0.121	0.062		
Hyperlipidaemia	0.190	0.003		
Cigarette smoking	0.080	0.215		
Family history of CVD	0.124	0.055		
Active stage	0.148	0.022		
BMI	0.228	<0.001		
Angiographic Type V	0.298	<0.001	3.681	<0.001
MBP	0.218	0.001	0.071	<0.001
Heart rate	0.110	0.088		
Hb	0.055	0.396		
FBG	0.103	0.111		
RDF	0.189	0.003	1.800	0.048
ESR	0.107	0.099		
hs-CRP	0.233	<0.001		
Corticosteroid	0.001	0.989		
Antiplatelet agents	-0.048	0.458		
Statins	0.100	0.121		
CCB	0.126	0.051		
β Blocker	0.039	0.549		
ACEI/ARB	-0.095	0.143		
Diuretics	-0.042	0.514		

TAK: Takayasu's arteritis; baPWV: brachial-ankle pulse wave velocity; CVD: cardiovascular disease; BMI: body mass index; MBP: mean blood pressure; Hb: haemoglobin; FBG: fasting blood glucose; RDF: renal dysfunction; ESR: erythrocyte sedimentation rate; hsCRP: high sensitive C-reactive protein; CCB: calcium-channel blockers; ACEI: angiotensin-converting enzyme inhibitors; ARB: angiotensin receptor blocker.

the presence of CVEs in TAK patients. This result was in line with the previous study conducted by our colleagues, which suggested that baPWV was an independent risk factor for adverse cardiac events and in-stent restenosis in TAK patients with percutaneous coronary intervention (23). Taken together, baPWV may serve as a potential predictor of CVEs in patients with TAK.

The association between baPWV and CVEs in TAK patients is complex. Increased arterial stiffness could lead to enhanced pressure wave reflection, resulting in augmented central blood pressure and ventricular workload, thereby conferring an increased risk of heart failure (24, 25). Perfusion of coronary artery could also be influenced by the abnormal wave reflection, leading to ischaemia of the coronary arteries (24, 26). Arterial stiffening also contributes to the elevated pulse pressure, which is recognised as a strong predictor of adverse cardiovascular disease events, including cardiovascular death, non-fatal stroke, and non-fatal myocardial infarction (27). Pulse pressure mediates the progression of atherosclerosis and induces the instability of atherosclerotic plaques, consequently participating in the pathogenesis of atherosclerosis and contributing to acute vascular complications (28, 29). Atherosclerosis impairs the arterial wall, and also exaggerates arterial stiffening (30). This vicious circle amplifies the correlation of arterial stiffness and cardiovascular events. Arterial stiffness may be the consequence of inflammation lesions of the affected arterial wall in TAK. Activated immune cells infiltrate, penetrating all layers of the affected vessel walls, and accelerating the production of proteases, such as matrix metalloproteinases (MMPs). This results in the destruction of elastic fibres in the vessel walls, thereby contributing to arterial stiffening (31-34). A previous study also confirmed that the TAK itself was an independent risk factor of arterial stiffness. In a strictly selected study of arterial stiffness in TAK patients, whose age, SBP and other clinical factors were comparable to the controls, Salles Rosa Neto *et al*. reported that the disease itself and MBP were the strongest determinants of cfPWV (35). Similar to their results, the present study also found that age, angiographic type V, MBP and RDF were independent risk factors of arterial stiffness, as measured by baPWV. Traditional cardiovascular risk factors, such as age, MBP and RDF also promote arterial stiffness in TAK. Advancing age accompanied by the physiological degeneration of arterial elasticity was observed in the general population, as well as in TAK patients (35, 36). Hypertension was one of the most common complications of TAK. The long-term elevation of MBP caused by the stenosis of the renal artery or aortic coarctation leads to decreased vascular compliance. Decreased renal function, as a result of renal artery involvement, also drives arterial stiffening through diffuse calcification in vessels (37, 38). Angiographic type V was another independent factor associated with baPWV in our study, implicating the more extensive involvement of the artery, and the more stiffening of arteries in TAK. Overall, the disease itself and traditional cardiovascular risk factors could accelerate the arterial stiffness in TAK (3, 35). As a simple measurement in clinical practice, baPWV could reflect the arterial stiffness of TAK, and may be a prognostic tool for CVEs.

Restricted by the cross-sectional nature of the present study, patients with previously diagnosed cardiovascular disease have been on antiplatelet agents, statins, β-blockers and diuretics before enrolment into the present study, thus leading to the higher usage of medications in patients with CVEs. Although these medications may exert a favourable effect on arterial stiffness (39, 40), baPWV remained higher in TAK patients present with CVEs than those absent. In the present analysis, baPWV was significantly associated with the presence of CVEs, but was independent of medication use. Therefore, the difference in medications in the present study may not affect these final conclusions. In addition, if present, this would have caused an underestimation of the associations.

Limitations

The major limitation of our research was its cross-sectional study design. Prospective studies are necessary to confirm the predictive value of baPWV for CVEs. Moreover, patients with an ABI of <0.9 and undetectable baPWV were not included in our study. Therefore, the conclusion of our study may not be applicable to the general population of TAK patients. Additionally, as in any observational studies, the possibility of confounding could not be ruled out, such as pre-hospital medications, although adjustments were attempted for these confounders. Regardless of these shortcomings, our study still illustrates the role of baPWV in assessing CVEs and its correlation factors in TAK in a relatively large sample size.

Conclusions

The present study indicated that the increased arterial stiffness measured by baPWV was independently associated with CVEs in patients with TAK. Traditional risk factors and TAK-related factors together correlated with baPWV in TAK. BaPWV is a simple and useful indicator for evaluating arteriosclerosis and may be a potential maker for predicting CVEs in TAK. However, prospective studies are needed to verify the role of baPWV in predicting CVEs in TAK.

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