Original paper

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Assessment of the arterial stiffness in patients with acute ischemic stroke using longitudinal elasticity modulus measurements obtained with Shear Wave Elastography.

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Abstract

Aim: Arterial wall elasticity including the circumferential and longitudinal modulus is a measure of sub-clinical cardiovascular disease; the circumferential modulus is increased in acute ischemic stroke (AIS). There are still no reports of non-invasive measurement of longitudinal elastic modulus of arterial wall and its prospect of clinical application. In this study, the longitudinal elastic modulus of the arterial wall was assessed using real-time shear wave elastography in patients with AIS. The technique's feasibility and its related factors were studied initially. **Materials and methods:** In this study 179 patients with AIS and 168 age- and sex-matched controls were examined. The pulse wave velocity (PWV) of the bilateral carotid arteries was measured using radio frequency ultrasound technology. The 20 areas of superficial walls of bilateral carotid artery were analyzed by real-time shear wave elastography (SWE), and the average values of longitudinal average elastic modulus (ME_{mean}), maximum elastic modulus (ME_{max}), minimum elastic modulus (ME_{min}), and elastic modulus standard deviation (ME_{SD}) were measured. **Results:** The PWV, ME_{mean}, ME_{max} and ME_{SD} of the carotid artery in patients with AIS were greater than those in the control group. Age, systolic blood pressure, PWV, and low-density lipoprotein were positively related to ME_{mean} and ME_{max} (r=0.221and r=0.248, r=0.174 and r=0.176, r=0.776 and r=0.716, r=0.173 and r=0.200, p<0.05) and were independent risk factors for ME_{mean} and ME_{max}. ROC curves for detection of ischemic stroke as decided by PWV, ME_{mean} and ME_{max}. The area under the curves were 0.55±0.03 (p≤0.05), 0.59±0.03 (p≤0.05) and 0.60±0.03 (p=0.023), respectively. The optimal PWV, ME_{mean} and ME_{max} cutoff values for the detection of ischemic stroke were 9.66 m/s, 55.4 kPa and 65.4 kPa, with 69%, 73% and 73% sensitivity and 89%, 53% and 51% specificity, respectively. **Conclusions:** SWE could measure non-invasively the longitudinal elastic modulus of the arterial wall and evaluate the arterial stiffness. It was equivalent to the PWV which showed circular elastic modulus of arterial wall on evaluating AIS. Age, systolic blood pressure, pulse wave velocity, and low-density lipoprotein were independent risk factors for longitudinal elastic modulus. SWE may be effective in the assessment of arterial stiffness and offer a potential clinical benefit.

Keywords: stroke, arterial stiffness, shear wave elastography, elastic modulus, pulse wave velocity

Introduction

Acute ischemic stroke (AIS) is the leading cause of death and disability worldwide, carotid artery disease being responsible for 15%–20% of all strokes [1]. The type of AIS is classified according to the TOAST classification: large artery atherosclerosis (LAAS), lacunar infarct (LAC), cardio-embolic infarct, stroke of other determined etiology, and stroke of undetermined etiology [2]. Among the subtypes of stroke, LAAS and LAC are more likely to be associated with arterial stiffness [3].

Various techniques are used to assess arterial stiffness and the measurement of pulse wave velocity (PWV) is one of the most representative and noninvasive techniques for this purpose [4]. PWV is directly linked to the circumferential elasticity modulus [5]. However, several studies have shown that the arterial wall exhibits different elasticity modulus in the longitudinal and circumferential directions [6]. The PWV provides an estimate of

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the circumferential elasticity modulus. There was still no reports on non-invasive measurement of longitudinal elastic modulus of the arterial wall and its prospect of clinical application. Longitudinal elastic modulus of arterial wall changing will lead to arterial diseases. A decrease in longitudinal elastic modulus can add the chances of aneurysm while an increase in it can add the speed of PWV and raise the cardiac afterload. Non-invasive measurement of longitudinal elastic modulus may have clinical significance for the treatment and prevention. Shear wave elastography (SWE) allows access to the longitudinal elasticity modulus because shear wave propagation is analyzed in a longitudinal direction [5].

SWE is a new ultrasound imaging method that can record up to 50,000 images per second. This high temporal resolution makes it possible to measure the arterial wall stiffness due to the remote palpation carried out by shear waves [7]. SWE has been used to quantify the elasticity modulus of a normal carotid vessel wall through the cardiac cycle [8]. We hypothesized that 1) due to the fact that shear wave propagation is analyzed in the longitudinal direction, the longitudinal elastic modulus of arterial wall may be assessed by SWE; 2) longitudinal elastic modulus may be equivalent to the PWV which showed circular elastic modulus of arterial wall on evaluating arteriosclerosis; 3) in patients with AIS a higher arterial stiffness is present and the longitudinal modulus and circumferential elasticity modulus would both increase. This study was conducted to clarify whether the SWE technique could assess the longitudinal elasticity of the carotid artery and predict AIS.

Materials and methods

Study Population

For inclusion, patients had to be admitted within 7 days of the onset of stroke. We studied 179 AIS patients admitted to our department from June 2014 to April 2015. Diagnosis had to be corroborated by a neurologist's investigation and cerebral imaging (magnetic resonance imaging or a computed tomography scan). A final diagnosis of ischemic stroke was confirmed with magnetic resonance imaging. The inclusion criteria were LAAS and LAC categorized by the TOAST classification [3]. We excluded patients with history of cerebrovascular events related to trauma or medical instrumentation, severe concomitant kidney or liver disease, autoimmune disease, cerebral vasculitis, or embolism from implants, such as an artificial heart valve or atrial fibrillation.

One hundred sixty-eight age- and sex-matched control subjects were recruited for comparison with our patients. In order to match patients with AIS and controls according to their cardiovascular risk factors and any previous cardiovascular morbidity, the presence of risk factors or a history of myocardial infarction, cerebrovascular disease, or peripheral vascular disease were not considered to be exclusion criteria. The exclusion criteria were current or recent (in the past 6 months) cerebrovascular disease, age <18 years and >80 years, acute myocardial infarction, and hemorrhagic stroke.

This study was approved by the Institutional Review Board of Shanghai General Hospital (2014158). Each patient or the legally authorized representative was informed about the study and gave their consent to participate.

Risk factor analysis for cerebrovascular disease and clinical assessments

Clinical characteristics, past and familial history were documented, and physical examination was performed prior to the ultrasound examination, including weight, height, and blood pressure measurements. Venous blood samples for biochemical analyses and hematological parameters were drawn after a 12-h fast before the patients received any medication. Fasting plasma glucose (FPG), serum creatinine, blood serum urea nitrogen (BUN), C-reactive protein (CRP), D-dimer, homocysteine, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglyceride (TG), and glycated hemoglobin (HbA1c) levels were recorded.

Carotid artery assessment

Standard carotid ultrasound, including intima-media thickness (IMT) and PWV, were performed using the ESAOTE Mylab Twice ultrasound system (ESAOTE Medical Systems, Genoa, Italy) equipped with a 4–13 MHz linear array transducer. The device also included software to evaluate the IMT (quality intima-media thickness) and arterial stiffness (quality arterial stiffness, which was the measurement used for the PWV). In supine position the measurement site was selected 1.5 cm proximal to the dilatation of the bifurcation plane (longitudinally). The probe was adjusted to ensure that ultrasound beam was vertical to the artery walls. Images were optimized so that the anterior and posterior walls of the common carotid artery (CCA) were clearly shown. If there were plaques on the carotid artery walls, the probe's position and direction was adjusted in order to avoid plaques. The PWV, IMT, and diameter (CCAD) of the CCA were automatically measured (fig 1a and 1b). The IMT, CCAD, and PWV on both the left and right sides were calculated with the software using high quality images of six cardiac cycles, which were displayed on the screen. The average IMT, CCAD, and PWV values were chosen for analyses. The SWE data were acquired with an Aixplorer ultrasound system equipped with an L15-4 probe (Supersonic Imagine, AIX-EN-PROVENCE, France). The measurement site of SWE was consistent with PWV and CIMT. The SWE region of interest (ROI) box size was adjusted to include the anterior and posterior walls of CCA (1 cm wide × 2 cm long). In this study, the measurement of superficial walls of bilateral carotid artery was analyzed by SWE (fig 1c and 1d). The blue and red areas on the elastogram corresponded to the low elasticity modulus (soft) and the high elasticity modulus (stiff), respectively, up to a maximum of 80 kPa. The observers acquired a 10-s SWE cine-loop, and each observer repeated the acquisition process on three separate occasions. The first two SWE frames were excluded in each clip, while the next five SWE frames were analyzed separately, a play back performed and were selected at diastolic end to measure (the largest diameter of CCA), as our experience suggested that this delay improved the image stability. The observers measured ten ROIs (measurement positions) on the superficial walls of carotid using the Aixplorer system's inbuilt Q-box analysis software. The Q-box tool quantified the elasticity values including the mean, minimum, maximum, and standard deviation (E_{mean}, E_{min}, E_{max}, and E_{SD}) for a circular ROI positioned by the observer (fig 1e and 1f). The 20 areas of superficial walls of bilateral carotid artery were measured, and the average values of longitudinal average elastic modulus (ME_{mean}), maximum elastic modulus (ME_{max}), minimum elastic modulus (ME_{min}), and elastic modulus standard deviation (ME_{SD}) were measured. All analyses were based on the mean elasticity modulus quantified in each Q-box for a size set to the minimum diameter of 1 mm. The size of Q-box was adjusted according to CCA wall thickness and fully included the CCA wall. IMT≥1.1mm was defined as plaque and was avoided. So the size of Q-box was set as 1mm.

Statistical Analysis

All analyses were carried out using IBM SPSS Statistics software, version 13.0 (SPSS Inc., Chicago, IL, USA). The Statistical Package for the Social Sciences (SPSS) version 13.0 statistical analysis software was adopted, and continuous variables were expressed as mean ± SD. Discrete variables were analyzed using the

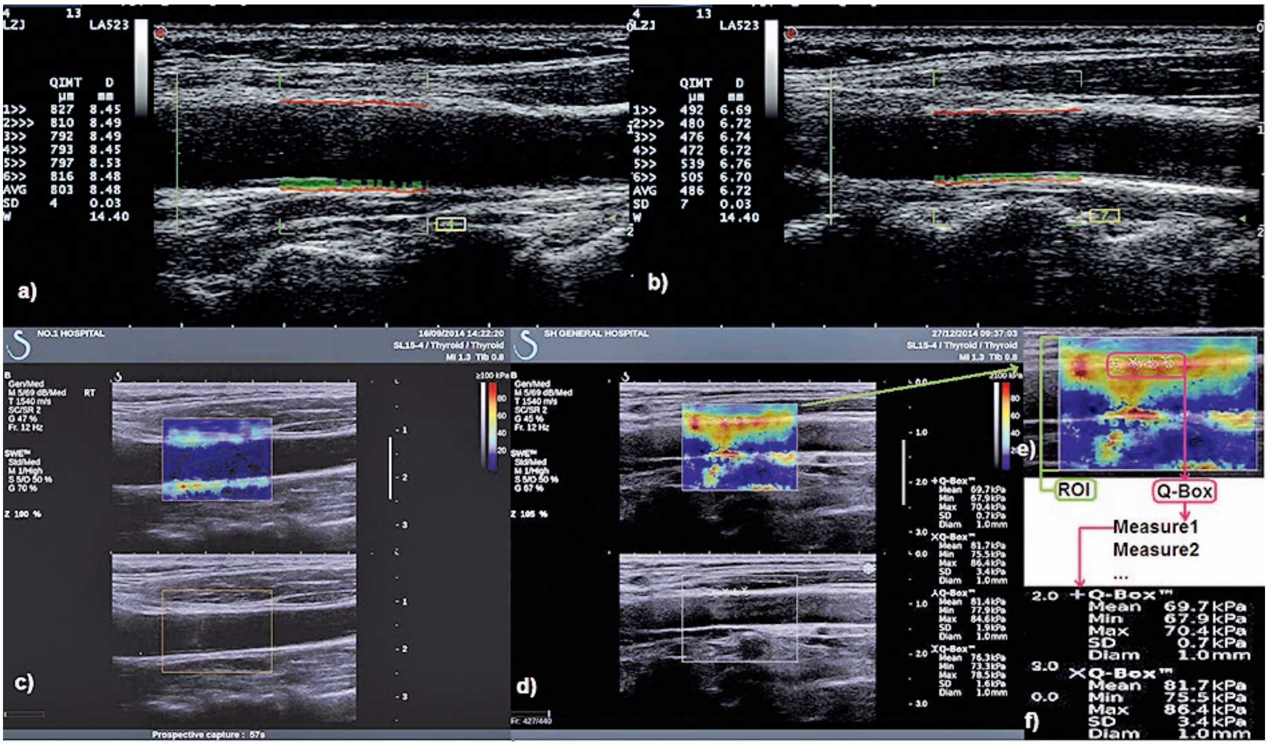

Fig 1. SWE^{RT} for evaluating carotid artery elasticity: a) The structure and function of carotid was evaluated by QIMT/QAS in AIS (CCAD=8.84mm, CIMT=803μm); b) The structure and function of carotid was evaluated by QIMT/QAS in the control group (CCAD=6.72mm, CIMT=486μm); c) Carotid artery elasticity and grey scale ultrasonography of the control group was evaluated by SWE^{RT}; d) Carotid artery elasticity of AIS was evaluated by SWE^{RT} (above). The value of elasticity modlus was color-coded and was superimposed on the grey scale ultrasonography. The larger value of elasticity modlus showed "red", and the smaller value was "blue". The grey scale ultrasonography was corresponding to AIS (below); e) Zooming in the fig.1d partially. The SWE region of interest (ROI) box size was adjusted to include the anterior and posterior walls of carotid (Light green box). f) The Q-box tool quantified the superficial walls of carotid elasticity values including the mean, minimum, maximum, and standard deviation (E_{mean}, E_{min}, E_{max} and E_{SD}) for a circular ROI positioned by the observer (Pink box).

independent t-test and Chi-square test. Receiver operator characteristics curve (ROC) was used to identify the ability of the CIMT, PWV, ME_{mean}, ME_{max}, ME_{min}, and ME_{SD} to predict AIS. Comparisons between areas under the curves were tested by the Z test. The ROC curve defined the optimal cutoff value of CIMT, PWV, ME_{mean}, ME_{max}, ME_{min}, and ME_{SD} that represented the presence of ischemic stroke. Multivariate linear regression analysis (stepwise) was performed to analyze the independent risk factors for ME_{mean}, ME_{max}, ME_{min}, and $ME_{SD.}$ Statistical significance was considered when $p<0.05$.

The reproducibility of the ME_{mean} was assessed in 20 randomly selected subjects (patients or controls) whose ME_{mean} values were measured independently by two different physicians and twice by the same physician, respectively. The repeatability evaluation adopted a linear correlation analysis and Bland-Altman plots. Bland-Altman plots were used to assess the inter-observer and intra-observer variability, based on the elasticity modulus value for each ROI averaged across five frames in each acquisition.

Results

Patient characteristics

The general characteristics of the participants were shown in Table I. The age, length, and weight of the AIS group/control group were similar ($p>0.05$). The systolic blood pressure (SBP) and diastolic blood pressure were significantly higher in the AIS group than in the control group ($p<0.05$). AIS patients demonstrated higher FPG, HbA1c, TG, LDL-C, and CRP values and lower TC and HDL-C values ($p<0.05$). The creatinine, BUN, D-dimer, and homocysteine values were similar in both the AIS and control groups ($p>0.05$). There were no differences in the prevalence of diabetes mellitus and hypertension between the groups ($p>0.05$).

Comparison of carotid artery structures, stiffness, and elasticity modulus

Compared to the control group, the patients with AIS had markedly higher CCAD, IMT, and PWV values ($p<0.05$). This trend suggested that the structure of the carotid artery had been remodeled and the arterial

Table I. Baseline characteristics of the study population.

Characteristics	Acute ischemic stroke group	Controls	t-Value	p-Value
Sex (F/M)	80/99	75/93	0.001	0.993
Age (years)	65.0 ± 10.4	64.5 ± 8.4	0.583	0.56
Length (cm)	166.4 ± 7.5	166.0 ± 7.1	0.435	0.664
Weight (kg)	67.4 ± 13.9	65.0 ± 11.5	1.811	0.071
Systolic blood pressure (mmHg)	138.9 ± 14.9	131.9 ± 17.7	4.133	<0.001
Diastolic blood pressure (mmHg)	86.2 ± 9.9	83.4 ± 10.1	2.669	0.008
Diabetes mellitus	64 (35.8%)	45 (26.8%)	3.235	0.072
Hypertension	68 (37.9%)	63 (37.5%)	0.009	0.925
Platelet aggregation inhibitor use	46 (25.7%)	32 (19%)	2.20	0.138
Beta-blocker therapy	35 (19.6%)	25 (14.9%)	1.323	0.250
ACE inhibitor therapy	39 (21.8%)	27 (16%)	1.839	0.175
Calcium channel blocker therapy	21 (11.7%)	15 (8.9%)	0.732	0.392
Diuretic therapy	34 (18.9%)	28 (16.7%)	0.320	0.572
Statin therapy	146 (81.6%)	129 (76.8%)	1.203	0.273
Ezetimibe therapy	53 (29.6%)	35 (20.8%)	3.526	0.060
Oral anti-diabetic therapy	35 (19.5%)	35 (20.8%)	0.088	0.766
Insulin therapy	51 (28.5%)	30 (17.8%)	5.477	0.019
FPG, mmol/L	6.3 ± 2.0	5.3 ± 1.1	5.586	<0.001
HbA1c, %	6.7 ± 1.5	5.7 ± 0.6	5.916	<0.001
TC, mmol/L	4.4 ± 1.1	6.0 ± 10.2	-2.081	0.038
TG, mmol/L	1.8 ± 1.3	1.4 ± 0.7	3.576	<0.001
HDL-cholesterol, mmol/L	1.1 ± 0.3	1.2 ± 0.3	-4.303	<0.001
LDL-cholesterol, mmol/L	3.1 ± 0.9	2.9 ± 0.9	2.599	0.01
Creatinine, µmol/L	74.5 ± 21.3	75.1 ± 17.7	-0.272	0.786
Blood urea nitrogen, mmol/L	5.1 ± 1. 7	5.1 ± 1.3	0.397	0.691
C-reactive protein, mg/L	5.1 ± 7.7	2.7 ± 4.7	3.412	0.001
D-dimer, mg/L	0.7 ± 1.8	1.1 ± 2.6	-1.389	0.166
Homocysteine, µmol/L	14.2 ± 11.2	15.8 ± 14.1	-1.024	0.307

Values are expressed as mean ± SD. SBP and DBP: systolic and diastolic blood pressures, respectively; TC: total cholesterol; TG: triglycerides; LDL: low-density lipoprotein; HDL: high-density lipoprotein; FPG: fasting plasma glucose; HbA1c: glycated hemoglobin; 1 mmHg = 0.133 kPa.

Table II. Assessment of the carotid using ultrasound.

Items	Acute ischemic stroke group	Controls	t-Value	p-Value
CCAD (mm)	8.8 ± 1.1	8.5 ± 0.9	3.316	0.001
IMT (μm)	694.7 ± 139.8	648.1 ± 145.1	3.174	0.002
PWV (m/s)	9.1 ± 2.3	8.6 ± 1.7	2.375	0.018
MEmean (kPa)	72.7 ± 27.3	61.9 ± 20.6	4.320	0.000
MEmin (kPa)	60.6 ± 26.2	55.9 ± 22.9	0.918	0.359
MEmax (kPa)	83.9 ± 31.2	71.5 ± 25.5	4.186	0.000
MESD (kPa)	7.3 ± 4.9	6.1 ± 4.3	2.314	0.021

CCAD: diameter of common carotid artery; IMT: intima-media thickness; PWV: pulse wave velocity; ME_{mean}: average values of longitudinal average elastic modulus; ME_{min}: average values of longitudinal minimum elastic modulus; ME_{max}: average values of longitudinal maximum elastic modulus ME_{SD}: average values of longitudinal elastic modulus standard deviation.

Table III. Multiple regression analysis of factors related to the longitudinal elastic modulus.

Items		Coefficients b	SE	Standardized coefficients (b')	t-value	p-value
MEmean	(Constant)	4.312	27.904	N/A	0.155	0.877
	AGE	0.740	0.229	0.268	3.234	0.001
	SBP	0.705	0.274	0.400	2.572	0.011
	PWV	12.241	4.306	0.949	2.842	0.005
	LDL-C	3.556	1.733	0.132	2.052	0.041
MEmin	(Constant)	-16.551	25.425	N/A	-0.651	0.516
	AGE	0.770	0.208	0.303	3.698	0.000
	SBP	0.702	0.250	0.433	2.809	0.005
	PWV	13.386	3.924	1.126	3.411	0.001
MEmax	(Constant)	10.651	32.200	N/A	0.331	0.741
	AGE	0.819	0.264	0.257	3.103	0.002
	SBP	0.758	0.316	0.372	2.396	0.017
	PWV	12.208	4.969	0.819	2.457	0.015
	LDL-C	4.624	2.000	0.149	2.312	0.022
MESD	(Constant)	8.627	5.289	N/A	1.631	0.104
	LDL-C	0.893	0.329	0.184	2.718	0.007

ME_{mean}: average values of longitudinal average elastic modulus; ME_{min}: average values of longitudinal minimum elastic modulus; ME_{max}: average values of longitudinal maximum elastic modulus ME_{SD}: average values of longitudinal elastic modulus standard deviation; SBP: systolic blood pressures; PWV: pulse wave velocity.

stiffness had increased in the AIS group. The elasticity modulus, ME_{mean}, ME_{max}, and $ME_{SD,}$ were also greater in the AIS group (p<0.05), which indicated that the arterial wall was markedly hardened and non-uniform in the AIS group. The ME_{min} was similar in both groups (p>0.05, Table II).

Analysis of carotid artery stiffness

Age, SBP, PWV, and LDL-C were all positively correlated with ME_{mean} (r=0.221, r=0.174, r=0.776, r=0.173, respectively, p<0.05). Multiple linear regression analysis showed that age, SBP, PWV, and LDL-C were independent risk factors for ME_{mean}. Age, SBP, PWV, and LDL-C were also all positively correlated with ME_{min} (r=0.197, r=0.161, r=0.773, and r=0.109, respectively, p<0.05). Multiple linear regression analysis additionally revealed that age; SBP, PWV, and LDL-C were independent risk factors for ME_{min}. Age, SBP, PWV, and LDL-C were all positively correlated with ME_{max} (r=0.248, r=0.176, r=0.716, and r=0.200, respectively, p<0.05). According to multiple linear regression analysis, age, SBP, PWV, and LDL-C were independent risk factors for increased ME_{max}, while age, SBP, PWV, and LDL-C were all positively correlated with ME_{SD} (r=0.158, r=0.071, r=0.262, and r=0.195, respectively, p<0.05). LDL-C was also revealed to be an independent risk factor for ME_{SD} upon multiple linear regression analysis (Table III).

ROC analysis showed the areas under the curves of IMT, PWV, ME_{mean}, ME_{max}, ME_{min}, and ME_{SD} to be 0.61±0.03 (p=0.001), 0.55±0.03 (p≤0.05), 0.59±0.03 (p≤0.05), 0.60±0.03 (p=0.023), 0.57±0.03, (p=0.561), and 0.55±0.03 (p=0.001), respectively. The Z-test was performed, and the difference of areas under the curves had not a statistical significance (p>0.05). The optimal IMT, PWV, ME_{mean}, ME_{max}, ME_{min}, and ME_{SD} cutoff values for the detection of ischemic stroke were 683 μm, 9.66 m/s, 55.4 kPa, 65.4 kPa, 57.5 kPa, and 3.2 kPa with 58%, 69%, 73%, 73%, 51%, and 80% sensitivity and 65%, 89%, 53%, 51%, 76%, and 67% specificity, respectively (fig 2).

Repeatability test

The repeatability test showed that intragroup and intergroup comparisons had a high degree of consistency (intragroup: r=0.755, p<0.01, with a mean difference of 1.07±9.42 kPa; intergroup: r=0.88, p<0.01, with a mean difference of −0.45±8.15 kPa) (fig 3).

Discussions

The main aim of this study was to determine the feasibility of the longitudinal elastic modulus using SWE in a vascular clinic on the carotid artery. We found that 1) longitudinal elastic modulus of arterial wall could be assessed by SWE; 2) longitudinal elastic modulus was equivalent to the PWV on evaluating arterial stiffness; 3) for patients with AIS, the longitudinal and circular elastic modulus were all increased and the arterial stiffness was added. Our study, which was based on SWE, assessed ischemic stroke patients and demonstrated changes in the carotid arterial structure; higher ME_{mean} and ME_{max} scores of the carotid artery suggested that the arteries were stiff and the longitudinal elastic modulus of the carotid artery was increased in AIS patients. At the same time, the PWV and the circular elastic modulus of the carotid artery were positively correlated with the ME_{mean} and ME_{max} and were independent risk factors for ME_{mean} and ME_{max}. These results indicated that the longitudinal and circular elastic modulus acted synergistically on the carotid artery. Our study also showed that the optimal PWV, ME_{mean}, and ME_{max} cutoff values for the detection of ischemic stroke were 9.66 m/s, 55.4 kPa, and 65.4 kPa, respectively. In particular, a PWV higher than 9.66 m/s could be a useful predictor of ischemic stroke. ME_{mean} and ME_{max} values higher than 55.4 kPa and 65.4 kPa, respectively, might also be effective indices for predicting ischemic stroke.

Atherosclerosis often accompanies cerebrovascular diseases. The findings from a previous study suggested that increased arterial stiffness was predictive for cerebrovascular events through an increase in the central brachial pulse pressure. The brachial pulse pressure is associated with carotid artery disease, including IMT and plaque area [9]. Gasecki et al showed that the PWV as an index of aortic stiffness is an independent predictor of a fatal stroke in patients with essential hypertension [10]. Elastic modulus, which includes both longitudinal and circular types, is a key parameter for evaluating arterial stiffness. The PWV mainly reflects the circular elastic modulus of an artery and is the gold standard in evaluation of the arterial stiffness. Our previous study demonstrated that arterial stiffness in different regions may have a separate role in cardiovascular disease and showed that

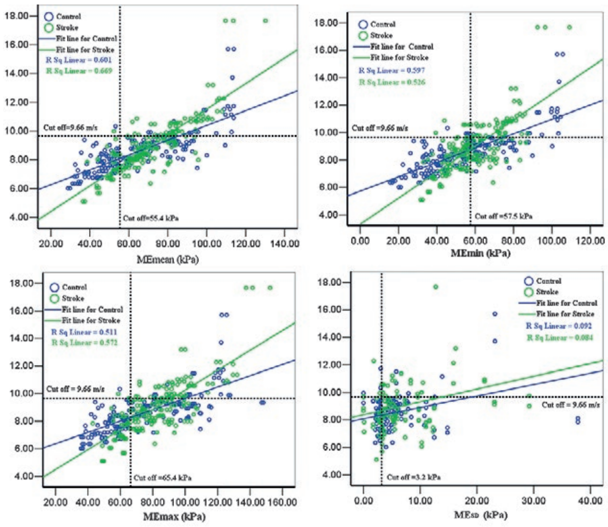

Fig 2. The overlay scatters for PWV, MEmean, MEmin, MEmax and MESD. The ROC curves were to define the optimal cutoff value of PWV, MEmean, MEmax, MEmin and MESD that represents the presence of an ischemic stroke. If PWV was considered as the ideal index, the control group (blue scatters) would appear below the "cut off" (in quadrant 3 and 4), and AIS (green scatters) would appear above the "cut off" (in quadrant 1 and 2). If ME was considered as the ideal index, the control group would appear on the left of the "cut off"(in quadrant 1 and 4), and AIS would appear on the right of the "cut off" (in quadrant 2 and 3). The four graphs showed the control group mainly distributed in quadrant 1 and the AIS was mainly in quadrant 2 and 3. These suggested that MEmean, MEmax and MESD were slightly better than PWV to identify AIS based on carotid elasticity; there was no significant difference between these parameters. The inter-group differences of MEmin evidenced no significant difference, so the blue and green scatters distributed relatively equally along the two sides of MEmin.

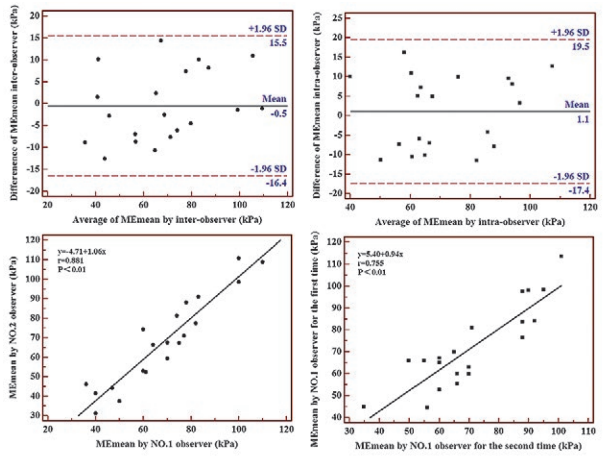

Fig 3. Repeatability was analyzed by linear correlation analysis and Bland-Altman Plots. Bland-Altman analysis showed a consistent trend in the difference value and the mean value of the MEmean by repeated measurement. The results showed that intragroup and intergroup comparison had a high degree of consistency.

among the central PWV measurements, an elevated PWV was most closely associated with coronary, cerebral, and peripheral arterial disease [11]. This study found that the PWV of the AIS group and the control group were 9.1±2.3 m/s and 8.6±1.7 m/s, respectively, with a statistically significant difference. These results indicate that the circular elastic modulus of the artery was higher and the arterial stiffness was increased in patients with AIS. In addition, the longitudinal elastic modulus of the artery was found to be approximately three times higher than the circular elastic modulus [12]. The longitudinal modulus and the circumferential modulus of the arterial wall therefore indicated different circumstances. Under normal conditions, the arterial wall had a lower elasticity modulus in a circumferential direction, so the wall showed good compliance in this direction and helped the heart pump blood throughout the body. On the other side, the longitudinal modulus was higher than the circumferential one, so it was easy to rapidly distribute the pressure in the arteries and maintain the arterial pressure of organs. If the longitudinal modulus were reduced, however, the shape of the arteries would be difficult to maintain; it would also be harder to ensure their dilation. As a result, the infernal circle will eventually lead to an aneurysm [13].

Compared with ultrasonic waves, shear waves have very different characteristics in human tissues. The speed of propagation of the shear waves is dependent on the local density and the elastic modulus of the tissue. Soft tissues can exhibit very strong contrasts in terms of shear modulus (or stiffness), while shear waves can encounter strong reflections or reverberations. Moreover, shear waves can propagate in our soft tissues only at low frequencies (1 to 1000 Hz) because of the important shear viscosity that occurs at a higher frequency (kHz), leading to centimetric wavelengths. Hence, for particular configurations (such as arteries), this shear wavelength becomes larger than local strong heterogeneities, leading to guided mode propagation. Recent studies have reported the potential clinical value of shear wave elastography in the diagnosis of malignancy in a range of applications, including the breasts [14], liver [15], thyroid [16], prostate [17], cervical lymph node [18], and salivary glands [19], though very few studies have considered vascular applications [20-21]. Ramnarine et al findings indicated that SWE can quantify Young's modulus of carotid plaque phantoms with good reproducibility [20-21] and could help establish the potential clinical value of the additional elasticity information for the identification of unstable carotid plaque and risk of stroke. Couade et al [21] study performed in healthy volunteers evaluated Young's modulus of the common carotid artery wall and found it to be higher during systole than diastole. SWE would quantify Young's modulus as arterial stiffness, as well as the potential clinical benefit. In our study, ME_{mean} and ME_{max}, which indicate the longitudinal elasticity modulus of a vessel based on SWE, showed a significant difference between the AIS group and the control group. The AIS group had higher ME_{mean} and ME_{max} scores than those of the control group. These findings suggest that the arterial stiffness was increased in the longitudinal axis. Our correlation analysis revealed that age, SBP, PWV, and LDL were independent risk factors for arterial stiffness along the longitudinal axis. These risk factors can also encourage arterial stiffness in the circular axis. Increased arterial stiffness may lead to vessel wall damage and atherosclerosis, while cerebral artery atherosclerosis can contribute to cerebral hypoperfusion and arterial embolism, resulting in LAC [22].

In our study, the good reproducibility of the longitudinal elasticity modulus in patients with AIS supported the feasibility of using SWE in vascular applications. However, there were limited cases in our study. In addition, the occurrence of LAAC and LAC were not compared, and neither was the presence or absence of carotid atherosclerosis plaque. In our study, the SWE measurement was temporarily unable to be simultaneously recorded by electrocardiograms, and the end diastolic images (the largest diameter of CCA) were obtained by a dynamic movie playback, so only certain deviations were available for analysis. Further research will be needed to assess the risk factors and to attribute different weights on arterial stiffness in longitudinal and circumferential directions and propose a different subtype of AIS.

AIS is closely related to the stability of atherosclerotic plaques. MRI is "gold standard" on assessing the AIS, but it has limitations of showing the the stability of atherosclerotic plaques in intracranial vessels. Despite its limitations, this study described the feasibility and demonstrated good reproducibility of SWE in the quantification of longitudinal elasticity modulus in the carotid artery. Ongoing clinical studies will help establish the potential clinical value of additional elasticity information for the identification of arterial stiffness.

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Conflict of interest: none

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