Evaluation of tensile stress in carotid artery: evidence from ultrasonography

CURRENT STATUS: ACCEPTED

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DOI:
10.21203/rs.2.13760/v1

SUBJECT AREAS
Nuclear Medicine & Medical Imaging

KEYWORDS
Shear wave dispersion, shear wave elastography, Tensile stress, Carotid artery, Viscoelasticity, Ultrasonography
Abstract

Background Arterial remodeling reflects adaptation of the vessel wall to mechanical and hemodynamic stimuli and contributes to the progression of cardiovascular and cerebrovascular diseases. Tensile stress (TS) is one of the mechanical properties of the artery wall. We sought to investigate the effects of carotid viscoelasticity on its tensile stress (TS) in different age subjects.

Methods Forty-five subjects were recruited and divided into the group1 (≥50 years old) and the group2 (<50 years old) according to the median age. The carotid arteries were examined by ultrasonography, including shear wave elastography (SWE), shear wave dispersion (SWD) and radiofrequency (RF) technologies. The values were obtained, including the carotid elastic modulus (SWE R) and viscous index (SWD R), as well as the peak and mean TS of the left and right carotid arteries (L-PTS, R-PTS, L-MTS and R-MTS). The correlations between SWE R, SWD R and tensile stress were investigated, respectively.

Results In the group1, the carotid arteries had lower SWE R and SWD R than those in the group2 (SWE R, [10.29±9.57] kPa vs. [17.24±14.07] kPa; SWD R [11.99±3.51] (m/s)/kHz vs. [13.97±3.71] (m/s)/kHz, all P values < 0.05). In addition, the R-PTS was also lower in the group 1 (P <0.05). Pearson correlation analysis showed that the carotid SWE R was positively correlated with tensile stress. R-values for R-PTS, R-MTS, L-PTS and L-MTS were r =0.218, r =0.359, r =0.209 and r =0.369, respectively (all P <0.05). However, the carotid SWD R was not significantly associated with TS.

Conclusion Ultrasonic shear wave imaging could be used to quantitatively assess carotid viscoelasticity. The carotid TS was related to its elasticity while little related to its viscosity, suggesting that mechanical properties of the arterial wall might be better revealed.
Background

Arterial remodeling reflects adaptation of the vessel wall to mechanical and hemodynamic stimuli and contributes to the progression of cardiovascular and cerebrovascular diseases [1, 2]. On the other hand, the biomechanical behaviors of arteries are adjusted to correspond to the arterial remodeling [3]. The circumferential tensile stress (TS) derived from Laplace’s law can be used to assess the transmural pressure of vascular, which is one of the mechanical properties of the artery wall. TS could exhibit different responses of the arterial wall to blood pressure, blood flow and arterial structure, and is an important indicator of atherosclerosis. In the clinically useful rang, TS also helps to assess the compliance of vascular grafts [4].

Arterial wall has been known as one of the most intricate type of structures and presents a certain biomechanical property of viscoelasticity [5]. This behavior presents a non-linear mechanical relationship and attributes in part to fluid transport within the solid matrix [6,7]. However, most of the arterial TS had been measured through biomechanical experiments in vitro, and little is known the nature of the adjustments to the arterial viscoelasticity, which corresponds to the altered wall TS.

In recent years, shear wave-based elastography techniques, such as shear wave elastography (SWE) and shear wave dispersion (SWD) have received wide attention for noninvasive assessment of elasticity and viscosity properties [6,7]. This study was to assess the carotid TS and viscoelasticity by ultrasonic technologies, and explored the relationship between them.

Methods

Study design and setting participants

The study was registered with Clinical trials (ChiCTR1800016590) and approved by the
Institutional Ethics Board of the hospital (2017KY009). Written informed consent was obtained from all subjects. Participants were enrolled from August 1, 2017 to May 1, 2018. They were selected based on the electronic medical record. The participants with active bleeding, history of cardiovascular or cerebrovascular events, vascular diseases of the extremities, immune diseases, severe liver, lung, kidney diseases, or malignant tumor were excluded. Forty-five participants met the inclusion criteria (age: 48.9±9.7 years, range: 20–80 years). Subsequently, the subjects were divided into 2 groups according to median age: group1 (≥50 years) and group 2 (<50 years). After being seated for at least 10 min, the blood pressure was determined by performing three systolic blood pressure (SBP), and diastolic blood pressure (DBP) measurements. Blood samples for measurement of the level of glucose, triglycerides (TG), total cholesterol (TC) and low-density lipoprotein-cholesterol (LDL) were obtained after 12h of fasting.

Instrument Setting and carotid artery Measurement

After high-resolution common carotid artery (CCA) images of were obtained, the viscoelasticity of the CCA was measured by an Aplio 900 ultrasound system (Canon Medical Systems Corporation, Otawara, Japan) with PVI-475BX curved abdominal transducer (frequency range:1-8-MHz and mid frequency: 5.0 MHz)[10]. Electrocardiography was recorded by synchronization. The arterial viscoelasticity could be evaluated after starting “TCS” button. QuadView was novel in the provision of 4 display maps for the single-shot acquisition, which provided different visual representations of the arterial shear wave profile, including the elastic map (Fig.1a), propagation map (Fig.1b), two-dimensional reference map (Fig.1c) and shear wave dispersion map (Fig.1d). After recording the motion of vascular wall for 10–20 cardiac cycles, measurements were obtained from a 1.0 cm circular region of interest (ROI) in systolic phase. Five ROIs were
placed selectively on the anterior and posterior walls of the bilateral carotid arteries, respectively (1 to 2 mm apart). Then shear wave elastic modulus (SWE<sub>R</sub>) and shear wave dispersion (SWD<sub>R</sub>) in electrocardiographic R wave were analyzed and their mean values were calculated for final analysis.

The carotid structure and tensile stress were measured by Mylab Twice ultrasound system (Esaote, Firenze, Italy) equipped with a LA523 linear transducer (4–13 MHz) and the software for ultrasonic radiofrequency analysis. The software was used for quantitative assessment of common carotid intima-media thickness (CIMT) and inner diameter (CCID) via a complex algorithm. Pressing the “Tools” button, the radiofrequency signal tracked the motion of vascular wall for at least six cardiac cycles and calculated automatically the mean values, including CIMT and CCID. The carotid peak tensile stress (PTS) and mean tensile stress (MTS) were calculated according to Laplace’s law. 

\[
\text{PTS} = \frac{\text{SBP}}{2} \times \frac{\text{CCID}_R}{\text{CIMT}} (\text{mmHg}), \quad \text{MTS} = \frac{\text{MBP}}{2} \times \frac{\text{CCID}_T}{\text{CIMT}} (\text{mmHg})[11].
\]

MBP was the mean blood pressure and calculated by \((\text{SBP+2×DBP})/3\). CCID<sub>R</sub> was the common carotid inner diameter at end of systole, while CCID<sub>T</sub> was at end of diastole. 1 dyne/cm<sup>2</sup> = \(7.5 \times 10^{-4}\) mmHg.

**Statistical analyses**

All statistical analyses were performed using SPSS 13.0 statics software program. The continuous variables were presented as the mean±SD and compared using Student’s t-tests, while categorical variables were expressed as percentages or number, and compared using chi-squared test. Agreement of measurement was evaluated by Bland-Altman plots. Pearson correlation analysis was done to assess the correlation between carotid viscoelasticity and TS. \(P<0.05\) was considered to be significant.

**Results**
Baseline characteristics

The baseline characteristics for two age groups were summarized in Table 1. Compared with group 2, the height was less, while SBP and DBP were higher in group 1 (all \( P<0.05 \)). No significant difference was observed in the gender, weight, body mass index, glucose, TG, TC, LDL-C, diabetes mellitus and hypertension respectively (all \( P>0.05 \)).

Comparison of carotid structure, viscoelasticity and tensile stress between two age groups

The \( \text{SWE}_R \) and \( \text{SWD}_R \), which exhibited the carotid viscoelasticity, were significantly lower in the group 1 than those in the group 2 (\( P = 0.040 \) and \( 0.043 \), respectively). The bilateral CIMT, CCID\(_T\) and CCID\(_R\), which assessed the carotid structure, were all higher in the group 1 (all \( P<0.05 \)). The PTS on the right carotid artery was lower in the group 1 (\( P<0.05 \)), while no significant difference was observed in the left PTS and bilateral MTS between two groups (all \( P>0.05 \)) (Table 2).

Correlation between the carotid viscoelasticity and tensile stress

Figure 2 and Table 3 showed that \( \text{SWE}_R \) correlated positively with R-PTS, R-MTS, L-PTS and L-MTS, respectively (\( r = 0.218, 0.359, 0.209, 0.369 \), respectively, all \( P<0.05 \)), whereas \( \text{SWD}_R \) did not correlate with them (all \( P>0.05 \)).

Agreement evaluation

A week later, a total of 22 subjects were randomly selected and participated the agreement evaluation. \( \text{SWD}_R \) and \( \text{SWE}_R \) were measured repeatedly by the same operator, and the results showed the biases were 3.3% and 3.9%, respectively. The Bland–Altman plots showed a good concordance between the values of the parameters obtained by two measurements (Figure 3).
Discussion

The cardiovascular and cerebrovascular diseases are still ranked amongst the main mortality causes in the world. However, it is known that the onset and progression of these diseases are associated with the alteration of the biomechanical properties of tissues. Therefore, some of the indicators describing this mechanical behavior, such as stress and strain might play the important roles in identifying the processes of arterial pathologies. For example, TS, an indictor based on Laplace’s law, gives a relation between the inflation pressure, wall thickness and inside diameter [12]. However, in vivo, TS of arterial wall is significantly connected to its viscoelasticity. In present study, the $SWE_R$ and $SWD_R$, being the parameters of viscoelasticity were lower in the older subjects than in the younger ones. We also observed that the PTS and MTS, describing the carotid peak and mean TS, showed less difference between two age groups, with only right carotid PTS in the older subjects showing lower values than the younger ones. Subsequently, the TSs, including PTS and MTS, were positively connected with $SWE_R$, while were not related to $SWD_R$. This suggested that the arterial elasticity contributed its mechanical behavior rather than viscosity.

Carotid structure was closely related to its mechanical properties. CIMT is a noninvasive ultrasound measurement and is strongly associated with cardiovascular and cerebrovascular events [13]. CIMT is a strong independent predictor of remolding and atherosclerosis. In this study, the CIMT was measured using ultrasonic radio-frequency technique. Based on the clear visualization of the two-dimensional vascular structure, it can receive complete RF signal, and detect the CIMT in six cardiac cycles in real-time, which is up to 10 µm. This technology is considered as a reliable and feasible method of clinical evaluation of arterial structure and function [14]. In this study, the CIMT increased
in the subjects who were ≥50 years old. This suggested that the carotid arteries remolding associated with increasing age. CIMT measurements respectively made on the left and right carotid arteries could represent separate phenotypes because their patterns of associations with risk factors are different. For example, on the left carotid artery, the CIMT is thicker and shows stronger associations with blood lipid, glucose and lower estrogens; while on the right carotid artery, the CIMT is thinner and significantly related to hemodynamics, such as hypertension and heart rate. These results suggest that the weights of risk factors are different on left and right carotid arteries [15]. The CCID is also an important indicator of remolding and atherosclerosis [16]. In this study, the CCID was enlarged in the older ones, while CCAD, i.e. the difference of CCID between diastole and systole was decreased. These results also exhibited that carotid artery occurred remodeling with age.

Carallo et al. [17] had demonstrated that the circumferential wall tension (WT) significantly increased with age [17]. Conversely, the present results showed the TS did not parallel the increase in CIMT and CCID. Only the right carotid PTS decreased with age, and no marked difference was observed in the parameters of TS, including bilateral MTS and left PTS. Various reasons for participating in that: (1) Mechanical models of artery, such as WT and TS, derived from Laplace’s law can be used to relate the arterial inner radius (r) and internal pressure (P). The WT was defined as \( P \times r \) [18]. The WT model assumes a very thin wall, and then handles the pressure, which does not take into account wall thickness. The TS, being a corrected Laplace model, was \( P \times r/CIMT \). TS could reflect the tensile response in circumference [11]. (2) The mechanical stretch can induce structural changes in the arterial wall, including VSMC hyperplasia and hypertrophy, as well as increased deposition of ECM collagen and elastin and result in arterial remodeling [19, 20]. On the other hand, the arterial remodeling could act on its mechanical properties
[21]. (3) The arterial tissue is viscoelasticity and show non-linear.

Alterations in the structural and mechanical properties of arteries are thought to be crucial for early demonstration of the atherosclerotic changes, which could serve as the indicators for future atherosclerotic diseases [22]. However, the arteries are of viscoelastic properties and exhibit the nonlinear stress-stain relations [23]. Several new non-invasive techniques have been used to study arterial elasticity, such as dimensional speckle-tracking imaging [24], ultrasonic radiofrequency tracking [25] and shear wave elastography [26,27]. However, in vivo, it is difficult to study the arterial viscosity due to its complex temporal changing behavior. Shear wave elasticity imaging may noninvasively evaluate the properties of soft tissues based on a group shear wave speed assuming that tissue is elastic; however, soft tissues are known to be viscoelastic, meaning the shear wave speed is dependent on the wave’s frequency content. Over the last years, there has been significant innovation in the area of describing the viscoelastic properties of soft tissue by the frequency-dependent: shear wave dispersion (SWD, the change in speed with frequency)[28]. In this work, the viscoelastic properties of carotid artery were evaluated by SWD. The SWE_R and SWD_R decreased with age. In addition, the TSs were positively connected with SWE_R, while were not related to SWD_R. This suggested that the arterial elasticity contributed its mechanical behavior rather than viscosity. The vascular smooth muscle cells, extracellular matrix proteins collagen and elastin play a crucial role in the viscoelastic properties, i.e. their spatial organization and interaction dominate the macroscopic non-linear vessel properties [29,30]. Higher vascular stiffness is typically found in older subjects because the elastic lamellae decreases with age, while the connective tissue and collagen fibers increase [31]. The mechanical characteristics of arteries were related to local pathologies of the arterial system, while wall viscosity change reflects a more general influence of age and diseases [32].
Despite the applied approach tried to use state-of-the-art methods, several limitations should be mentioned. A limitation in the present study was the small sample size. In addition, the curved abdominal transducer was used to evaluate the carotid viscoelasticity, while transducer of linear array could provide better images and measurements. The arterial viscoelasticity in the patients with cardiovascular or cerebrovascular diseases merited further investigation.

Conclusion

Ultrasonic shear wave imaging could be used to quantitatively assess carotid viscoelasticity. The carotid TS was related to its elasticity while little related to its viscosity, suggesting that mechanical properties of the arterial wall with age might be better revealed.

Abbreviations

TS: Tensile stress; SWE: Shear wave elastography; SWD: Shear wave dispersion; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; TG: Triglycerides; TC: Total cholesterol; LDL: Low-density lipoprotein-cholesterol; CCA: Common carotid artery; $SWE_R$: Shear wave elastic modulus in electrocardiographic R wave; $SWD_R$: Shear wave dispersion in electrocardiographic R wave; CIMT: Common carotid intima-media thickness; CCID: Common carotid inner diameter; PTS: Peak tensile stress; MTS: Mean tensile stress; WT: Wall tension.

Declarations

Ethics approval and consent to participate

Clinical investigations were performed according to the Declaration of Helsinki. The study protocol was approved by the ethics committee of Shanghai General Hospital (2017KY009) and registered with the official website of China Clinical Trial Registration Center
(ChiCTR1800016590).

Consent for publication

Consent for publication was obtained from the patients and family members.

Availability of data and materials

Not applicable.

Conflict of interest

The authors declare that they have no conflict of interest.

Funding

This work was supported by the Three - year Plan for Clinical Skills and Innovation in Municipal Hospitals (16CR3105B), Shanghai Science and Technology Committee Fund (16411969300), Interdisciplinary Program of Shanghai Jiao Tong University (YG2015MS28), Shanghai Health and Family Planning Commission Fund (201640043) and Shanghai Songjiang District Science and Technology Project (18sjkjgg72 and 18sjkjgg53).

Authors’ contributions

XHL and ZJL designed this study. ZJL, RW and LFD conducted the ultrasound scans and measurements. ZJL analyzed the data. XHL wrote the manuscript.

Acknowledgements

Not applicable.

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Tables

| Variable                        | Group 1 (n=23) | Group 2 (n=22) | t/χ² | P     |
|---------------------------------|---------------|---------------|------|-------|
| Gender (F/M)                    | 11/12         | 11/11         | 0.023| 0.879 |
| Height, cm                      | 162.9±7.1     | 167.5±7.9     | -2.301| 0.025 |
| Weight, kg                      | 66.3±17.3     | 66.7±15.6     | 0.348| 0.729 |
| Body mass index, kg/m²          | 25.8±7.4      | 23.5±4.1      | 1.444| 0.154 |
| SBP, mmHg                       | 139.6±11.1    | 125.7±9.1     | 5.102| 0.001 |
| DBP, mmHg                       | 87.9±7.2      | 79.7±6.1      | 4.607| 0.001 |
| Glucose, mmol/L                 | 6.1±1.61      | 5.2±1.21      | 1.001| 0.327 |
| Total cholesterol, mmol/L       | 4.6±1.11      | 4.4±0.81      | 0.763| 0.456 |
| Triglycerides, mmol/L           | 1.7±1.31      | 1.2±0.81      | 1.12 | 0.275 |
| Low-density lipoprotein, mmol/L  | 2.9±1.01      | 2.7±0.81      | 0.77 | 0.433 |
| Diabetes mellitus (n)           | 3             | 1             | 0.156| 0.693 |
| Hypertension (n)                | 5             | 3             | 0.044| 0.833 |

1 mm Hg =0.133 kPa.
Table 2. Comparison of carotid viscoelasticity, structure and tensile stress between groups

| Variable | Group 1 (n=23) | Group 2 (n=22) | t    | p   |
|----------|----------------|----------------|------|-----|
| **Viscoelasticity** | | | | |
| SWE_R kPa | 10.29±9.57 | 17.24±14.07 | -2.236 | 0.040 |
| SWD_R (m/s)/kHz | 11.99±3.51 | 13.97±3.71 | -2.129 | 0.043 |
| **Structure** | | | | |
| R-CIMT (μm) | 677.6±138.4 | 449.1±131.9 | 6.321 | 0.001 |
| L-CIMT (μm) | 674.7±119.8 | 503.9±193.2 | 3.976 | 0.001 |
| R-CCID_T (mm) | 8.23±0.89 | 6.43±0.40 | 5.946 | 0.001 |
| L-CCID_T (mm) | 7.93±0.99 | 6.50±0.41 | 7.575 | 0.001 |
| R-CCID_R (mm) | 8.57±1.03 | 7.00±0.55 | 7.095 | 0.001 |
| L-CCID_R (mm) | 8.20±1.09 | 7.04±0.56 | 5.000 | 0.001 |
| R-CCAD (μm) | 339.9±142.7 | 571.1±148.2 | -5.946 | 0.001 |
| L-CCAD (μm) | 273.6±98.6 | 535.4±153.9 | -7.575 | 0.001 |
| **Tensile stress** | | | | |
| R-PTS (mmHg) | 920.4±160.3 | 1073.6±285.8 | -2.474 | 0.017 |
| R-MTS (mmHg) | 783.8±189.9 | 884.4±224.0 | -1.812 | 0.076 |
| L-PTS (mmHg) | 648.1±117.4 | 723.8±195.5 | -1.758 | 0.084 |
| L-MTS (mmHg) | 600.9±108.2 | 644.6±168.2 | -1.156 | 0.253 |

SWE_R: shear wave elastic modulus in electrocardiographic R wave; SWD_R: shear wave dispersion in electrocardiographic R wave; L-CIMT: left common carotid intima-media thickness; R-CIMT: right common carotid intima-media thickness; L-CCID_T and R-CCID_T: left and right common carotid inner diameters at end of diastole, respectively. L-CCID_R and R-CCID_R: left and right common carotid inner diameters at end of systole, respectively. L-CCAD and R-CCAD: difference of CCID between diastole and systole on left and right. R-PTS and R-MTS: right carotid peak tensile stress and mean tensile stress; L-PTS and L-MTS: left carotid peak tensile stress and mean tensile stress.

1 dyne/cm² = 7.5×10⁻⁴ mmHg.
### Table 3. Correlation analysis between carotid viscoelasticity tensile stress [rP]

| Variable | $SWE_R$       |            |            | $SWD_R$       |            |
|----------|---------------|------------|------------|---------------|------------|
|          | All subjects  | Group1     | Group 2    | All subjects  | Group1    |
| R-PTS    | 0.218 (0.021) | 0.137 (0.313) | 0.159 (0.241) | 0.096 (0.314) | -0.404 (0.002) |
| R-MTS    | 0.359 (0.001) | 0.276 (0.040) | 0.353 (0.008) | 0.054 (0.568) | 0.068 (0.619) |
| L-PTS    | 0.209 (0.027) | 0.196 (0.148) | 0.142 (0.298) | 0.067 (0.485) | -0.352 (0.008) |
| L-MTS    | 0.369 (0.001) | 0.415 (0.001) | 0.313 (0.019) | 0.005 (0.956) | 0.086 (0.530) |

$SWE_R$: shear wave elastic modulus in electrocardiographic R wave; $SWD_R$: shear wave dispersion in electrocardiographic and R-MTS: right carotid peak tensile stress and mean tensile stress; L-PTS and L-MTS: left carotid peak tensile stress and mean tensile stress.

**Figures**
Figure 1

QuadView of 4 display maps for the arterial shear wave profile. (a) Elastic map, (b) propagation map, (c) two-dimensional reference map and (d) shear wave dispersion map.
Correlation between the carotid viscoelasticity and tensile stress. (a) SWER correlated positively with right and left carotid peak tensile stress, respectively. (b) SWER correlated positively with right and left carotid mean tensile stress, respectively.

Bland-Altman plots for agreement in SWER (a) and SWDR (b) measurements.