Femoral Artery Sclerosis Evaluation by Tissue Doppler in Patients with Hypertension

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Background: The aim of this study was to evaluate the early femoral sclerosis in hypertensive patients by using tissue Doppler imaging (TDI).

Material/Methods: One hundred patients with hypertension were recruited and divided into group A (femoral artery intima-media thicknesses (IMT) ≥1.0 mm) and group B (femoral artery IMT <1.0 mm) with 50 cases in each group based on the femoral IMT. In addition, 50 healthy controls were also included in this study. Femoral wall structure and femoral artery IMT were examined by using high frequency ultrasound. Pulsed wave (PW)-TDI was used to obtain the motion curve of the posterior wall of the femoral artery. First (T1) and second (T2) peak duration were also obtained.

Results: The IMT of group A, group B, and the healthy control group were 1.17±0.12 mm, 0.74±0.11 mm, and 0.71±0.09 mm respectively with significant statistical difference (P<0.05). The first peak duration (T1) of the 3 groups (group A, group B, and healthy control group) were 135.6±16.6 ms, 134.5±18.5 ms, and 129.8±12.4 ms, respectively without statistical difference (F=1.868 P=0.158). The second peak duration (T2) of group A, group B, and the healthy control group were 234.7±39.8 ms, 209.3±34.9 ms, and 169.8±19.5 ms respectively with statistically significant difference (F=50.411 P=0.000). The diagnostic sensitivity, specificity area under the curve (AUC) and cut-off value for early arteriosclerosis diagnosis of femoral artery by T1 was 56.0% (95% CI: 41.3–70.0%), 66.0% (95% CI: 51.2–78.8%), AUC=0.54 (95% CI: 0.42–0.66) and 130.5 ms respectively. And it was 64.0% (95% CI: 49.2–77.1%), 62.0% (95% CI: 47.2–75.4%), AUC=0.69 (95% CI: 0.59–0.80) and 214.5 ms respectively for T2.

Conclusions: TDI can be used as an effective index for early femoral artery sclerosis before femoral artery IMT changes.

MeSH Keywords: Amyotrophic Lateral Sclerosis • Echocardiography, Doppler • Femoral Artery • Hypertension

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Background

The major characteristics of hypertension include the arteriosclerosis and elasticity attenuation of the main artery [1,2]. With long-term elevation of blood pressure under changes in hemodynamic force, the endarterium is damaged and causes the aggregation of vascular smooth muscle cell of the artery wall, macrophage, and T-lymphocytes [3,4]. Changes can include the hyperplasia of connective tissues such as collagen and proteoglycan, and vascular smooth muscle cells; the reduction of elastic fibers; the elasticity attenuation of the vascular wall; the increase in arterial stiffness; and the formation of wall calcified athero-plaque. The changes and dysfunctions are the pathological basis for the occurrence of cardiovascular and cerebrovascular events [5]. Elasticity attenuation is the specificity and sensitivity index of the blood vessel changes at the early stage, which reflects the function state of the vessel and is earlier than the structural change. Elasticity attenuation of the vessel discovery and diagnosis at the early stage are valuable for the prevention and treatment of cardiovascular and cerebrovascular diseases.

Cardiovascular and cerebrovascular diseases caused by atherosclerosis are a leading causes of crippling and death [6]. Therefore, early detection and intervention have crucial clinical significance to the reduction of the occurrence of cardiovascular and cerebrovascular diseases. Currently, the clinical diagnosis of arteriosclerosis mainly relies on morphological changes, and the available methods for functional inspection of blood vessels are insufficient. This study aimed to develop an effective way to evaluate atherosclerosis before morphological changes occur, providing a reliable imaging method for the clinical prevention of atherosclerosis.

Material and Methods

Patients

One hundred patients with hypertension who received treatment from October 2015 to December 2016 were recruited as participants. This study was approved by the Ethics Committees of Tianjin Union Medicine Center and in accordance with the Declaration of Helsinki. All patients signed written informed consent. The inclusion criteria were as follows: 1) patients who satisfy the diagnostic reference of WHO/ISH; 2) patients aged 45–65 years old; and 3) patients with 10–20 years of hypertension medical history. The exclusion criteria were as follows: 1) patients with secondary hypertension, 2) patients with renal insufficiency, 3) patients with thyroid dysfunction or combined metabolic disease, 4) patients with diabetes, and 5) patients with connective tissue disease. All patients were examined with high-frequency ultrasonic detection of the femoral artery and were divided into 2 groups according to the intima-media thickness (IMT) inside the femoral artery. Group A was the hypertension group (100 femoral arteries) that comprised 50 patients (23 males and 27 females) aged 46–65 years old (average, 53.3±7.3 years) with an IMT ≥1.0 mm. Group B was the hypertension group (100 femoral arteries) that comprised 50 patients (24 males and 26 females) aged 47–67 years old (average, 54.7±7.4 years) with an IMT <1.0 mm. Fifty healthy controls (25 males and 25 females) aged 45–65 years old (average, 53.0±9.0 years) at the same time were selected as control group. The inclusion criteria for healthy controls were participants without hypertension, hyperlipidemia, diabetes, coronary heart disease, or renal insufficiency; no alcohol consumption and no smoking history; the blood pressure within the normal scope; and the high-frequency ultrasound showed an IMT <1.0 mm and the absence of the echo of attached plaque.

Instrument

We used PhilipsIU22 probe S5-1 with a frequency of 2.5–5 MHZ and probe l9-3 with a frequency of 5–10 MHZ. A Riva-Rocci sphygmomanometer branded Yutu from Shanghai Medical Equipment Co., Ltd. was used.

Blood pressure measuring

The patients were required to rest for 10 minutes before taking their blood pressure and were forbidden to smoke and drink coffee within 30 minutes. We requested that their bladders should be empty. The participants sat down, and the brachial artery blood pressure of their right upper limbs was measured with a table mercury sphygmomanometer that has been calibrated regularly. Two measurements were performed continuously, with a 1–2 minutes interval, and the average value was obtained. The measurement was repeated when the systolic or diastolic pressure value of the 2 measurements differed by over 5 mmHg. The average value of 3 measurement results was recorded.

Measuring the intima-media (IMT) of the femoral artery

After laying prone with completely exposed limbs, the linear array probe was used to observe the morphological features (e.g., presence of plaque) of the vascular wall of the femoral artery, such as the wall thickness. The IMT thickness at the section of the long axis of the femoral artery (the distance between the first strong echo area to the second echo area formed by the tunica media and tunica externa) (Figure 1A) was continuously measured 3 times, and the average value was used.

Measuring the motion curve of the paries posterior tissues of the femoral artery

The cuff of the Riva-Rocci sphygmomanometer was placed at the remote end of the femoral artery to measure the blood
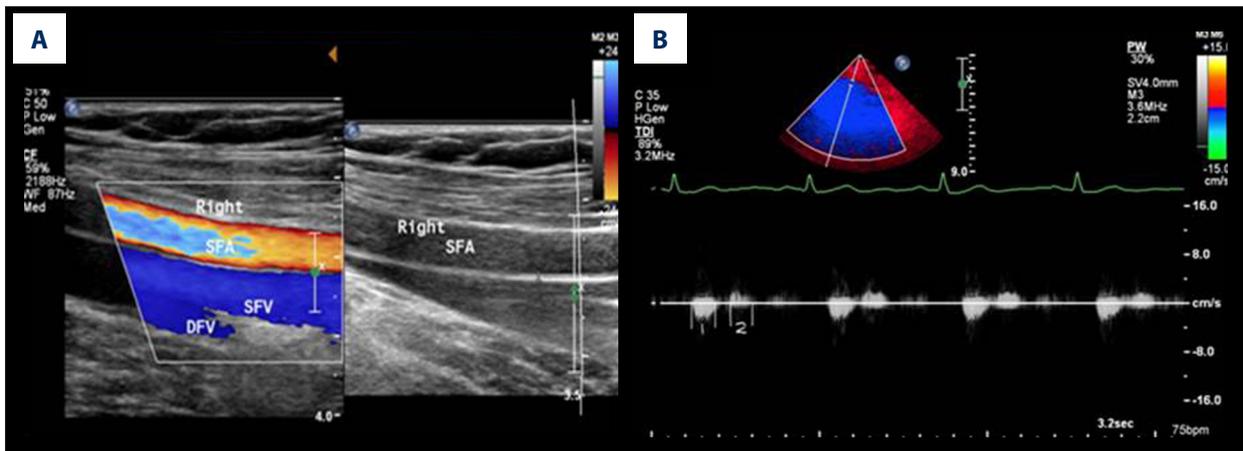
Figure 1. Inspection of the IMT and the paries posterior tissue motion curve of the femoral artery under the tissue Doppler pulse mode. The left side (**A**) shows the color 2D diagram of the femoral artery along the axis, whereas the right-side figure of the femoral artery paries posterior observation site of femoral vein forks shows the intima-media measurement site of the femoral artery. After the femoral artery far-end of (**B**) was blocked, motion curve 1 of the femoral artery paries posterior tissue measured by PW-TDI imaging was negative for the first peak while motion curve 2 was positive for the second peak. IMT – intima-media thickness, PW-TDI – pulsed wave-tissue Doppler imaging.

pressure, and the mercury column was situated in a region that was 10 mmHg larger than the systolic pressure of the femoral artery to block the blood stream. The observation site was placed at the paries posterior of the femoral artery that was in front of the femoral vein branch. The S5-1 phased array probe was placed at the vertical section for probing. The tissue Doppler pulse mode was used to place the sample frame at this observation site. The sampling line should be perpendicular to the vessel direction, and the width of the sampling gate was 4 mm. The motion curve of the paries posterior tissues of the femoral artery was obtained, and 3 curves of the complete cardiac cycle were recorded and stored on a hard disk. The durations of the first and second peaks of the motion curve of the paries posterior tissues of the femoral artery within the same cardiac cycle were measured (Figure 1B). Three cardiac cycles were selected for the aforementioned measurements, and the average value was obtained and recorded.

Statistical analysis

SPSS 17 software (SPSS, Inc., Chicago, IL, USA) was used for statistical analysis. The measurement data of normal distribution was expressed by mean and standard deviation, and the 2 groups A and B were compared with the control group with independent sample t-test, and the T1 and T2 of the 3 groups were compared with the analysis of variance. The count data are expressed in frequency. The difference of $P<0.05$ was statistically significant.

## Results

IMTs comparison

The IMTs of 300 femoral artery vessel ultrasonic detections of 150 study participants is clearly displayed. One hundred high-frequency ultrasonic vessels of the 50 cases in the control group displayed smooth endarterium without attached plaques. The IMT thickness of the femoral artery was 0.71±0.09 mm. The 50 cases in group A (hypertension group, with an IMT ≥1.0 mm), 100 vessels, exhibited thickened endarterium, was rough and unsmooth, in which 46 vessel lumen had attached plaques. Color Doppler flow imaging (CDFI) displayed that part of the vessel filling-detect, without narrowing. IMT thickness was (1.17±0.12) mm. The high-efficiency ultrasound of 100 vessels of the 50 cases of group B indicated that the endarterium of the femoral artery was smooth and without attached plaques. CDFI displayed good blood filling, without the filling-detect. IMT thickness was 0.74±0.11 mm (Table 1). The IMT of group A was significantly higher than that of the control group ($P<0.05$). No significant difference in IMT was found between group B and the healthy control group ($P>0.05$).
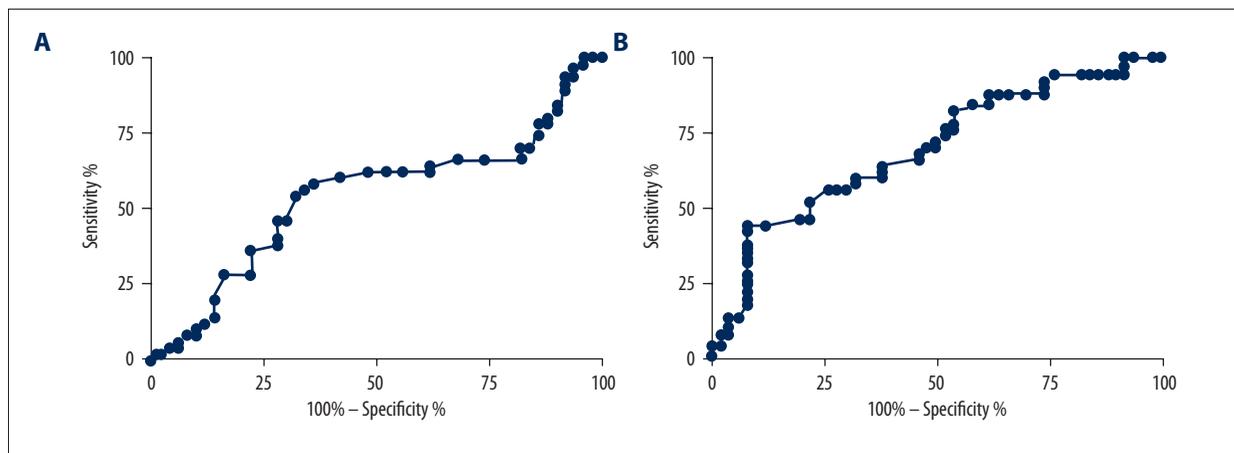
Peak duration

The peak duration of the first, second peaks of the posterior wall of the femoral artery were compared for the 3 groups after the femoral artery was blocked by the distal blood flow. The first peak duration (T1) of 3 groups (group A, group B and healthy control group) were 135.6±16.6 ms, 134.5±18.5, and 129.8±12.4 ms, respectively. There was no statistically significant difference among the three groups (F=1.868 P=0.158).

Table 1. The first, second peak duration and IMT of three groups.

Group	Femoral arteries (n)	IMT (mm)	T1 (ms)	T2 (ms)
A	100	1.17±0.12	135.6±16.6	234.7±39.8
B	100	0.74±0.11	134.5±18.5	209.3±34.9
Control	100	0.71±0.09	129.8±12.4	169.8±19.5
P	–	<0.0001	0.158	<0.0001
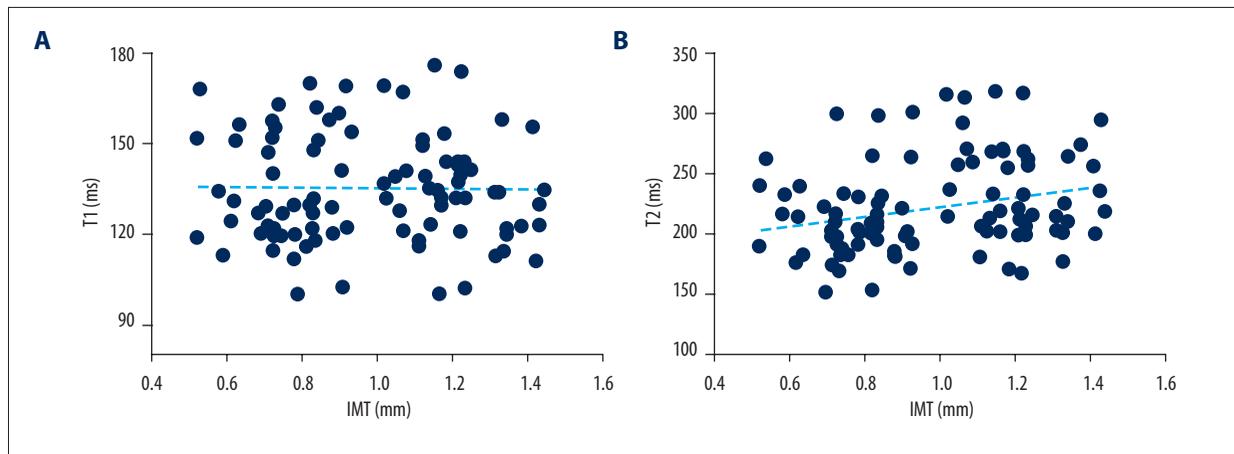
Figure 2. Scatter plot of Pearson correlation between IMT and T1: T2 (**A**): T1 and IMT; (**B**) T2 and IMT. IMT, intima-media thickness.

Figure 3. ROC curve was used to evaluate T1 and T2 as reference for evaluation the value of early arteriosclerosis of femoral artery:
(**A**) T1 as the reference; (**B**) T2 as the reference. ROC, receiver operating characteristic.

The second peak duration (T2) of group A, group B, and the healthy control group were 234.7±39.8 ms, 209.3±34.9 ms, and 169.8±19.5 ms respectively with statistically significant (F=50.411 *P*=0.000), Table 1.

Correlation between IMT and T1, T2

Significant positive correlation between T2 and IMT was found in patients with hypertension (r=0.25, *P*=0.01), Figure 2B. However, the T1 and IMT was not correlated (*P*>0.05), Figure 2A.

T1 and T2 as reference for evaluation arteriosclerosis of femoral artery

The diagnostic sensitivity, specificity area under the curve (AUC) and cutoff value for early arteriosclerosis of femoral artery by T1 was 56.0% (95% CI: 41.3–70.0%), 66.0% (95% CI: 51.2–78.8%), AUC=0.54 (95% CI: 0.42–0.66) and 130.5 ms respectively (Figure 3A). It was 64.0% (95% CI: 49.2–77.1%), 62.0% (95% CI: 47.2–75.4%), AUC=0.69 (95% CI: 0.59–0.80) and 214.5 ms respectively for T2 (Figure 3B).

Discussion

Traditional ultrasound [7,8], magnetic resonance imaging (MRI) [9], and computed tomography (CT) only determine the vessel wall structure, plaque morphology, and nature, which can only provide anatomical and biological information and not mechanical characteristics. Another classic method for detecting the artery wall elasticity is pulse wave velocity (PWV), which uses a pulse wave gauge [10–12]. Although simple and easy to use, PWV has many insufficiencies [13]. First, the true length of the artery that the pulse wave passes cannot be obtained and thus it is a rough estimated using the body distance. Second, within the area, the deformation of the blood vessel and the replacement of the aortic internal pressure with the brachial artery affect the PWV value and result in deviation. As a new technology, blood vessel elasticity imaging is mainly used for evaluating the morphology of artery atheroplaque and determining the vulnerable plaques. Few studies focused on the early elasticity change of the vessel wall, and medical imaging combined with invasive catheterization techniques have a high cost and requirement for expert operators. Therefore, it is difficult to promote in the clinic. Through blocking the far-end blood flow at the femoral artery for hypertensive patients, this study established a transformation model of hemodynamics; testing the motion curve of the femoral artery paries posterior tissues was found to be easy and noninvasive. CDFI displayed a good blood filling without damage, and reflected the femoral artery wall elasticity before the morphology of the femoral artery wall changed and thus provided reliable evidence for the early diagnosis of atherosclerosis. Previously published studies [14] have shown that femoral arteriosclerosis could indirectly predict coronary arteriosclerosis and could be more sensitive and accurate than other peripheral vessels.

Tissue Doppler imaging (TDI) has been shown to have high sensitivity for the function evaluation of the myocardial velocity and have a good resolution of time and space [15]. It can detect substantial movement with low velocity and can be suitable for the detection of femoral artery wall motion at any time in the cardiac cycle, realistically reflecting the motion state of the vessel wall *in vivo*. In addition, it can intuitively evaluate the artery elasticity [15–18], and is practical and feasible for measuring femoral artery motion. Once the far-end blood flow of the femoral artery was blocked in this study, the blood flow resistance and its lateral pressure to the vessel wall increased. The motion extent of the vessel wall increased and made the motion curve of the femoral artery wall tissue clearer and easy to measure, which reduced deviation. The first peak of the motion curve of the femoral artery paries posterior measured by PW-TDI was negative, while the second peak and its formation mechanism were positive. The first peak was formed by the rapid blood flow of the heart to the lateral pressure of the femoral artery wall, the compliance of the vasodilation, and the elastic recoil of the femoral artery. The active force was produced by heart blood flow and did not reflect the self-elasticity of the vessel. No significant difference in the duration of the first peak was found among the 3 groups in this study. Once the cardiac diastolic arterial cavity pressure rapidly decreased, the arterial wall elasticity at the blocked position retracted and produced high-speed blood flow. The lateral pressure to the vessel wall from the blood flow, the femoral artery compliance, and the elastic recoil produced the second peak. The active force was the elastic recoil of the femoral artery, which reflected the self-elastic function of the artery. The worse the vessel compliance and artery elasticity were, the longer the duration of the wave was; conversely, the better the artery elasticity and compliance were, the shorter the duration was. The second peak duration of the patients in the 3 groups in this study was significant, which was in accordance with Nicolle et al. findings [15].

The comparison of the 3 groups of IMTs indicated that the IMT in group A was significantly larger than that in the control group, whereas the IMT in group B was not significantly different from that in the control group. However, significant differences were found in the second peak duration of the motion curve of the participants' paries posterior tissues of the femoral artery. This result suggests that the vessel wall elasticity function already decreased before the IMT of the femoral artery thickened. Meanwhile, early sclerosis of the femoral artery was evaluated on the basis of the ROC (receiver operating characteristic) curve using T1 and T2 as references. The ROC area under the curve (AUC) using T1 and T2 as references to evaluate the early sclerosis of the femoral artery were AUC=0.54 and AUC=0.69, respectively. The AUC value of T2 was comparatively higher than that of T1, which indicated that Doppler imaging could be an effective index for evaluating the early sclerosis of the femoral artery before the femoral artery IMT changes.

Conclusions

The application of TDI in detecting the second peak duration of the femoral artery paries posterior motion curve was a reliable index for evaluating the femoral artery elasticity before the femoral artery wall structure changed. It has low requirements in terms of devices and is easy to use, noninvasive, repeatable, and applicable in hospitals with different levels of resources. However, due to the small sampling capacity and monocentric study, it exhibited a limited statistical efficiency. Therefore, in the future, large-scale polycentric and forward-looking diagnosis studies should be carried out to explore and discuss the clinical value of Doppler imaging for evaluating early sclerosis before the femoral artery IMT changes.

Conflict of interest

None.

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