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Evaluating Arterial Stiffness in Type 2 Diabetes Patients Using Ultrasonic Radiofrequency*

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Summary: Differences in arterial stiffness between the two sides of the carotid arteries were investigated using ultrasonic radiofrequency in 88 patients with type 2 diabetes and 70 controls. The compliance coefficient (CC), pulse wave velocity (PWV), intima-media thickness (CIMT) and diameter (CCAD) of the common carotid arteries (CCAs) were measured. The ratio of the left to right CCAs was calculated to provide four indexes: CC ratio, PWV ratio, CIMT ratio and CCAD ratio. In the diabetes group, the PWV on the left side was significantly higher than that on the right side, while the CC on the left side was significantly lower than that on the right side. The bilateral CIMT was thicker and CCAD was wider, the left PWV traveled faster, and the right CC was higher in the diabetes group than in the control group. The PWV ratio between the two groups was significantly different and correlated positively with duration of diabetes and systolic blood pressure (SBP). The differences between the two sides of CCAs in patients with diabetes suggested that disease duration and SBP were important risk factors for arterial stiffness. Identifying the difference could potentially lead to the much earlier diagnosis of arteriosclerosis.

Key words: type 2 diabetes; intima-media thickness; stiffness; pulse wave velocity

Arteriosclerosis is a major complication of diabetes and affects multiple organs. Approximately 30% of ischemic strokes are caused by carotid arteriosclerosis[1]. Early diagnosis and intervention in vascular diseases are important to control the cerebrovascular and cardiovascular events, such as stroke and transient ischemic attack. The pulse wave velocity (PWV) is considered as an important indicator for evaluating arteriosclerosis. Many studies evaluate arteriosclerosis of the arterial tree and the risk factors using PWV[2]. However, it has been poorly elucidated the difference of arteriosclerosis and the risk factors on the left and right sides of CCAs, respectively.

For the common carotid artery (CCA), there exists difference with the structure and function on left and right sides, respectively. By ultrasonic radiofrequency, the PWV can be measured on left and right sides respectively, so the arterial stiffness can be evaluated respectively. Our previous studies revealed as to the carotid intima-media thickness (CIMT), there remained some differences between the two sides of the carotid arteries, and each side was influenced by different factors[3]. The levels of blood biochemical indexes were strongly correlated to the left CIMT, while hemodynamic factors influenced much more strongly on the right CIMT. We supposed the structures of the left and right carotid arteries were different, and such differences might be represented in much earlier stage of arteriosclerosis in patients with type 2 diabetes. In this study, we reflected the differences of carotid arteriosclerosis in patients with diabetes with some new indexes. These four indexes were defined as the difference between the CCA function and structure: (1) thickness, CIMT ratio=L-CCA-IMT/R-CCA-IMT; (2) diameter, CCAD ratio=L-CCAD/R-CCAD; (3) compliance coefficient (CC) ratio=L-CC/R-CC; and (4) the PWV ratio=L-PWV/R-PWV (where L and R were left and right, respectively). We evaluated progression of arteriosclerosis, which was considered to be a risk factor of cardiovascular disease, using new indexes and ultrasonic radiofrequency in type 2 diabetes patients.

1 MATERIALS AND METHODS

1.1 Subjects

This observational study involved 88 consecutive patients with type 2 diabetes (54 men and 34 women, aged 36–78 years, and mean age 56.0±11.7 years) from January 2013 to December 2013 in our hospital. The average diabetic history was 8.4±7.1 years (ranging from 1–30 years). Tests had shown no marked evidence of carotid arteriosclerosis in these patients. Carotid atherosclerosis was defined as luminal stenosis >0% (according to North American Symptomatic Carotid Endarterectomy Trial criteria)[4]. Seventy healthy subjects, age- and sex-matched to the type 2 diabetes patients, were enrolled (38 men and 32 women, aged 35–78 years, and mean age 53.4±8.6 years). The control group had no medical history of hypertension or coronary heart disease,

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and had normal results for physical examination, electrocardiography, echocardiography and blood tests of hepatic and renal functions. This study was approved by the ethics committee of Shanghai General Hospital, Shanghai Jiaotong University (China). The purpose of the research was explained to every prospective participant and they participated freely. Written informed consent was provided by all participants.

1.2 General Procedures

Blood pressure, taken as the average of three readings, was measured between 8–10 a.m. with a mercury sphygmomanometer on the right arm after patients sat for 10 min or longer. Blood samples were collected in the early morning following 12-h fasting to test fasting blood glucose (FBG), triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and hemoglobin A1c (HbA1c). Body height and weight were also measured and medical histories recorded.

1.3 Vascular Analysis

Vascular properties were measured and analyzed using Mylab Twice echocardiographic scanner (ESAOTE Medical Systems, Genova, Italy) with 4–13 MHz linear array transducer. The device was equipped with software for evaluation of the intima-media thickness (quality intima-media thickness software program, QIMT) and arterial stiffness (quality arterial stiffness software program, QAS). Local arterial construction and stiffness was automatically measured. This technology can precisely detect the vessel wall along each radiofrequency vector line in real time, and track the diameter waveform as a function of time using a complex cross-correlation model, and acquire the cardiac cycle based on the waveform periodicity[5].

While in a supine position, the measurement site was selected as 1.5 cm proximal to the dilatation of the bifurcation on view of long axis. The probe was adjusted to ensure the two-dimensional ultrasound beam was vertical to the artery walls. Images were optimized so that the anterior and posterior walls of the CCA were clearly shown. Once the systolic blood pressure (SBP) and diastolic blood pressure (DBP) were entered within the QIMT and QAS functions, the local carotid systolic pressure (Loc-Psys) and diastolic pressure (Loc-Pdia) were automatically estimated. The CIMT, CCAD, CC and PWV were calculated by the software from high quality images of six cardiac cycles, which were displayed on the screen (fig. 1). The values of CIMT ratio (L-CCA-IMT/R-CCA-IMT), CCAD ratio (L-CCAD/R-CCAD), CC ratio (L-CC/R-CC) and PWV ratio (L-PWV/R-PWV) were calculated with the above parameters.

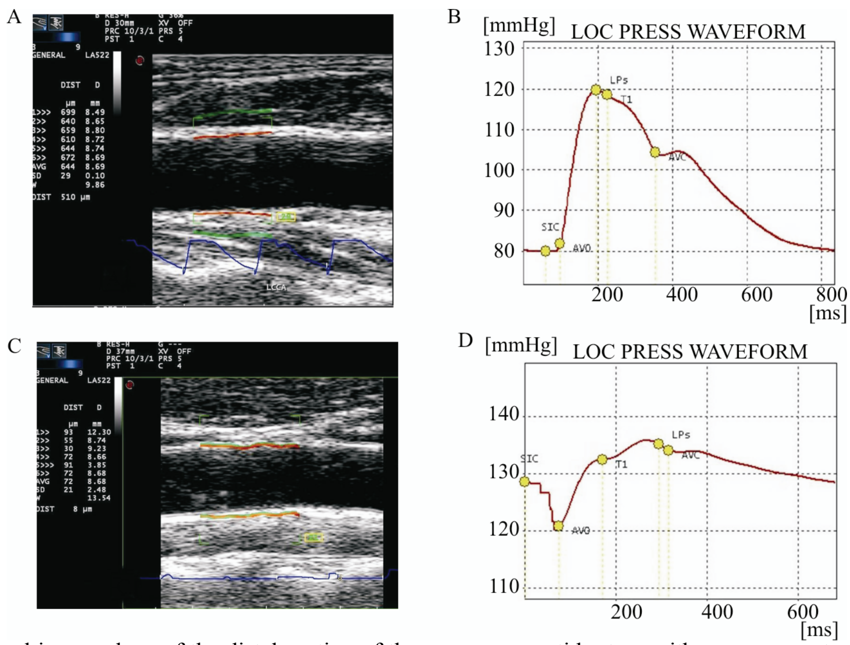

Fig. 1 The longitudinal image plane of the distal portion of the common carotid artery with measurement of the intima-media thickness (IMT) of the bilateral walls in control group (A) and patients with type 2 diabetes (C). The interfaces between lumen and intima and between media and adventitia were traced automatically using a quality intima-media thickness software program (QIMT), which further provides multiple distance measurements between both interfaces. The mean IMT in this sample is shown, and computed as the average of multiple distance measurements. The pressure waveform of the common carotid artery was measured by the quality arterial stiffness software program which automatically measures the local arterial construction and stiffness in control group (B) and patients with type 2 diabetes (D).

SIC: starting point of isovolumic contraction phase; AVO: aortic valve opens; LPS: end-point of systolic pressure of the left common carotid artery; T1: Forward waves stacking up reflected wave from the small arteries; AVC: aortic valve closes

These parameters were calculated using the following formulas[5], in which D and △D were the diastolic diameter and the change of diameter in systole, respectively, Ps and Pd were SBP and DBP, △P was pulse pressure (PP), and ρ was the blood density.

The parameter CC was the relative change in vessel diameter during systole for a given pressure change and was calculated as follows:

$$CC=\frac{\pi\cdot 2\cdot D\cdot \Delta D+\Delta D^{2}}{4\cdot \Delta P}$$

The parameter PWV was calculated as follows:

$$\text{PWV}=\sqrt{\frac{D^2\cdot\Delta \text{P}}{\rho\cdot(2\cdot D\cdot\Delta D+\Delta D^2)}}$$

1.4 Statistical Analysis

The difference within groups resulted from left and right comparison and the difference between the groups was from the same side comparison. The results were expressed as $\bar{x}\pm s$. The *t*-test was used to compare the numerical variables between the two groups, respectively. The paired *t*-test was used to compare the variables between the two sides of the carotid arteries and the Pearson correlation coefficient was calculated. The statistical analyses were performed using SPSS 13.0 and the statistical significance set at $P<0.05$. Subsequently, variables whose association with the vascular stiffness parameters achieved statistical significance (i.e. $P<0.05$) as well as other factors that may affect arterial stiffness (age, disease course, weight, BMI and metabolic parameters) were entered into a stepwise linear regression model to determine independent predictors of vascular parameters. Repeatability was evaluated by linear correlation analysis and Bland-Altman Plots.

2 RESULTS

2.1 Clinical and Biochemical Characteristics

The SBP, DBP, TG, FPG and HbA1c values were significantly higher in the group with diabetes than those in the control group ($P<0.01$). There were no significant differences in gender, age, height, body weight, TC, LDL and HDL between the two groups ($P>0.05$) (table 1).

Table 1 General characteristics of two groups

Variables	T2DM group	Control group	*t* value	*P* value
Demographics				
Gender (F/M)	34/54	38/32	1.925	0.181
Age (years)	56.05±11.70	53.43±8.57	1.571	0.118
Disease course (years)	8. 22±6.76	–		N
Height (cm)	165.21±7.15	165.77±8.73	–0.445	0.657
Weight (kg)	64.19±10.98	62.69±8.82	0.932	0.353
BMI (kg/m^2)	26.31±2.79	24.44±2.15	1.503	0.135
SBP (mmHg)	133.44±17.25	119.22±12.33	5.927	<0.001
DBP (mmHg)	82.73±8.05	77.72±8.65	3.831	<0.001
Metabolic parameters				
TC (mmol/L)	4.92±1.20	4.54±0.75	1.578	0.118
TG (mmol/L)	1.94±0.88	1.38±0.30	3.432	0.001
LDL-cholesterol (mmol/L)	2.65±0.91	2.31±0.56	1.887	0.062
HDL-cholesterol (mmol/L)	1.29±0.28	1.35±0.27	–0.954	0.343
FPG (mmol/L)	8.63±2.58	4.96±0.73	7.610	<0.001
Hemoglobin A1c (%)	7.92±1.65	4.85±0.63	9.875	<0.001

Values are expressed as $\bar{x}\pm s$. BMI: body mass index; 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; 1 mmHg=0.133 kPa

2.2 Difference in Structure and Function

In the group with diabetes, the PWV of the left carotid artery was significantly higher than that of the right carotid artery, while the CC of the left carotid artery was significantly lower than that of the right carotid artery ($P<0.05$). The CIMT and CCAD did not show significant differences between the two sides ($P>0.05$). In the control group, there were no significant differences in CIMT, CCAD, CC and PWV between the two sides of the carotid arteries (table 2).

Table 2 Differences of structure and function between left and right carotid arteries in two groups

Variables	Left carotid artery	Right carotid artery	*t* value	*P* value
T2DM group				
CIMT (μm)	659.89±153.38**	643.11±131.63**	1.457	0.149
CCAD (mm)	7.72±0.90**	7.86±0.94**	–1.344	0.183
CC (mm^2/kPa)	0.89±0.48	0.99±0.41*	–2.568	0.012
PWV (m/s)	8.15±2.36*	7.48±1.83	2.929	0.004
Control group				
CIMT (μm)	575.89±122.36	555.11±128.10	1.526	0.132
CCAD (mm)	7.24±0.63	7.12±0.88	1.373	0.174
CC (mm^2/kPa)	0.79±0.33	0.78±0.39	0.257	0.798
PWV (m/s)	7.43±1.38	7.81±2.02	–1.876	0.065

Values are expressed as $\bar{x}\pm s$. CIMT: carotid intima-media thickness; PWV: pulse wave velocity; CCAD: diameter of the common carotid; CC: compliance coefficient of the common carotid

$^{*}P<0.05$, $^{**}P<0.01$ *vs*. healthy control subjects

The indexes of left and right CCAs were compared between groups. The bilateral CIMT of patients with type 2 diabetes was thicker than that of the control subjects, and the bilateral CCAD was wider ($P<0.05$). The left PWV of diabetes group traveled faster than that of control subjects, and the right CC in the diabetes group was higher than that of the control group (table 2).

2.3 Difference in New Indexes of Stiffness and Correlation Analysis

The values of the PWV ratio (L-PWV/R-PWV) and the CC ratio (L-CC/R-CC) were calculated to evaluate the difference in carotid stiffness between the bilateral carotid arteries. The PWV ratio was greater than 1 in the group with diabetes, and less than 1 in the control group. At the same time, the CC ratio was less than 1 in the group with diabetes, and greater than 1 in the control group. There was a significant difference in PWV ratio and CC ratio between the two groups ($P<0.05$, table 3).

Table 3 Difference in new indexes of stiffness between diabetic group and control group

Variables	T2DM group	Control group	*t* value	*P* value
IMT ratio	1.03±0.18	1.06±0.22	–0.801	0.424
CCAD ratio	0.99±0.16	1.03±0.15	–1.509	0.133
CC ratio	0.95±0.47	1.15±0.52	–2.579	0.011
PWV ratio	1.10±0.27	0.98±0.20	3.101	0.002

IMT ratio: LCCA-IMT/RCCA-IMT; CCAD ratio: L-CCAD/R-CCAD; CC ratio: L-CC/R-CC; PWV ratio: L-PWV/R-PWV

Correlation analysis showed that the PWV ratio was correlated positively with diabetes, SBP and DBP (r=0.334, 0.277 and 0.172, $P<0.05$). Multiple linear regressions suggested that diabetes, SBP, age, weight, BMI and TG were independent risk factors for higher PWV ratio. CC ratio was negatively correlated with SBP and positively with FBG and HDL-C. HDL-C and age were the independent risk factors for CC ratio. Values of the CIMT ratio and CCAD ratio revealed no significant differences between the two groups ($P>0.05$), suggesting there was no significant difference in the carotid structure between the left and right common carotids in the patients and control subjects (tables 4 and 5).

Table 4 Correlation analysis between new indexes of stiffness and risk factors

Variables	IMT ratio	CCAD ratio	CC ratio	PWV ratio
Age (years)	–0.067	0.028	0.046	–0.006
Height (cm)	–0.043	0.114	–0.092	0.005
Weight (kg)	0.111	0.075	–0.045	–0.026
BMI (kg/m^2)	0.167*	0.011	0.022	–0.056
Disease course (year)	0.163	0.282**	–0.105	0.334**
SBP (mmHg)	–0.065	–0.155*	–0.166*	0.277**
DBP (mmHg)	0.074	–0.133	–0.135	0.172*
FPG (mmol/L)	0.193	0.002	0.231*	–0.094
TC (mmol/L)	–0.044	–0.222	0.023	0.072
LDL-c (mmol/L)	–0.061	0.006	–0.176	0.144
HDL-c (mmol/L)	0.003	0.035	0.291*	–0.051
TG (mmol/L)	0.077	0.071	0.139	–0.189

$^*P<0.05$, $^{**}P<0.01$

Table 5 New indexes of stiffness and risk factors analyzed with multiple linear regression

Dependent	Model	Unstandardized coefficients (B)	Standard error of B	Standardized coefficients (B’)	*t* value	*P* value
PWV ratio						
	Age	–0.006	0.003	–0.268	–2.363	0.022
	Weight	0.084	0.042	3.660	2.015	0.049
	BMI	–0.255	0.115	–3.421	–2.214	0.031
	Disease course	0.017	0.005	0.402	3.421	0.001
	TG	0.203	0.085	–0.576	–2.385	0.021
	SBP	0.010	0.003	0.533	3.153	0.003
CC ratio						
	Age	0.009	0.004	0.268	2.173	0.034
	HDL-c	0.652	0.326	0.625	2.002	0.050

2.4 Repeatability

One week later, 15 research objects were randomly selected for a repeatability test. Namely, the same observer measured CIMT and PWV again. Intra-group comparison had a higher correlation (for CIMT, r=0.970, $P<0.01$; for PWV, r=0.885, $P<0.01$), and mean difference was −4.467±28.487 μm for CIMT, and −0.145±0.852 m/s for PWV respectively. Blant-Altman analysis showed a consistent trend in the difference value and the mean value of the CIMT and PWV by repeated measurement (fig. 2).

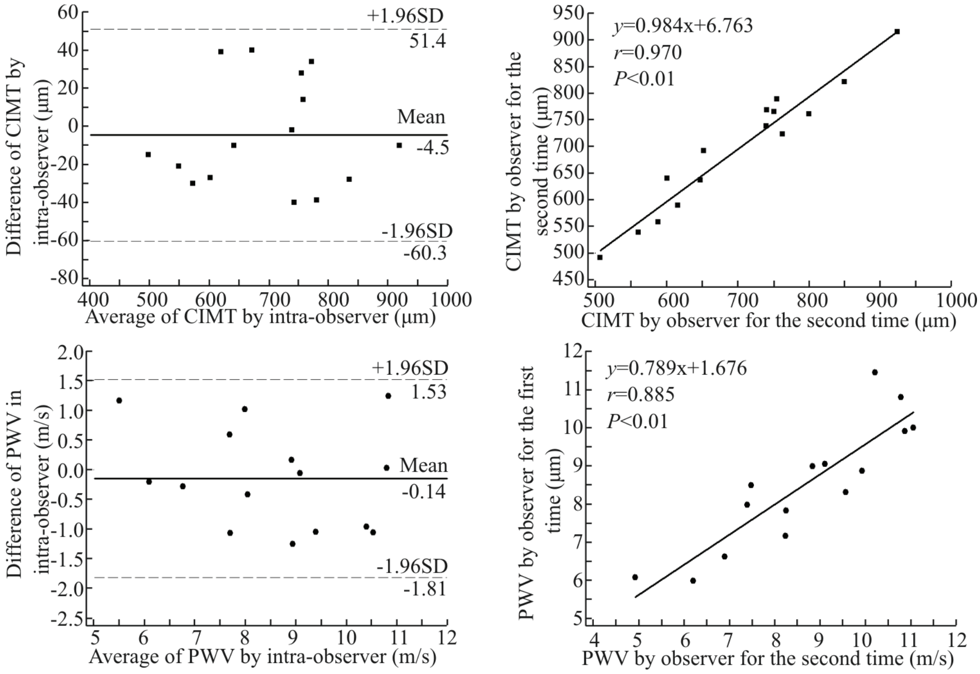

Fig. 2 Intra-observer variability of PWV and CIMT measurements

Blant-Altman analysis showed a consistent trend and linear regression analysis showed good agreement between measurements for PWV and CIMT.

3 DISCUSSION

In this study the difference of arterial stiffness between the two sides of the carotid arteries was shown in patients with diabetes, which made the diagnosis of arteriosclerosis much earlier. This study showed that the mean values of PWV ratio (L-PWV/R-PWV), which was calculated for evaluating the difference in carotid stiffness between the two sides, were greater than 1 in diabetes group and less than 1 in the control group. These results suggested the arterial stiffness developed much more rapidly on the left side in patients with diabetes. Further, for arterial function, this difference between the two sides was related to the subject's age, SBP and history of diabetes. This might be one of the reasons why the ratio of the two sides of carotid stiffness converted in patients with diabetes and could sensitively reflect the segmental arteriosclerosis and impairment of arterial functions under pathological conditions.

Type 2 diabetes is a metabolic disorder characterized by chronic hyperglycemia. Metabolic disorders damage the vascular system, which can lead to systemic arteriosclerosis[6]. Diabetes and other cardiovascular risk factors lead to different degrees of arteriosclerosis in different arteries. A study revealed the arteriosclerosis in degree was different with different segments of the arterial tree for patients with type 2 diabetes. In the same study, aging was associated with the increased stiffness of central arteries more than that of peripheral arteries. Gender also affected the PWV of lower extremity arteries. Therefore, different factors were involved in differently segmental stiffness. Increased arterial stiffness is an indicator of arteriosclerosis and is a critical index that can be used to evaluate the morbidity and mortality of cerebrovascular diseases[1]. PWV is considered to be the golden standard for evaluating arterial stiffness because of its ability to reflect the early stage of arteriosclerosis in type 2 diabetes patients[7]. There are two methods of measuring PWV. One is the two-point method (a traditional method)[8, 9], in which the carotid-femoral PWV (cfPWV), heart-femoral PWV (hfPWV), and brachial-ankle PWV (baPWV) are calculated based on waveform analysis combined with electrocardiac signals and cardiac sound signals. The other single-point method (a new method)[10] is based on primitive radiofrequency signals whereby the PWV of a local vascular segment is calculated by real-time and dynamic analysis of the change of the vascular diameter. This method can analyze the difference of arteriosclerosis in various arteries. Arteriosclerosis is a process that gradually develops. It can be induced by factors such as hypertension, diabetes, metabolic syndrome and a variety of risk factors. As such, the pathogenic mechanisms contribute to differences in the sequence and degree of arteriosclerosis in different arteries. Previous studies revealed the atherosclerosis in degree was different with different segments of arterial tree, and vascular elasticity could be improved by drugs[9–11]. The cfPWV, hfPWV and baPWV were used to evaluate different arteries[12–14]. cfPWV and hfPWV were used to evaluate the stiffness of large arteries, such as the aortic and carotid arteries. They were reported to be independent predictors for cardiovascular events, and were used to evaluate the improvement of vascular function after drug intervention[14]. Many studies found angiotensin converting enzyme inhibitors, calcium antagonists and nitrate medication improved the elasticity of main arteries and decreased PWV. Other studies showed the baPWV mainly represented the PWV of the lower extremities, and reflected stiffness of elastic arteries and some muscular arteries. The antilipemic agent and simvastatin improved the compliance of peripheral arteries, but had no significant effect on main arteries[15]. These suggest vascular elasticity of different segments are improved by different mechanisms[16, 17]. The changes in the vascular wall and the interaction between the heart and blood vessels contribute to arterial stiffness. Different arterial segments undertake different weights of risk factors, so their elasticity is different[18].

Thickened CIMT is the earlier lesion of arteriosclerosis[19]. This study showed that CIMT and diameter of both sides of the carotid arteries increased in diabetes group, suggesting that vascular structural changes had occurred in these patients. In the early stages, the functional changes of the arterial walls, such as the decrease of elasticity and increase of stiffness, had occurred. Therefore, the stiffness of arteries in patients with diabetes occurs prior to the onset of diabetes[20]. Hypertension, which is a common complication in diabetes, is closely correlated with arteriosclerosis[21]. Increased blood pressure leads to increased arterial stiffness and vice versa. Higher blood pressure leads to vascular wall fibrosis in great vessels, wall thickening in small vessels, and finally increased arterial stiffness. On the other hand, the growth and proliferation of vascular smooth muscle cells improve the accumulation of collagen and the cellular matrix, resulting in increased arterial stiffness and vascular reconstruction[22]. This study showed that carotid stiffness was significantly increased in patients with diabetes, with a higher stiffness of the left carotid artery than that of the right one. New indexes (IMT ratio, CCAD ratio, CC ratio and PWV ratio) were introduced to further investigate the structural and functional differences of the two sides of the carotid. The results revealed a significant difference in the PWV ratio between the two sides of the carotid artery in patients with diabetes. This difference indicated the degree of damage varied in different arteries. The carotid stiffness and the difference between the two sides of the carotid arteries in patients with diabetes might indicate much earlier stage of arteriosclerosis[23]. This study also showed that the PWV ratio was correlated positively with diabetic history and SBP, suggesting stiffness of arteries was relevant to the duration of diabetes and level of SBP. However, the difference of vascular elasticity could be precisely detected using a new method based on an ultrasonic radiofrequency technique. It was proved to be a remarkably powerful way of evaluating the development of arteriosclerosis.

In conclusion, type 2 diabetes is a major risk factor for the progression of arteriosclerosis. There was difference in arterial stiffness between left and right sides of CCAs. PWV ratio tested by ultrasound radiofrequency should be required to detect progression of arteriosclerosis and thereby prevent cardiovascular events.

Conflict of Interest Statement

The authors declare that there is no conflict of interest with any financial organization or corporation or individual that can inappropriately influence this work.

REFERENCES

1 Junyent M, Martínez M, Borràs M, *et al*. Predicting cardiovascular disease morbidity and mortality in chronic kidney disease in Spain. The rationale and design of NEFRONA: a prospective, multicenter, observational cohort study. BMC Nephrol, 2010,11(1):1-8

2 Wilkinson IB, Prasad K, Hall IR, *et al*. Increased central pulse pressure and augmentation index in subjects with hypercholesterolemia. J Am Coll Cardiol, 2002, 39(6):1005-1011

3 Luo X, Yang Y, Cao T, *et al*. Differences in left and right carotid intima-media thickness and the associated risk factors. Clin Radiol, 2011,66(5):393-398

4 Henderson RD, Eliasziw M, Fox AJ, *et al*. Angiographically defined collateral circulation and risk of stroke in patients with severe carotid artery stenosis. North American Symptomatic Carotid Endarterectomy Trial (NASCET) Group. Stroke, 2000,31(1):128-132

5 Niu L, Zhang Y, Meng L, *et al*. Detection of subclinical atherosclerosis in asymptomatic subjects using ultrasound radiofrequency-tracking technology. PLoS One, 2014, 9(11):e111926

6 Li ZJ, Du LF, Luo XH. Evaluation of ventricular-vascular coupling in patients with type 2 diabetes mellitus using 2-dimensional speckletracking imaging. J Huazhong Univ Sci Technolog Med Sci, 2014,34(6):929-934

7 Watson NL, Sutton-Tyrrell K, Youk AO, *et al*. Health ABC Study. Arterial stiffness and gait speed in older adults with and without peripheral arterial disease. Am J Hypertens, 2011,24(1):90-95

8 Matsui Y, O'Rourke MF, Ishikawa J, *et al*. Association of changes in ambulatory arterial stiffness index and pulse wave velocity during antihypertensive treatment: the J-CORE study. Am J Hypertens, 2012,25(8):862-868

9 Tsao CW, Seshadri S, Beiser AS, *et al*. Relations of arterial stiffness and endothelial function to brain aging in the community. Neurology, 2013,81(11):984-991

10 Chen LZ, Wang B, Zhang H, *et al*. Analyses of carotid intima-media thickness and quantitative arterial stiffness in type 2 diabetes mellitus patients with follow-ups. Zhonghua Yi Xue Za Zhi (Chinese), 2013,93(12):927-929

11 Matsui Y, O'Rourke MF, Hoshide S, *et al*. Combined effect of angiotensin II receptor blocker and either a calcium channel blocker or diuretic on day-by-day variability of home blood pressure: the Japan Combined Treatment With Olmesartan and a Calcium-Channel Blocker Versus Olmesartan and Diuretics Randomized Efficacy Study. Hypertension, 2012,59(6):1132-1138

12 Miljkovic D, Perret-Guillaume C, Alla F, *et al*. Correlation between peripheral blood pressure and pulse-wave velocity values in the institutionalized elderly persons 80 years of age and older: the PARTAGE study. Am J Hypertens, 2013,26(2):163-173

13 Hidvégi EV, Illyés M, Benczúr B, *et al.* Reference values of aortic pulse wave velocity in a large healthy population aged between 3 and 18 years. J Hypertens, 2012,30(12): 2314-2321

14 Girerd N, Legedz L, Paget V, *et al*. Outcome associations of carotid-femoral pulse wave velocity vary with different measurement methods. Am J Hypertens, 2012,25(12):1264-1270

15 Figueroa A, Gil R, Wong A, *et a*l. Whole-body vibration training reduces arterial stiffness, blood pressure and sympathovagal balance in young overweight/obese women.

Hypertens Res, 2012,35(6):667-672
16 Mäki-Petäjä KM, Booth AD, Hall FC, *et al*. Ezetimibe and simvastatin reduce inflammation, disease activity, and aortic stiffness and improve endothelial function in rheumatoid arthritis. J Am Coll Cardiol, 2007,50(9):852-858
17 Yuan LJ, Xue D, Duan YY, *et al*. Maternal carotid remodeling and increased carotid arterial stiffness in normal late-gestational pregnancy as assessed by radio-frequency ultrasound technique. BMC Pregnancy Childbirth, 2013,13:122
18 Giannarelli C, Bianchini E, Bruno RM, *et al*. Local carotid stiffness and intima-media thickness assessment by a novel ultrasound-based system in essential hypertension. Atherosclerosis, 2012,223(2):372-377
19 Keymel S, Heinen Y, Balzer J, *et al*. Characterization of macro-and microvascular function and structure in patients with type 2 diabetes mellitus. Am J Cardiovasc Dis, 2011,1(1):68-75
20 Low LC. The epidemic of type 2 diabetes mellitus in the Asia-Pacific region. Pediatr Diabetes, 2010,11(4):212-215
21 Vyssoulis G, Pietri P, Vlachopoulos C, *et al*. Early adverse effect of abnormal glucose metabolism on arterial stiffness in drug naive hypertensive patients. Diab Vasc Dis Res, 2012,9(1):18-24
22 Butt MU, Zakaria M. Association of common carotid intimal medial thickness (CCA-IMT) with risk factors of atherosclerosis in patients with type 2 diabetes mellitus. Pak Med Assoc, 2009,59(9):590-593
23 Castellon X, Bogdanova V. Screening for subclinical atherosclerosis by noninvasive methods in asymptomatic patients with risk factors. Clin Interv Aging, 2013,8:573-580

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