Carotid Artery Elasticity Variables as Predictors for the Risk of Coronary Arterial Lesions in Patients With Coronary Artery Disease

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Abstract

Background: Carotid artery can be considered as the window to reflect systemic artery atherosclerosis. Nowadays, the evaluation of carotid artery lesions both from the structural and functional aspects in patients with coronary artery disease (CAD) by ultrasonographic imaging is one of the preferable tools.

Materials and Methods: Patients with suspected CAD underwent coronary angiography and were assigned to one of four groups (non-CALs, atherosclerosis, single-lesion and multi-lesion) based on the results. Carotid artery intima-media thickness (IMT) and arterial stiffness were investigated by quality intima-media thickness (QIMT) and quality arterial stiffness (QAS) techniques. Univariable and multivariable modeling were used to investigate arterial elasticity predictors of CALs. Area under the receive operating characteristic curve (AUC) was used to evaluate diagnostic accuracy.

Results: Carotid IMT and stiffness variables pulse wave velocity (PWV), α , β and compliance coefficient (CC) were statistically different between every two-group comparisons. Multivariable logistic regression analyses demonstrated that the odd ratio (OR) for patients with CALs were 1.73, 1.67, 1.19, 1.23 and 0.56 accordingly as IMT, PWV, α , β and CC were concerned. The OR values were similar with or without. The AUC of IMT, PWV, α , β and CC were 0.9257, 0.8910, 0.8016, 0.9383, 0.8581 with correctly classified rate of 88.16%, 83.77%, 78.07%, 86.84%, and 81.58%, respectively.

Conclusions: The ultrasonographic variables derived from QIMT and QAS analysis present favorable diagnostic values for patients with CALs. The vascular stiffness changes predicted by QAS variables highlighted the hypothesis that functional impairment might predate structural damages as we can detect.

1. Introduction

Coronary atherosclerosis is the leading cause of coronary artery disease (CAD). Radiologic advances make non-invasive evaluation of vascular disease possible, especially to identify the asymptomatic individuals at high risk for cardiovascular (CV) disease. For those who are suspected of CAD, the widely used imaging modalities are coronary calcium scanning and carotid ultrasound. Coronary angiography is the preferred method for direct evaluation of CAD; however, it is an invasive procedure, which limits its use as a routine screening method for high-risk populations. Atherosclerosis is a systemic disease; coronary atherosclerosis and carotid atherosclerosis have the same risk factors and pathological basis, and are closely related to each other in occurrence and development. The clinical evaluation of vascular morphology and function of the common carotid artery (CCA) is the preferred means for detecting coronary lesions (CALs) [1–4].

In recent years, quantitative detection of vascular intima-media thickness (IMT) and arterial stiffness have become superior techniques to the traditional ultrasonic spatial resolution methods [5]. Ultrasound radio frequency (RF) data technology is a newly developed method for evaluating vascular elasticity of the carotid artery [6–8]. The measurement of arterial elasticity is based on the monitoring of RF signals

transmitted by ultrasound, and the acquired data gives an accurate reflection of the change in both structural and functional aspects. The parameters measured by RF data technology have good reproducibility and are more accurate; it has become a commonly used technique in vascular research in recent years. Reports on the relationship between large arterial structures and elastic indexes in CV events indicate the possibility of early detection of CAD noninvasively [5, 9, 10]. In the present study, we adapted this method for analyzing carotid artery with the aim of assessing arterial wall changes in patients with CAD. In addition, we discussed change tendencies in the CCA according to different stages of coronary arterial lesions as verified by coronary angiography and the predictive performance of these variables by using this superior technology.

2. Materials And Methods

2.1 Patients

From April 2018 to September 2020, 228 consecutive patients (146 men and 72 women; mean age, 55.30 $\pm$ 10.73 years) undergoing coronary angiography for the assessment of suspected CAD were enrolled in the study. Patients presenting with diabetes, nephropathy and carotid stenosis $\geq$ 50% were excluded from the study. The subjects were divided into four groups according to the results of coronary angiography: patients without CALs (non-CALs group, n = 54); patients with coronary atherosclerosis and coronary stenosis < 50% (atherosclerosis group, n = 41); patients with involvement of one major coronary artery, meanwhile, the coronary stenosis $\geq$ 50% (single-lesion group, n = 55); patients with involvement of more than one coronary arteries and at least one major coronary artery was detected with coronary stenosis $\geq$ 50% (multi-lesion group, n = 78).

Prior to ultrasonography, patients underwent a physical examination, and the following physical and laboratory parameters were assessed: body mass index (BMI), body surface area (BSA), smoking status, low density lipoprotein (LDL), high density lipoprotein (HDL) and clinical blood pressure, which was determined by performing three measurements of systolic blood pressure (SBP) and diastolic blood pressure (DBP). Hypertension was defined as SBP > 140mmHg and DBP > 90mmHg. The investigation conforms to the principles outlined in the Declaration of Helsinki. All subjects included in the study provided written informed consent. The study protocol was approved by the ethics committee of the Fourth Military Medical University Tangdu Hospital (Xi'an, China) and all the methods were performed in accordance with the relevant guidelines and regulations.

2.2 Coronary angiography

All patients had previously undergone a coronary angiography by an experienced physician with a Digital Subtraction Angiography System (GE INOVA3100, GE Healthcare) due to a suspicion of CAD. The narrowing caused by the most severe lesion in each coronary artery was recorded. Significant stenosis of the major coronary arteries was used to classify the patients as having single- or multi-vessel disease.

2.3 Ultrasound examination

Ultrasound examinations were conducted with a Mylab Twice color Doppler ultrasound diagnostic system (Esaote, Firenze, Italy), using a 5–13 MHz vascular probe, LA523, with built-in QIMT and QAS analysis software. Each patient was placed in the supine position, and the left common carotid artery (LCCA), carotid bulb and portions of the internal carotid arteries on both sides were scanned. The region of interest (ROI) was defined as 30 mm proximal to the beginning of the dilation of the bifurcation bulb.

Examination of the CCA was performed by two experienced ultrasound physicians who had been trained in vascular screening. The physicians were blinded to any clinical information about the subjects.

2.3.1 QIMT analysis

Similar to our previous study [11], subjects were placed in the correct position, so that the CCA was shown in longitudinal view. The ultrasonographic imaging was focused on the QIMT measurement site, ensuring that the anterior and posterior walls of the CCA were clearly shown. The IMT was measured at ROIs, which were plaque-free sites of the CCA. Atherosclerotic plaque was defined as a lesion with a focal IMT ≥ 1.5 mm, with localized protrusion of the vessel wall into the lumen. The QIMT function was started, and a radiofrequency signal tracked the leading edge of the lumen-intima boundary to the leading edge of the media-adventitia interface at the posterior wall of the selected vascular segment. The software automatically acquired six cardiac cycle measurements of QIMT (Fig. 1). When the standard deviation (SD) value became less than 15, the image was frozen and stored for further analysis.

2.3.2 QAS analysis

QAS measurements were carried out at the same time as QIMT measurements. Similar to previous study [11], a radiofrequency signal tracked the vascular wall (the red line), and another signal tracked the motion of the vascular wall (the green line) for at least six cardiac cycles. The mean and SD values were calculated automatically; again images were frozen when the SD value became less than 15 (Fig. 2). A derived carotid pressure waveform was calibrated by brachial end diastolic and mean arterial pressure, which allowed the calculation of the arterial stiffness, including pulse wave velocity (PWV, m/s), compliance coefficient (CC, mm^2/kPa), α and β .

2.4 Statistical analysis

All continuous variables were expressed as mean $\pm$ SD. The χ^2 test was used to compare the distributions of the studied variables between two groups for categorical data. The two-sample Student's t test was used to calculate the difference between the two groups for continuous variables with normal distribution. The Wilcoxon tank-sum test was used to determine the difference between the two groups for continuous variables with non-normal distribution. The reproducibility of the arterial stiffness measurements was tested in the younger subjects of non-CALs group, and the intra- and inter-observer variability was assessed by linear correlation analysis and Bland-Altman plots. Smoking was stratified into two categories: never smoker and ever smoker, which included former smoker and current smoker. A

Spearman correlation coefficient was used to examine the correlation among all vascular stiffness variables. Linear regression analysis was performed to assess correlations among all variables. The ORs and corresponding 95% CI were calculated to evaluate the association of risk of CALs and various risk factors using univariate and multivariate regression analyses. Performance of the stiffness variables as predictive factors was tested using receiver operating characteristic (ROC) curve analysis. The stiffness variables predictions for the assessment of coronary lesions were expressed in terms of area under ROC curve (AUC), sensitivity, specificity and positive and negative predictive values. The optional cutoff threshold values were determined at the point on the ROC curve at which Youden's index (YI, sensitivity + [100%-specificity]) was maximal. The level of significance was set at $p < 0.05$. Statistical analyses were carried out using the Stata 11.0 statistical software package (StataCorp LP, College Station, TX).

3. Results

3.1 Characteristics of the study subjects

The clinical, laboratory and ultrasonographic data for study participants are summarized in Table 1. No significant differences were found between two groups' gender, BMI, and BSA. Patients in the multi-lesion group were older than single-lesion patients (57.265 ± 8.550 v.s. 53.454 ± 11.593 , $P = 0.0313$). The percentage of smoker was much higher in multi-lesion group compared with that in non-CALs patients (55% v.s. 30% , $P = 0.004$). Meanwhile, patients with CALs were more likely to be hypertensive than non-CALs subjects ($P = 0.014$, $P = 0.001$, $P < 0.0001$ according to atherosclerosis, single-lesion and multi-lesion). Laboratory test indicated that patients with CALs had much lower HDL profiles compared with non-CALs patients with all $P < 0.05$. Patients in single-lesion and multi-lesion group had a higher level LDL than others. As expected, almost all the arterial elasticity variables in different group presented significant difference among intergroup comparisons, except for CC in comparison between single-lesion and atherosclerosis group (0.801 ± 0.385 v.s. 0.867 ± 0.319 , $P = 0.2055$). IMT, PWV, α , and β increased greatly with the severity of CALs, while CC decreased ($P < 0.0001$, $P < 0.0001$, $P = 0.01$, $P = 0.012$, $P = 0.042$). The associations of the arterial elasticity variables were showed in Fig. 3. IMT, PWV, α , and β positively correlated with each other ($P < 0.0001$), and with CC negatively ($r = -0.5656, -0.4500, -0.4073$, $P < 0.0001$). In multiple linear regression analyses, each 0.5m/s increment in PWV, α , and β was associated with an increase in IMT by 15 μm , 11 μm , and 8 μm in all subjects, while 0.2 mm^2/kPa reduction in CC was related to an increment in IMT by 33 μm .

Table 1
Characteristics of the study participants

Characteristic	Non-CAD Group (n = 54)	Atherosclerosis group(n = 41)	Single-lesion group(n = 55)	Multi-lesion group(n = 78)
Gender	34(63)	28(68)	35(64)	49(63)
Male, n (%)	54.167 ± 12.495	55.561 ± 10.533	53.454 ± 11.593	57.265 ± 8.550 [#]
Age (y)	25.214 ± 4.041	24.893 ± 3.481	24.537 ± 3.706	24.816 ± 3.837
BMI (kg/m ²)	1.817 ± 0.148	1.820 ± 0.131	1.787 ± 0.131	1.790 ± 0.116
BSA (m ²)	117.241 ± 10.332	115.536 ± 9.813	122.473 ± 11.303 ^{*^}	121.461 ± 12.073 ^{*^}
SBP (mmHg)	82.407 ± 6.2989	83.634 ± 10.317	85.8 ± 10.640	86.192 ± 7.816 [*]
DBP (mmHg)	9(17)	16(39) [*]	26(47) [*]	37(47) [*]
HP, n (%)	1.338 ± 0.163 [*]	15(36)	25(45)	43(55) [*]
Smoking satus	9(17)	1.338 ± 0.163 [*]	1.216 ± 0.225 ^{*^}	1.213 ± 0.225 ^{*^}
Ever, n (%)	16(30)	2.956 ± 0.327	3.084 ± 0.357 [*]	3.121 ± 0.365 ^{*^}
HDL (mmol/l)	1.411 ± 0.166	756.6 ± 50.66 [*]	838.9 ± 58.37 ^{*^}	953.2 ± 105.4 ^{*^#}
LDL (mmol/l)	2.933 ± 0.46	7.302 ± 1.386 [*]	8.744 ± 1.216 ^{*^}	11.04 ± 3.732 ^{*^#}
IMT (μm)	686.1 ± 72.77	0.867 ± 0.319 [*]	0.801 ± 0.385 [*]	0.654 ± 0.297 ^{*^#}
PWV (m/s)	6.273 ± 1.296	5.685 ± 2.052 [*]	6.968 ± 2.811 ^{*^}	8.831 ± 4.773 ^{*^#}
CC (mm ² /Kpa)αβ	1.334 ± 0.471	9.701 ± 3.164 [*]	12.60 ± 4.037 ^{*^}	16.77 ± 7.098 ^{*^#}
	4.199 ± 1.491			
Abbreviations: BMI, body mass index; BSA, body surface area; SBP, systolic blood pressure; DBP, diastolic blood; HP, hypertensive(was defined as SBP > 140 mmHg and DBP > 90mmHg); HDL, high density lipoprotein; LDL, low density lipoprotein; IMT, intima-media thickness; PWV, pulse wave velocity; CC, compliance coefficient.				
Value are presented as mean ± SD or number of subjects				
*Significantly different from the Non-CAD group (p < 0.05)				
^Significantly different from the Atherosclerosis group (p < 0.05)				
# Significantly different from the Single-lesion group (p < 0.05)				

Characteristic	Non-CAD Group (n = 54)	Atherosclerosis group(n = 41)	Single-lesion group(n = 55)	Multi-lesion group(n = 78)
	6.584 ± 1.718			
Abbreviations: BMI, body mass index; BSA, body surface area; SBP, systolic blood pressure; DBP, diastolic blood; HP, hypertensive(was defined as SBP > 140 mmHg and DBP > 90mmHg); HDL, high density lipoprotein; LDL, low density lipoprotein; IMT, intima-media thickness; PWV, pulse wave velocity; CC, compliance coefficient.				
Value are presented as mean ± SD or number of subjects				
*Significantly different from the Non-CAD group (p < 0.05)				
^Significantly different from the Atherosclerosis group (p < 0.05)				
# Significantly different from the Single-lesion group (p < 0.05)				

3.2 Risk association of arterial elasticity

Table 2 presents the risk estimates for each elasticity variable. The OR for IMT, PWV, α , and β , without adjustment, was 1.73, 1.67, 1.19, and 1.23, respectively, which meant that each 20 μm increment in IMT, 0.5m/s in PWV, 1.5 in α and 1.0 in β measurements and 0.2 mm^2/kPa reduction in CC increased the risk of CALs by 73%, 67%, 68%, 51%, and 44%. After being adjusted by gender, age, BSA, BMI, smoking status, blood pressure, HDL, and LDL, all the carotid vascular variables exhibited similar OR values to that of without adjustment analysis.

Table 2
Adjusted relative risk of coronary artery disease in relation to arterial stiffness parameters.

	OR (95%CI)	<i>P</i>	OR ^a (95%CI)	<i>P</i>	OR ^b (95%CI)	<i>P</i>
IMT	1.73(1.57–1.90)	< 0.0001	1.78(1.60–1.97)	< 0.0001	1.78(1.60–1.99)	< 0.0001
PWV $\alpha\beta$					1.69(1.52–1.89)	< 0.0001
CC	1.67(1.51–1.85)	< 0.0001	1.72(1.54–1.92)	< 0.0001	1.17(1.11–1.23)	< 0.0001
	1.19(1.13–1.25)	< 0.0001	1.19(1.14–1.26)	< 0.0001	1.22(1.16–1.28)	< 0.0001
	1.23(1.18–1.29)	< 0.0001	1.24(1.19–1.30)	< 0.0001	0.56(0.47–0.65)	< 0.0001
	0.56(0.49–0.65)	< 0.0001	0.54(0.47–0.63)	< 0.0001		
^a Adjusted by age, gender, BSA, BMI.						
^b Adjusted by age, gender, BSA, BMI, hypertensive status, smoking status, LDL, and HDL.						

Using the non-CALs group as reference, OR value of IMT, PWV, α , β and CC was 1.44 (95% CI: 1.21–1.72; $P < 0.0001$), 1.40 (95% CI: 1.15–1.71; $P < 0.0001$), 1.25 (95% CI: 1.09–1.45; $P = 0.001$), 1.45 (95% CI: 1.21–1.67; $P < 0.0001$), and 0.51 (95% CI: 0.37–0.70; $P < 0.0001$) respectively for the atherosclerosis group with adjustment. Similarly, dose-dependent relationships were also evident for single-lesion and multi-lesion group, with the OR of 3.88 (95% CI: 1.89–7.98) and 4.27 (95% CI: 1.46–12.39) for variable IMT, 2.79 (95% CI: 1.73–4.51) and 3.70 (95% CI: 1.85–7.37) for variable PWV. However, the OR values were reduced to 1.41 (95% CI: 1.20–1.65), 2.45 (95% CI: 1.56–3.83), 0.28 (95% CI: 0.17–0.47) for multi-lesion group compared with 1.45 (95% CI: 1.22–1.74), 3.29 (95% CI: 1.58–6.85), 0.57 (95% CI: 0.43–0.77) for single-lesion group as variable α , β and CC indicated (Table 3).

Table 3

Risk estimates of IMT, PWV, α , β , and CC for coronary artery disease in multivariate analysis

Variables	N	OR^a	(95% CI)	P
IMT	54	1.00	(1.21–1.72)	Ref. ^b
Non-CAD	41	1.44	(1.89–7.98)	< 0.0001
Atherosclerosis	55	3.88	(1.46–12.39)	< 0.0001
Single-lesion	78	4.27		0.008
Multi-lesion				
PWV	54	1.00	(1.15–1.71)	Ref. ^b
Non-CAD	41	1.40	(1.73–4.51)	0.001
Atherosclerosis	55	2.79	(1.85–7.37)	< 0.0001
Single-lesion	78	3.70		< 0.0001
Multi-lesion				
α	54	1.00	(1.09–1.45)	Ref. ^b
Non-CAD	41	1.25	(1.22–1.74)	0.001
Atherosclerosis	55	1.45	(1.20–1.65)	< 0.0001
Single-lesion	78	1.41		< 0.0001
Multi-lesion				
β	54	1.00	(1.21–1.67)	Ref. ^b
Non-CAD	41	1.45	(1.58–6.85)	< 0.0001
Atherosclerosis	55	3.29	(1.56–3.83)	0.001
Single-lesion	78	2.45		< 0.0001
Multi-lesion				
CC	54	1.00	(0.37–0.70)	Ref. ^b
Non-CAD	41	0.51	(0.43–0.77)	< 0.0001
Atherosclerosis	55	0.57	(0.17–0.47)	< 0.0001
Single-lesion	78	0.28		< 0.0001
Multi-lesion				
^a Adjusted by age, hypertensive status, gender, smoking status, BSA, BMI, LDL, and HDL.				
^b Reference group.				

3.3 Diagnostic performance validation

The predicted probability was used to construct the ROC curve. The AUC of carotid artery elasticity variables IMT, PWV, α , β and CC were 0.9257, 0.8910, 0.8016, 0.9383, 0.8581 with correctly classified rate of 88.16%, 83.77%, 78.07%, 86.84%, and 81.58%, respectively (Fig. 4).

The predictive performance of these variables for different CALs, which compared with non-CALs group, including the AUC, sensitivity, specificity and corresponding cutoff values were further evaluated as Table 4 indicated. IMT showed a good predictive performance in the multi-lesion (AUC = 0.9909, $P < 0.0001$) and single-lesion groups (AUC = 0.9408, $P = 0.0110$). The AUC for β values was higher than other variables in both atherosclerosis group and single-lesion group with AUC of 0.8042 and 0.9689 ($P < 0.0001$). This indicated that the diagnostic performance of these variables were dependent of disease status.

Table 4
Predictive performance of the stiffness variables as independent factor for the assessment of coronary lesions

Variables	AUC	95% CI	P value	Cut off	Sensitivity(%)	Specificity(%)
For Atherosclerosis	0.783	0.6894to0.8766	< 0.0001	702.0	97.56	59.26
	0.7157	0.6114to0.8200	=	5.980	87.8	40.74
	0.7161	0.6091to0.8231	0.0003	6.935	87.8	55.56
	0.8042	0.7147to0.8937	< 0.0001	4.150	78.05	57.41
	0.7995	0.7118to0.8872	< 0.0001	0.895	58.45	83.33
For Single-lesion	0.9408	0.8991to0.9820	< 0.0001	821.5	98.18	81.40
	0.9187	0.8695to0.9679	< 0.0001	7.465	85.05	81.48
	0.8131	0.7345to0.8917	< 0.0001	5.885	64.45	85.19
	0.9689	0.9420to0.9958	< 0.0001	8.91	90.91	92.59
	0.8359	0.7611to0.9107	< 0.0001	0.885	67.27	85.19
For Multi-lesion	0.9909	0.9793to1.001	< 0.0001	905.5	96.15	96.3
	0.9637	0.9367to0.9906	< 0.0001	8.165	87.18	90.74
	0.8517	0.7885to0.9150	< 0.0001	6.980	60.26	98.15
	0.8517	0.9711to1.003	< 0.0001	9.18	96.15	96.3
	0.9046	0.8566to0.9525	< 0.0001	0.8050	73.08	90.74

The diagnostic accuracy of the variables in differentiating the multi-lesion group from the atherosclerosis, single-lesion group and single-lesion group from atherosclerosis group were also evaluated, respectively (Fig. 5). The analysis demonstrated that compared with other variables, IMT had a much higher accuracy in discriminating multi-lesion from atherosclerosis lesion (AUC = 0.9742; 95% CI, 0.9501 to 0.9982),

single-lesion (AUC = 0.8735; 95% CI, 0.7706 to 0.9044), and also single lesion from atherosclerosis lesion (AUC = 0.8561, 95% CI, 0.7836 to 0.9286)(Fig. 6).

3.4 Repeatability comparison

Good agreement was found in the intragroup and intergroup comparisons for IMT (intragroup mean bias: $10.32 \pm 33.06 \mu\text{m}$; intergroup mean bias: $8.15 \pm 26.11 \mu\text{m}$) and PWV values (intragroup mean bias: $0.0126 \pm 0.643 \text{ m/s}$; intergroup mean bias: $0.007 \pm 0.194 \text{ m/s}$). Bland-Altman analysis showed a consistent trend in the difference and mean values of IMT and PWV by repeated measurements.

4. Discussion

With the development of imaging modalities, imaging parameters of vascular changes might reflect the long-lasting effects of some disease such as CAD, diabetes and so on. Thus, the guidelines for assessment of CV risk published in 2010 recommended some vascular imaging parameters should be used as the biomarkers [12, 13]. Extra-cranial carotid artery is the most widely accepted window to predict CV disease, especially when IMT measurement and arterial stiffness evaluation by ultrasonographic method became available.

IMT has long been measured in routine clinical examinations, and is considered a good indicator of any future CV disease. An increase in carotid IMT has been reported to be associated with an increased risk of ischemic heart disease and cerebrovascular disease [14–17], but other studies have disagreed [18–20]. Nowadays, RF-based devices provide more accurate measurement because they are based on the signals with higher spatial resolution [21, 22]. Previous studies suggested that IMT measurements should be proposed for screening of CV events. While, in population with different risk profiles (e.g. with vs. without previous cerebrovascular disease (CVD) or diabetes mellitus (DM), on vs. off treatment), these parameters need to be verified the added value in individual risk prediction. For that reason, in the present study, we choose to include the variable only to comparison carotid properties and angiographic coronary lesions. In the present study, vascular morphological changes in IMT differed greatly between groups and were also found to be positively correlated with angiographic coronary lesions. Each $20 \mu\text{m}$ increment in IMT increased the risk of atherosclerosis of coronary artery increased by 78% after adjustment. Similar reports by Hodis et al [23] showed that they performed serial carotid IMT measurement and quantitative coronary angiography on 146 patients with history of coronary artery bypass graft surgery for an average follow-up of 8.8 years and found that for each 0.03 mm increase per year in CIMT there was an increase in the relative risk of coronary event of 3.1. Another study by a meta-analysis of 8 large, prospective studies found that each 0.1 mm increment in carotid IMT was associated with a 10–15% to increase the risk of myocardial infarction [24]. Current guidelines state that a common carotid IMT $> 900 \mu\text{m}$ can be regarded as a conservative estimate of existing abnormalities [25]. The cut-off value of carotid IMT for predicting CAD in our study was $821.5 \mu\text{m}$, which was much lower than previous reports. When the IMT increased to $905.6 \mu\text{m}$, the patients became prone to have multiple coronary damages. As discussed before, the technique of measuring carotid IMT measurement could be sufficiently standardized before

widespread clinical screening, particularly when the sub-millimeter difference in IMT will be treated as an important factor to separate low-risk and high-risk groups [26]. Nevertheless, as a measurement, IMT has the benefit of standardized acquisition to be considered as one of the best predictor of arterial atherosclerotic disease.

Arterial distensibility, defined as the change in arterial lumen diameter during the cardiac cycle and contract with cardiac pulsation and relaxation, can be evaluated by ultrasound imaging using wall-tracking systems. Reduced compliance in large arteries reflects structural remodeling in response to elevated pressure, aging, or disease. The arterial remodeling of local and elastic arteries increases the risk for future CV disease. The QAS technique provides a series of standard parameters for assessing arterial stiffness by vessel-wall echo tracking technique [8, 11, 27]. As the most useful and robust index of arterial stiffness [21, 28–30], the assessment of PWV is considered to be the “gold standard” measurement of aortic stiffness. Stiffness parameters α and β are the elastic coefficients from Meinders Hoeks exponential formula, the latter is normalized on the diameters. CC, the fractional change in cross-sectional area relative to the change in arterial pressure, is a good parameter identifying changed arterial compliance. The local vascular stiffness values we measured (PWV, α , and β) increased and CC decreased with increasing severity of CALs.

It has been suggested that clinical features and circulating biomarkers sometimes may be incapable of predicting the risk of CV disease for the past few years [26, 31]. In present study, independent of all the clinical and laboratory variables, each ultrasonographic variable was associated with CALs. The OR values were similar when with or without adjustment analyses. A literature search highlighted that high PWV was associated with roughly two-fold risks of cardiovascular events [32]. Statistical analysis showed that each increment of 0.5m/s in PWV, 1.5 in α and 1.0 in β measurements was associated with a 67%, 68%, and 51% increase in the risk of angiographic coronary atherosclerosis. The reduction of CC with each 0.2 mm²/ kPa meant the increased risk of coronary lesion by 44%. A threshold PWV value of greater than 10m/s could be considered as an indicator of sub-clinical organ damage in hypertensive patients [13]. The QAS variables were correlated with each other in all patients in a dose-dependent manner, showing that the technology provided consistent reference for the evaluation of arterial stiffness. Some reports indicated that functional impairment of the arterial wall may occur early in the atherosclerotic process [33], and arterial stiffening may be a process independent of arterial thickening [34]. Although the relationship between carotid structural and functional changes was obvious, the mechanism of the interaction still remained to be elucidated.

Besides IMT, PWV, α , β , and CC did show good diagnostic performance of in discriminating different coronary lesion in our study. However, there was still a little difference. At an earlier stage, for the patients with only coronary atherosclerosis, β presented the highest diagnostic accuracy, even higher than that of IMT, which might be a support that functional impairment of the arterial wall may occur early in the atherosclerotic process [33]. Furthermore, β also exhibited excellent diagnostic accuracy of single-lesion with sensitivity of 90.91% and specificity of 92.59%. Functional arterial changes may be a marker for the onset of vascular disease before manifestation of symptoms or for the detection of preclinical

atherosclerotic lesions [35, 36]. PWV was found to have the high diagnostic accuracy for the prediction of multiple coronary lesions (AUC = 0.9637). The results, for the first time, raised the concern that different stage during coronary atherosclerotic changes might need different biomarkers to predict or diagnose.

There were some limitations to our study. First, the IMT measurement site in the study was plaque-free. Total 43 (14%) subjects were found to have plaques locating exactly right the measurement site in the posterior wall of carotid wall. We had to choose an adjacent site as the ROIs. Considering that both the effect of plaque and different hemodynamics, the stiffness would be different. Second, we did not account the presence of plaques and the value of plaque scores, which was confirmed to be strongly correlated with CAD by several studies [37–39]. Further research with quantitative analysis of carotid plaques should be carried out to verify the present results and validate the predictive value of CCA morphological and functional variables in diagnosing CAD. Last, the number of patients in each group was relatively small, resulting in low statistical power.

Ultrasonographic modalities provide great opportunity to non-invasive imaging both vascular structural and functional changes in large-scale population study. The changes were closely related with detectable coronary lesions. Both QIMT and QAS techniques applied in carotid artery are likely to play a role in CV risk prediction of patients with CAD.

Abbreviations

AUC Area under the receive operating characteristic curve

BMI Body mass index

BSA Body surface area

CAD Coronary artery disease

CALs Coronary lesions

CC Compliance coefficient

CCA Common carotid artery

CV Cardiovascular

CVD Cerebrovascular disease

DBP Diastolic blood pressure

DM Diabetes mellitus

HDL High density lipoprotein

IMT Intima-media thickness

LCCA Left common carotid artery

LDL Low density lipoprotein

OR The odd ratio

PWV Pulse wave velocity

QAS Quality arterial stiffness

QIMT Quality intima-media thickness

ROC Receiver operating characteristic

ROI The region of interest

SBP Systolic blood pressure

SD Standard deviation

RF Radio frequency

Declarations

Ethics approval and consent to participate

This study received ethical approval from the ethics committee of the Air Force Medical University Tangdu Hospital (Xi'an, China). Informed consent was obtained from all individual participants included in this study.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article [and its supplementary information files].

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Wen-Bin Cai drafted the manuscript and carried out data processing. Yi Wang collected data. Jia Wang recruited the patients. Li-Jun Yuan and Yun-You Duan carried out data processing and guidance. Li Zhang designed the research, conceptualized the manuscript and involved in data processing.

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Figures

Figure 1

QIMT analysis of CCA. The red line represents the RF signal tracking the leading edge of the lumen-intima boundary; the green line represents the RF signal tracking the leading edge of the media-adventitia interface. IMT and vascular diameter were calculated automatically for six cardiac cycles shown on the left side of the picture.

Figure 2

QAS analysis of CCA. The red line represents the RF signal tracking the leading edge of the lumen-intima boundary; the green line represents the RF signal tracking the leading edge of the media-adventitia interface. A derived carotid pressure waveform was calibrated by brachial end diastolic and mean arterial pressure after six cardiac cycles. Then the arterial stiffness was calculated automatically.

Figure 3

Correlations between QIMT and QAS stiffness values.

Figure 4

ROC curves of IMT, PWV, α , β , and CC as the independent variables for coronary arterial disease.

Figure 5

Correlations of QIMT and QAS variables with coronary lesions.

Figure 6

ROC curves of IMT, β , PWV, CC and DC for multi-lesion group (A), single-lesion group (B) and atherosclerosis group (C).