Original Article

Quantifying carotid stiffness in chronic kidney disease using ultrafast ultrasound imaging

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Background: The mortality and disability of chronic kidney disease (CKD) are highly linked to the incidence of atherosclerotic cardiovascular events. Numerous clinical biochemical indicators of renal function often only increase in advanced stages of CKD, driving an urgent need for reliable indicators of atherosclerosis in early CKD. Ultrafast pulse wave velocity (ufPWV) can evaluate the stiffness of the straight carotid *in vivo* and quantitatively reflect the degree of early atherosclerosis. However, the use of ufPWV in CKD has not yet been reported. In this study, we aimed to explore the association between carotid stiffness, quantified using ufPWV, and renal function in CKD patients.

Methods: This cross-sectional study enrolled a total of 582 participants between March 2017 and May 2022 in the Affiliated Hospital of Nanjing University of Traditional Chinese Medicine. Among those, 205 individuals without a history of CKD and estimated glomerular filtration rate (eGFR) ≥90 mL/min/1.73 m^2 were included as controls. According to the Kidney Disease Outcomes Quality Initiative (K/DOQI) expert group of the American Kidney Foundation staging for CKD, 44 stages 1 and 2 CKD patients were included in the early CKD group, whereas 49 stages 3, 4, and 5 CKD patients were included in the advanced CKD group. Clinical and serum parameters, ultrasonic characteristics including carotid intima-media thickness (cIMT), and pulse wave velocity at the beginning of systole (PWV-BS) and pulse wave velocity at the end of systole (PWV-ES) of systole were analyzed. One-way analysis of variance (ANOVA) and least significant

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difference (LSD) tests were performed to compare cIMT, PWV-BS, and PWV-ES among subgroups in pairs. Pearson's correlation analysis, scatter plots, and subgroups correlation analysis were used to determine the relationships among ultrasound characteristics (cIMT, PWV-BS, PWV-ES), and major cardiovascular risk factors.

Results: PWV-BS and PWV-ES for the early and advanced CKD groups were significantly higher than those for controls (all P<0.05). PWV-ES had the greatest correlation with age (r=0.474, P<0.001). PWV-ES had the greatest increase with age in the early CKD group (r=0.698, P<0.001).

Conclusions: ufPWV can be used for the quantitative evaluation of carotid stiffness in CKD patients. PWV-ES may be more advantageous in the assessment of carotid atherosclerosis in early CKD patients.

Keywords: Chronic kidney disease (CKD); atherosclerosis; pulse wave velocity (PWV); carotid stiffness; ultrafast ultrasound imaging

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Introduction

The morbidity, mortality, and disability associated with chronic kidney disease (CKD), a global public health problem, have increased significantly with the aging population (1). Several studies have reported a high incidence of cardiovascular diseases in CKD patients (2-4). Experiments in mice have demonstrated that CKD greatly accelerates the progression of atherosclerosis (3). CKD is often accompanied by pathophysiological conditions, such as inflammation and oxidative stress, that damage smooth muscle and endothelial cells, cause vascular calcifications (4,5), and increase arterial stiffness (6). Intimal and intermediate calcifications are associated with renal function decline in CKD patients (7). Early intervention can reduce global morbidity, cardiovascular mortality, and all-cause mortality in CKD patients (8). Clinical biochemical indicators of renal function often only increase in advanced stages of CKD. Therefore, there is an urgent need for reliable indicators of atherosclerosis in early CKD.

Carotid intima-media thickness (cIMT) can be used as a predictor for cardiovascular events and death in CKD patients on dialysis (9). Increased cIMT may indicate declining renal function in early stages of CKD (10). However, cIMT measured using ultrasonography is highly operator-dependent and lacks standardization, resulting in unstable measurements and poor reproducibility (11). Moreover, recent studies have demonstrated that cIMTs in CKD patients were similar to those without a history of CKD (0.78±0.21 and 0.65±0.16 mm, respectively, P=0.11) (12). In addition, increased cIMT is a morphological change; it is functional carotid artery stiffness, caused by vascular endothelial dysfunction, that occurs in the early stages of CKD (13). Consequently, it is important to find reliable indicators to reflect early pathological changes in the carotid arteries of CKD patients.

Pulse wave velocity (PWV) can be used for visual assessment of atherosclerosis and was recommended as the gold standard in the 2018 European Society of Cardiology/European Society of Hypertension guidelines for the management of arterial hypertension (14). Previous PWV techniques, such as cervical-femoral PWV, showed significantly increased central arterial stiffness in stage 3B CKD. Meanwhile, cervical-radial PWV, which reflects peripheral arterial stiffness, did not show these findings (15). Distinct from all those PWV techniques, ultrafast PWV (ufPWV) is a unique PWV technology that directly records the propagation of carotid pulse wave via ultrafast instantaneous ultrasonography in real-time assessment (>2,000 frame/s) (16). ufPWV can indirectly evaluate the stiffness of the straight carotid *in vivo* and quantitatively reflect the degree of systemic atherosclerosis (17). In recent years, ufPWV has been used for the evaluation of pre-hypertension (16), coronary artery disease (17), diabetes (18), and valvular heart disease (19). Previous studies validated the stability and reproducibility of ufPWV and confirmed its utility in subclinical atherosclerosis (20,21). However, the use of ufPWV in CKD has not yet been reported.

The present study explored the association between carotid stiffening, quantified using ufPWV, and renal function injury, and developed an indicator for early renal

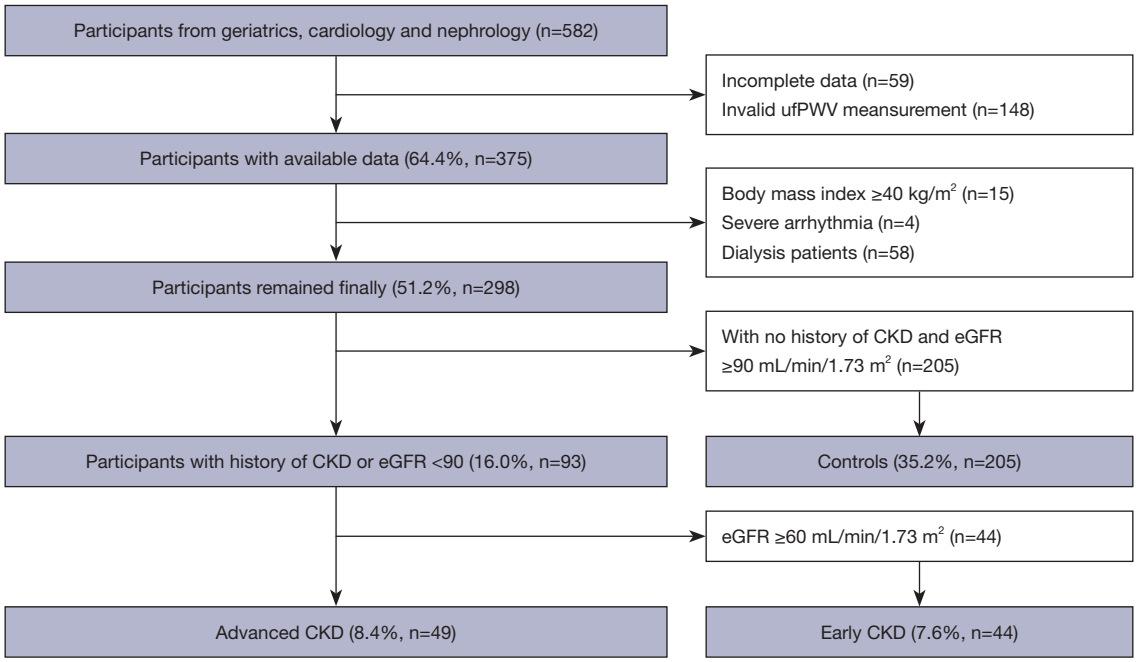

Figure 1 Study flow chart. ufPWV, ultrafast pulse wave velocity; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

damage. We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-23-503/rc).

Methods

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Affiliated Hospital of Nanjing University of Chinese Medicine (No. 2017NL-048-02) and the requirement for individual consent for this retrospective analysis was waived.

Study design and participants

Between March 2017 and May 2022, 582 participants aged 19–80 years were enrolled in this retrospective study. The sample included outpatients (62%) and inpatients (38%) from the geriatric (26%), cardiology (57%), and nephrology (17%) departments of the Affiliated Hospital of Nanjing University of Traditional Chinese Medicine. The patients underwent ufPWV examination and baseline data collection, including clinical interviews, physical examinations, and laboratory investigations. The CKD Epidemiological Cooperation equation was used to calculate the estimated glomerular filtration rate (eGFR) (22). CKD was divided into 5 stages according to eGFR by the Kidney Disease Outcomes Quality Initiative (K/DOQI) expert group of the American Nephrology Foundation (23). Patients who met any of the following conditions were excluded: (I) lack of complete data (including serum creatinine and serum urea; n=59); (II) invalid ufPWV measurements (detailed in the carotid ultrasonography section; n=148); (III) clinical conditions that could affect PWV reliability, including body mass index (BMI) ≥40 kg/m^2 (n=15) and severe arrhythmias (n=4); and (IV) dialysis patients (n=58). After exclusion of these patients, a total of 298 (51.2%) participants were included. The control group included 205 (35.2%) patients without a history of CKD and eGFR ≥90 mL/min/1.73 m^2 (100 males and 105 females; average age, 51.96±10.37 years). Stages 1 (n=28) and 2 (n=16) CKD patients were included in the early CKD group (n=44), whereas stages 3 (n=12), 4 (n=21), and 5 (n=16) patients were included in the advanced CKD group (n=49) (*Figure 1*, *Table 1*).

Carotid ultrasonography

The Aixplorer ultrafast commercial scanner (SuperSonic Imagine, Aix-en-Provence, France) was used to determine the cIMT and ufPWV with a linear array probe SL10-2 (frequency: 2–10 MHz; center frequency: 8.0 MHz). In the supine position, the neck was fully exposed and relaxed, and

Table 1 Participant characteristics

Variables	Total (n=298)	Controls (n=205)	Early CKD (n=44)	Advanced CKD (n=49)	P value
Baseline characteristics					
Age (years)	52.49±11.05	51.96±10.37	51.48±12.38	55.63±12.17	0.090
Male	151 (50.7)	100 (48.8)	22 (50.0)	29 (59.2)	0.423
BMI (kg/m^2)	24.34±3.30	24.15±2.92	25.73±3.99	23.90±3.81	0.009
CKD duration (years)	7.19±8.92	–	4.65±8.84	9.48±8.45	0.008
Hypertension	179 (60.1)	128 (62.4)	13 (29.5)	38 (77.6)	<0.001
Diabetes	29 (9.7)	5 (2.4)	11 (25.0)	13 (26.5)	<0.001
Smokers	68 (22.8)	44 (21.5)	14 (31.8)	10 (20.4)	0.301
SBP (mmHg)	132.67±17.85	129.34±15.66	131.77±13.46	147.41±22.30	<0.001
DBP (mmHg)	81.34±11.48	81.10±11.42	80.43±10.42	83.18±12.64	0.444
BPM use	161 (54.0)	126 (61.5)	10 (22.7)	25 (51.0)	<0.001
Statin use	85 (28.5)	51 (24.9)	20 (45.5)	14 (28.6)	0.023
Laboratory findings					
TC (mmol/L)	4.91±1.17	4.90±0.95	5.18±1.36	4.75±1.70	0.190
TG (mmol/L)	1.68±1.28	1.52±1.18	1.94±1.58	2.13±1.27	0.004
LDL (mmol/L)	2.74±0.78	2.79±0.77	2.62±0.75	2.60±0.82	0.162
HDL (mmol/L)	1.48±0.34	1.54±0.33	1.35±0.36	1.32±0.27	<0.001
FBG (mmol/L)	5.47±1.08	5.39±0.74	5.61±1.29	5.73±1.83	0.092
Cr (μmol/L)	113.30±152.14	68.60±13.92	75.08±19.33	334.60±286.70	<0.001
eGFR (mL/min/1.73 m^2)	126.45±43.59	144.15±18.66	134.20±25.76	45.45±39.90	<0.001

Data are presented as mean ± standard deviation or n (%). CKD, chronic kidney disease; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; BPM, blood pressure medication; TC, total cholesterol; TG, triglyceride; LDL, low-density lipoprotein; HDL, high-density lipoprotein; FBG, fasting blood glucose; Cr, creatinine; eGFR, estimated glomerular filtration rate.

the head was turned to one side. In mode B, the common carotid artery was scanned longitudinally to obtain a clear sonogram of the intima-media. cIMT measurements were performed after image optimization. The measurement system was used to determine the sampling frame, with a fixed width of 1.0 cm, to automatically track and record posterior wall cIMT of the distal segment of common carotid artery (1.0–1.5 cm below the carotid bulb). The ratio, obtained by dividing the length of cIMT segment by the sampling frame width, was used as a quality control index; measurements >70% were considered valid (*Figure 2A*). Each carotid was measured 3 times and the average was calculated. The average value for both sides was then calculated to obtain the final value.

The participants were then instructed to hold their breath and the "PWV" key was pressed to activate ultrafast imaging acquisition, which was completed within 3 seconds. After obtaining a stable ufPWV image, a region of interest (ROI) was selected and adjusted to cover a section of the common carotid artery. The software automatically recorded the PWV at the beginning of systole (PWV-BS) and PWV at the end of systole (PWV-ES) with their respective standard deviations (SDs) (denoted by Δ±; *Figure 2B*). For quality control, Δ± ≤2.0 m/s was considered valid for ufPWV acquisition. Invalid measurements included those with (I) failure to calculate PWV-BS or PWV-ES; (II) Δ± of >2.0 m/s; and (III) improper ROI localization with the tracing line outside of the arterial wall (20,21). The means of three valid PWV-BS and PWV-ES values for bilateral common carotid arteries were taken as their respective final values.

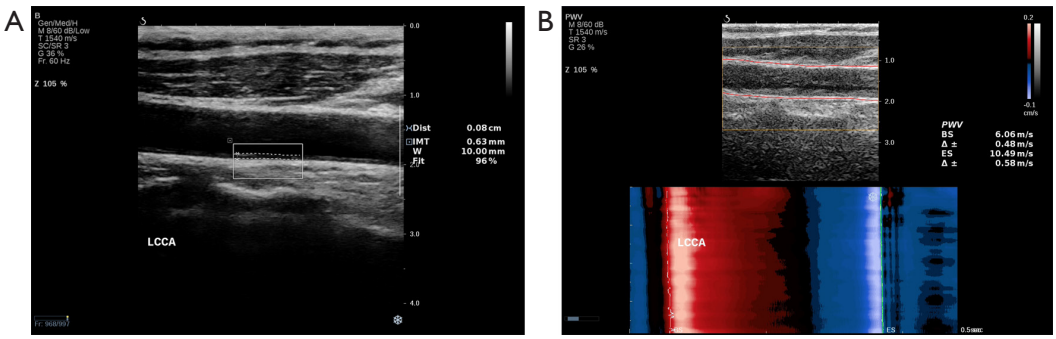

Figure 2 Protocols for the assessment of cIMT and ufPWV. (A) Measurement of cIMT was performed. A white ROI box was drawn at the posterior wall of the LCCA; the intimal and medial lines of the LCCA were automatically recorded with two dotted lines, and the mean cIMT of the ROI was obtained with a fit of 96%. (B) PWV-BS and PWV-ES were measured by using ufPWV. Using ufPWV imaging, a yellow ROI box covered and a red line automatically tracked the anterior and posterior walls of the LCCA. The PWV-BS and PWV-ES values were calculated in the ROI with Δ± ≤2.0 m/s, respectively. Dist, distance; IMT, intima-media thickness; W, width; LCCA, left common carotid artery; PWV, pulse wave velocity; BS, beginning of systole; Δ±, standard deviation; ES, end of systole; cIMT, carotid IMT; ufPWV, ultrafast PWV; ROI, region of interest; PWV-BS, PWV at the BS; PWV-ES, PWV at the ES.

Statistical analysis

Continuous variables were expressed as mean ± SD, whereas categorical variables were expressed as counts and ratios. One-way analysis of variance (ANOVA) and chi-square test were used to compare the continuous and categorical variables of participant characteristics between groups in total, respectively. The least significant difference (LSD) test was further used to compare cIMT, PWV-BS, and PWV-ES between groups in pairs, respectively. Pearson's correlation analysis was used to analyze the relationships among ultrasound characteristics (cIMT, PWV-BS, PWV-ES) and major cardiovascular risk factors [including age, BMI, CKD duration, systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), fasting blood glucose (FBG), and eGFR]. Scatter plots and subgroups correlation analysis were used to determine the correlated r for each group of cIMT, PWV-BS, and PWV-ES, linked to age. Statistical analyses were performed using the software SPSS 22.0 (IBM Corp., Armonk, NY, USA), and two-sided P<0.05 was considered statistically significant.

Results

Participant characteristics

The early CKD group included 22 males and 22 females (average age, 51.48±12.38 years), whereas the advanced CKD group included 29 males and 20 females (average age, 55.63±12.17 years). Baseline demographic, clinical, and laboratory characteristics are summarized in *Table 1*. All clinical measurements except for age, male sex, smoking, and DBP differed significantly according to CKD status. Similarly, significant differences were found in major serum biomarkers except for TC, LDL, and FBG. Cases in the advanced CKD subgroup demonstrated a remarkable increase in creatinine and CKD duration, and decrease in eGFR compared with cases in the control and early CKD subgroups (P<0.001 in total and P<0.001 for all pairwise comparisons).

Comparison of cIMT and carotid stiffening

For decades, ultrasonic imaging characteristics such as cIMT, which is currently a surrogate measure for atherosclerosis, were frequently used to identify early atherosclerosis, and to predict future cardiovascular events. In this study, there were no significant overall differences in cIMT among the control, early CKD, and advanced CKD groups (P=0.240), but the overall significant differences were found in both PWV-BS and PWV-ES, as shown in *Table 2* (P=0.002 and P<0.001). Pairwise comparisons showed no significant differences in cIMT (P=0.092, 0.796, and 0.249 for controls *vs.* early CKD, early *vs.* advanced CKD, and controls *vs.* advanced CKD, respectively; *Figure 3A*). The PWV-BS and PWV-ES for early and advanced CKD groups were significantly higher than those for controls

Table 2 Sonographic carotid measurements

Variables	Controls (n=205)	Early CKD (n=44)	Advanced CKD (n=49)	Comparing in total		Controls *vs.* early CKD		Early *vs.* advanced CKD		Controls *vs.* advanced CKD	
				F value	P value	SE	P value	SE	P value	SE	P value
cIMT (cm)	0.060±0.012	0.057±0.014	0.060±0.012	1.433	0.240	0.0020	0.092	0.0025	0.796	0.0019	0.249
PWV-BS (m/s)	5.73±1.07	6.33±1.34	6.14±1.19	6.499	0.002	0.1884	0.002	0.2355	0.419	0.1803	0.024
PWV-ES (m/s)	8.09±1.69	8.77±1.85	9.29±2.07	10.250	<0.001	0.2954	0.023	0.3692	0.153	0.2827	<0.001

Data are mean ± standard deviation. CKD, chronic kidney disease; SE, standard error; cIMT, carotid intima-media thickness; PWV-BS, pulse wave velocity at the beginning of systole; PWV-ES, pulse wave velocity at the end of systole.

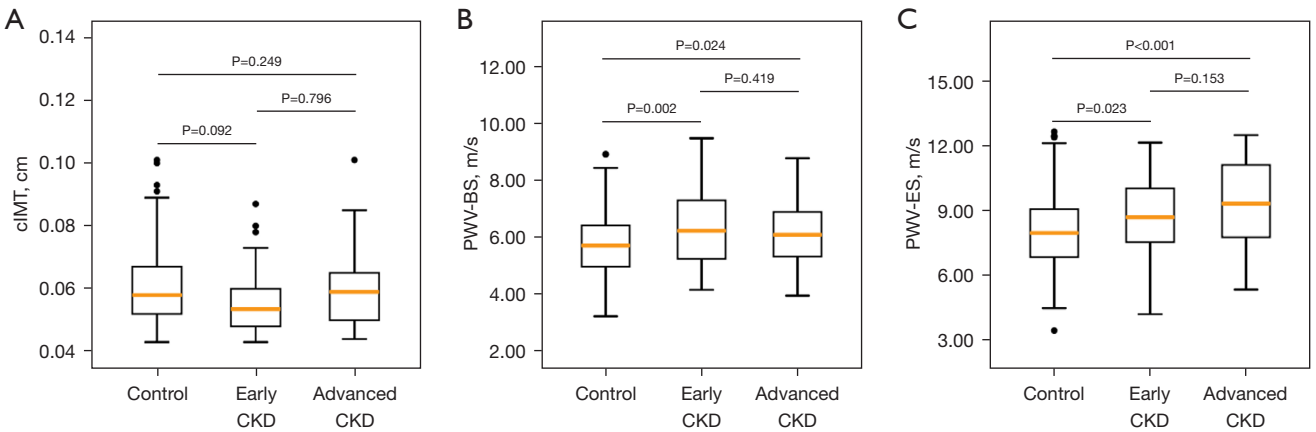

Figure 3 Comparison of ultrasonic characteristics among control and CKD subgroups. Boxplots of cIMT (A), PWV-BS (B), and PWV-ES (C) measurements compared in pairs among the control (n=205), early CKD (n=44), and advanced CKD subgroups (n=49), respectively. CKD, chronic kidney disease; cIMT, intima-media thickness; PWV-BS, pulse wave velocity at the beginning of systole; PWV-ES, pulse wave velocity at the end of systole.

(P=0.002 and 0.024 for PWV-BS; P=0.023 and P<0.001 for PWV-ES; *Table 2*, *Figure 3B,3C*), but there was no significant difference between the early and advanced CKD groups (P=0.419 for PWV-BS; P=0.153 for PWV-ES; *Table 2*, *Figure 3B,3C*).

Correlation analysis of cIMT, PWV-BS, PWV-ES, and cardiovascular risk factors

Atherosclerosis is a lifelong disease process that progresses slowly at a young age and may accelerate with the accumulation of numerous cardiovascular risk factors. Among those risk factors, age (r=0.408, P<0.001), BMI (r=0.254, P<0.001), SBP (r=0.210, P<0.001), DBP (r=0.140, P=0.016), LDL (r=0.195, P=0.001), and FBG (r=0.251, P<0.001) correlated significantly with cIMT. PWV-BS only correlated significantly with age (r=0.158, P=0.006) and eGFR (r=−0.128, P=0.027). PWV-ES correlated significantly with age (r=0.474, P<0.001), SBP (r=0.211, P<0.001), FBG (r=0.154, P=0.008), and eGFR (r=−0.188, P=0.001); the correlation was the greatest with age (*Table 3*).

Correlation analysis of cIMT, PWV-BS, PWV-ES, and age

As we all know, age is the dominant driver of atherosclerosis, cardiovascular risk factors, and cardiovascular events. cIMT increased with age in all three groups, with the strongest correlation for early CKD group, followed by advanced CKD and control groups (r=0.573, P<0.001; r=0.434, P=0.002; and r=0.360, P<0.001, respectively) (*Figure 4A*). PWV-BS did not correlate significantly with age in the early and advanced CKD groups (all P>0.05), but had a weak positive correlation in controls (r=0.192, P=0.006)

Table 3 Correlation analysis of cIMT, PWV-BS, PWV-ES, and cardiovascular risk factors

Variables	cIMT			PWV-BS			PWV-ES		
	r value	Covariance	P value	r value	Covariance	P value	r value	Covariance	P value
Age (years)	0.408	0.054	<0.001†	0.158	2.018	0.006†	0.474	9.599	<0.001†
BMI (kg/m^2)	0.254	0.010	<0.001†	0.077	0.293	0.185	0.041	0.247	0.481
CKD duration (years)	0.095	0.011	0.363	−0.089	−1.004	0.394	0.045	0.788	0.671
SBP (mmHg)	0.210	0.045	<0.001†	0.025	0.511	0.670	0.211	6.907	<0.001†
DBP (mmHg)	0.140	0.019	0.016†	0.026	0.034	0.660	0.071	1.492	0.222
TC (mmol/L)	0.091	0.001	0.117	−0.017	−0.022	0.775	−0.102	−0.218	0.079
TG (mmol/L)	−0.012	<0.001	0.842	−0.051	−0.075	0.382	−0.021	−0.050	0.715
LDL (mmol/L)	0.195	0.002	0.001†	−0.025	−0.022	0.671	−0.053	−0.076	0.359
HDL (mmol/L)	−0.001	<0.001	0.989	0.013	0.005	0.818	−0.068	−0.042	0.243
FBG (mmol/L)	0.251	0.003	<0.001†	0.098	0.123	0.090	0.154	0.306	0.008†
eGFR (mL/min/1.73 m^2)	0.005	0.003	0.930	−0.128	−6.438	0.027†	−0.188	−15.040	0.001†

†, significant P values at <0.05. cIMT, carotid intima-media thickness; PWV-BS, pulse wave velocity at the beginning of systole; PWV-ES, pulse wave velocity at the end of systole; BMI, body mass index; CKD, chronic kidney disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; LDL, low-density lipoprotein; HDL, high-density lipoprotein; FBG, fasting blood glucose; eGFR, estimated glomerular filtration rate.

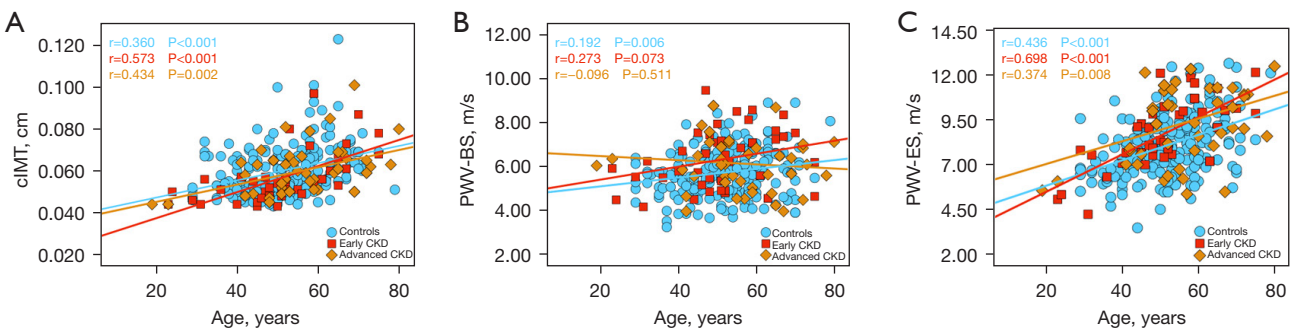

Figure 4 Subgroup correlations between ultrasonic characteristics and age. (A) Pearson's correlation analysis (n=298) is shown between age and cIMT in controls (r=0.360, P<0.001), early CKD (r=0.573, P<0.001), and advanced CKD participants (r=0.434, P=0.002). (B) Pearson's correlation analysis (n=298) is shown between age and PWV-BS in controls (r=0.192, P=0.006), early CKD (r=0.273, P=0.073), and advanced CKD participants (r=−0.096, P=0.511). (C) Pearson's correlation analysis (n=298) is shown between age and PWV-ES in controls (r=0.436, P<0.001), early CKD (r=0.698, P<0.001), and advanced CKD participants (r=0.374, P=0.008). CKD, chronic kidney disease; cIMT, carotid intima-media thickness; PWV-BS, pulse wave velocity at the beginning of systole; PWV-ES, pulse wave velocity at the end of systole.

(*Figure 4B*). PWV-ES also increased with age, with the strongest correlation for the early CKD group, followed by the control and advanced CKD groups (r=0.698, P<0.001; r=0.436, P<0.001; and r=0.374, P=0.008, respectively) (*Figure 4C*).

Discussion

CKD accelerates the progression of atherosclerosis, which leads to increased mortality (24). It has been demonstrated that atherosclerosis of large arteries begins in the early stages

of CKD, when renal function is only slightly reduced (13). In CKD patients with decreased renal function, PWV may be used to assess the cardiovascular risk and predict CKD progression and mortality (25). Our previous studies validated satisfactory intra- and inter-operator reproducibility of ufPWV measurements (20,21), and demonstrated that the ufPWV parameter, PWV-ES, can be used for early diagnosis and quantitative assessment of the degree of atherosclerosis (20), and to identify carotid atherosclerosis in healthy adults without major cardiovascular risk factors (21). Consistent with previous studies (13,20,25), our findings indicate that PWV-ES is significantly higher in early CKD patients than in controls ($P<0.05$), and has a significantly positive correlation with age in all three groups. However, the correlated r of PWV-ES linked to age were higher than those of cIMT in the control and early CKD populations, yet lower in advanced CKD. The increase in arterial stiffness begins in the early stages of CKD and slows down in the progressive stages. This is perhaps because an increase in arterial stiffness might not unendingly correlate with continuously increasing cIMT (20,21), and indicates that ufPWV might be a quantitative tool more suitable for assessing early atherosclerosis in CKD.

Ageing is the dominant driver of carotid stiffening and atherosclerosis, which promotes the rupture of elastin fibers in arterial walls and increases collagen accumulation, leading to arteriosclerosis (26). Li *et al.* (27) found that carotid PWV increased with age in CKD patients, but was alleviated in patients who underwent kidney transplantation after removal of major atherosclerotic risk factors, such as chronic renal insufficiency and arteriovenous fistulae. An analysis of end-stage renal disease patients by Tripepi *et al.* (28) demonstrated that the correlation between PWV and cardiovascular events was greater in younger ages. Our previous study using ufPWV confirmed a strong positive correlation between age and arterial stiffness, represented by PWV-ES (r=0.710) (20). The results of the present study were consistent with previous studies (20,26-28), and it further demonstrated that CKD patients had greater arterial stiffness, which was most strongly correlated with age in the early stages (r=0.698, $P<0.001$). Besides, PWV-ES performed better than PWV-BS at assessing age-related atherosclerosis in prior and our studies (20,21). This is probably due to differences in the wall recoil during the cardiac cycle, since early systolic expansions powered by left ventricular ejection may hinder detection of minute differences in wall stiffness. Therefore, PWV-ES may be used to evaluate age-related decrease in arterial elasticity in healthy individuals and CKD patients.

A histopathological study (18) suggested that the increase in intima-media thickness may be mainly due to lipid deposition in the intima and outward migration of smooth muscle cells, which leads to collagen proliferation, reduced elastin, and increased vascular stiffness. Previous studies (29-31) have indicated that eGFR is negatively correlated with cIMT and PWV, potentially damaging the structure and function of large blood vessels in CKD patients. Meanwhile, another study (32) found that cIMT had a limited role in the assessment of structural and functional vascular abnormalities in different stages of CKD. Although cIMT increases with age, it lags behind ufPWV as an indicator for age-related atherosclerosis (20). The present study also demonstrated that cIMT correlates positively with age (r=0.408, $P<0.001$), and may be influenced by various atherosclerosis risk factors. However, there were no significant differences among different stages of CKD, which was consistent with the results of previous studies (20,32). This is because cIMT, the traditional index for structural atherosclerosis, changes later than ufPWV.

This study had some limitations. First, the single-center study had a small sample size, and further multi-center studies may be needed to validate these findings. Second, even comprehensive adjustments cannot eliminate the role of confounding factors, including poor lifestyle, medication use, and concomitant tumors, in observational clinical studies. Although CKD may be caused by diabetes, the influence of hyperglycemia on carotid stiffness cannot be ruled out. Third, CKD patients, particularly those in middle and advanced stages, are often hypertensive, which itself is a strong risk factor for atherosclerosis. Fourth, almost a quarter of cases (25.4%, 148/582) had an invalid ufPWV measurement in this study, which likely reflects predictable challenges when introducing this new technology for CKD assessment. Finally, it should be noted that this study was conducted on subgroups through correlation analysis and hence the possibility of the effect of nonlinear and multivariate regression relationships on carotid properties was not considered in this study.

Conclusions

ufPWV can be used to quantitatively assess carotid stiffness in CKD patients and predict the risk of atherosclerosis. PWV-ES may be superior to PWV-BS and cIMT for the assessment of carotid atherosclerosis in early CKD patients.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-23-503/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-23-503/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Affiliated Hospital of Nanjing University of Chinese Medicine (No. 2017NL-048-02) and the requirement for individual consent for this retrospective analysis was waived.

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