Original Paper

Common Carotid Artery Stiffness Is Associated with Left Ventricular Structure and Function and Predicts First Hospitalization for Acute Heart Failure

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Key Words

Common carotid artery · Speckle tracking · Arterial stiffness · Left ventricular function · Acute heart failure

Abstract

Aims: Proximal aortic stiffness may be more important than carotid-femoral pulse wave velocity (cf-PWV) in the pathogenesis of heart failure. The present study investigated the associations of common carotid artery (CCA) stiffness, which might be a surrogate for proximal aortic stiffness, with left ventricular (LV) structure and function, and the development of acute heart failure (AHF). **Methods and Results:** Outpatients without a history of heart failure (114 subjects aged 63.5 ± 17.5 years) were enrolled for comprehensive noninvasive cardiovascular examinations. The LV mass index, the LV ejection fraction (EF), and the ratio of the early diastolic transmitral flow velocity to the early septal mitral annular diastolic velocity (E/E') were measured by echocardiography. CCA mechanical properties, including the incremental elastic modulus (Einc), β stiffness index, CCA distensibility (CD) and circumferential strain (CS), were assessed by carotid artery ultrasonography. cf-PWV was measured by arterial tonometry. CD was significantly associated with the LV mass index, and all CCA stiffness indices were significantly associated with EF and E/E' independently of age, mean blood pressure, and cf-PWV. During a mean follow-up of 265 ± 106 days, 9 patients presented with AHF. Einc (hazard ratio 6.56, 95% confidence interval 1.64–26.26, by quartile analysis), CS (6.82, 1.70–27.35), and β

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stiffness index (3.91, 1.05–14.57) but not cf-PWV (1.62, 0.41–6.51) significantly predicted the events. **Conclusions:** In patients at risk for heart failure, CCA stiffness was significantly associated with LV structure and function independently of cf-PWV. In addition, CCA stiffness but not cf-PWV predicted first AHF.

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Introduction

The left ventricle pumps pulsatile flow into the arterial system, which functions as both a conduit and a reservoir so that the peripheral tissue and end organs receive blood supply with minimal pulsatility. The arterial function declines with stiffening of large arteries, the aorta in particular, mainly due to the aging process. Increased central aortic stiffness has been identified as an independent risk factor for heart failure [1–3] and end-organ damage [4], likely due to the increased afterload on the heart, and the harmful effect of excessive pressure and flow pulsatility in the peripheral microcirculation.

Carotid-femoral pulse wave velocity (cf-PWV) measures the stiffness over a large part of the aorta but spares the ascending aorta, which may play a pivotal role in the pathogenesis of heart failure [3, 5, 6]. Although cf-PWV is associated with various indices of left ventricular (LV) structure and function [7] and is increased in patients with heart failure and preserved ejection fraction (EF) [8, 9], few epidemiological studies directly support that high baseline cf-PWV predicts future development of heart failure [10, 11].

Common carotid arteries (CCA) are usually considered as part of the central conductance vessels rather than the peripheral muscular arteries, due to their high content of elastin and close proximity to the ascending aorta [12, 13]. However, there is an impedance mismatch between the more compliant ascending aorta and the stiffer CCA in young, healthy adults, which may serve to reduce the harmful effect of pressure and flow pulsatility on the cerebral microcirculation [14]. Measures of the CCA stiffness have been associated with risk of ischemic stroke and dementia but not of coronary artery disease [14–18]. However, with advancing age, disproportionately increased proximal aortic stiffness may match the stiffness of CCA [14], reduce the impedance mismatch, and tighten the link between CCA stiffness and LV structure and function [9, 19]. In this context, measures of the CCA stiffness may become a surrogate for ascending aortic stiffness and provide additional information on the pathogenesis of heart failure beyond cf-PWV, an index of arterial aging [9, 20]. Therefore, in the present study, we investigated the associations of mechanical properties of the CCA with indices of LV structure and function, and development of acute heart failure (AHF) in subjects without a history of heart failure.

Methods

Study Population

Patients without typical signs (e.g. elevated jugular venous pressure, pulmonary crackles, and displaced apex beat) [21] or history of heart failure were eligible to be included in the present study. The study population consisted of 114 patients that were consecutively enrolled due to showing possible structural or functional reasons for the development of heart failure [22], among 259 subjects who were primarily invited to participate in a prospective study investigating the associations between vascular aging and renal functions. Patients with uncontrolled hypertension, uncontrolled diabetes mellitus, and documented history of myocardial infarction within 1 month were excluded. To be eligible for the present study, patients with atrial fibrillation, valvular heart disease, recent stroke (within 3 months) or established peripheral artery disease were also excluded. The investigation conformed to the principles outlined in the Declaration of Helsinki. A written informed consent approved by our institutional review board was obtained from each patient before enrollment.

Study Protocol

All participants underwent a comprehensive echocardiographic study including carotid artery sonography, and assessments of arterial stiffness and wave reflections. Data of the patients' medical history, including hypertension, diabetes and coronary artery disease, and demographics were recorded. Coronary artery disease was diagnosed by history of cardiac catheterization. The estimated glomerular filtration rate was calculated by using a modified Modification of Diet in Renal Disease equation based on the Chinese population [23].

Measurements of LV Structure and Function

LV mass (LVM) and LV end-diastolic volume (LVEDV) indexed to the body surface area, and LV EF were calculated from the M-mode measurements and biplane Simpson's method using a multifrequency transducer incorporated in an Artida Echocardiograph (Toshiba Medical Systems Corporation, Tokyo, Japan). The LV relative wall thickness was calculated as the ratio of $2 \times$ posterior wall thickness to LV end-diastolic internal dimension. The ratio of early to late diastolic transmitral inflow velocity (E/A) was measured by Doppler sampling between the tips of the anterior and posterior mitral leaflets. Deceleration time of the early diastolic flow velocity was also measured. Early diastolic velocity of the septal mitral annulus (E') was recorded in the apical four-chamber view using the tissue Doppler technique. E/E' was the ratio of the early diastolic transmitral flow velocity to the early septal mitral annular diastolic velocity. All measures were the average of 4 consecutive beats.

Patients with an LV EF <45% were considered to have systolic dysfunction [24]. Patients with a diastolic dysfunction had an LV EF $\geq$ 45% and met the following criteria: (1) LVEDV index <97 ml/m² and E/E' >15, or (2) LVEDV index <97 ml/m², $8 < E/E' < 15$, and abnormal LV filling (E/A_{>50years} <0.5, deceleration time_{>50years} >280 ms), or (3) LVEDV index <97 ml/m², $8 < E/E' < 15$, and LVM index >122 g/m² in women or >149 g/m² in men [21, 24]. The remaining subjects were categorized as having normal LV function.

Measurements of Arterial Stiffness and Wave Reflections

Supine brachial systolic (SBP) and diastolic (DBP) blood pressures, and simultaneous right CCA and right femoral arterial pressure waveforms were obtained with a commercially available device using the oscillometric and arterial tonometric techniques (VP-2000, Colin Corporation, Komaki, Japan) [25]. The difference between SBP and DBP was pulse pressure (PP). Brachial mean blood pressure (MBP) was calculated as DBP plus 1/3 PP. cf-PWV was calculated as the travelling distance between the right CCA and right femoral artery divided by the foot-to-foot pulse transit time [25]. Carotid SBP was the peak value of an ensemble-averaged carotid artery pressure waveform calibrated to brachial DBP and MBP [25]. Carotid augmentation index (cAI) was calculated by identification of the inflection point on the pressure waveform [25]. Intra- and interobserver reproducibility was evaluated in 20 randomly selected patients by calculating the intraclass correlation coefficient (ICC). The intra- and interobserver ICCs were 0.989 and 0.988 for cf-PWV, and 0.999 and 0.984 for cAI, respectively.

Two-dimensional grayscale images of the right CCA were swept from the proximal CCA to the carotid bifurcation to survey the CCA anatomy using a 7.5-Hz linear transducer incorporated in the Artida Echocardiograph. Cine loops of transverse CCA at the level of approximately 1 cm proximal to the carotid bulb were acquired for the online analyses using the premounted software in the Artida Echocardiograph (Toshiba Medical Systems Corporation).

On images of the cross-sectional CCA, the image frame at the end of the electrical diastole (start of QRS wave) was identified, and the vessel on this frame was manually marked with a contour at the lumen-intima boundary (fig. 1). The circumferential strain (CS) was then obtained to represent the prolongation along the circular perimeter of the carotid artery in the systole. The intra- and interobserver ICCs for CS were 0.998 and 0.991, respectively.

Two-dimensional long-axis grayscale cine loops of the right CCA were also obtained, and the CCA systolic and diastolic diameters as well as the intima-media thickness of the posterior wall at the same level were measured. CCA incremental elastic modulus (Einc) [7] was calculated according to the equation: $E_{inc} = (4a^2b\Delta P)/[(b^2 - a^2)\Delta D]$, where 'a' is the internal radius, 'b' the external radius of the wall obtained from the sonogram, and 'ΔP' and 'ΔD' are the CCA pressure and diameter changes over the cardiac cycle [7]. CCA distensibility (CD) was obtained according to the formula: $CD = 2[(D_s - D_d)/D_d]/\Delta P$ [26], where 'D_s' and 'D_d' are CCA systolic and diastolic diameters. β stiffness index was calculated using the equation: $\ln(SBP/DBP)/[(D_s - D_d)/D_d]$, where SBP and DBP are brachial blood pressures [27]. The intra- and interobserver ICCs were 0.994 and 0.978 for Einc, 0.986 and 0.943 for CD, and 0.995 and 0.959 for β stiffness index, respectively.

Fig. 1. An example showing the measurement of CS of the CCA.

Follow-Up

Patients were followed up at outpatient clinics or by regular telephone consultations for up to 1 year to check if there were any adverse cardiovascular events including hospitalization due to AHF and death. These adverse cardiovascular events were confirmed by review of medical records by an independent investigator (J.N.L.) who was blinded to the measurements of cardiovascular function. AHF was verified based on the simultaneous presence of at least 2 major Framingham criteria for congestive heart failure [28] or an elevated N-terminal pro-brain natriuretic peptide level if available. The period of event-free survival was defined as the interval between the cardiovascular evaluation and the date of the first adverse event or the end of follow-up.

Statistical Analysis

Between-group comparisons were performed using one-way ANOVA with Bonferroni post hoc analysis or χ^2 test, where appropriate. Multiple linear regression analysis was used to describe the associations between various indices of global and regional arterial stiffness, and LV structure and function, after accounting for age and brachial MBP, and even cf-PWV. Collinearity in the multiple linear regression models was examined by calculating the variance inflation factor. No significant collinearity was found in any of the multiple linear regression models. Significant indicators of impaired cardiac function, defined as systolic or diastolic dysfunction, identified from the univariate binary logistic regression analysis, were further examined in the multiple regression models. The quartile values of each variable were tested to evaluate the best cutoff value for the prediction of AHF. The Kaplan-Meier survival analysis with a log rank test was used to characterize the clinical impact of the CCA stiffness indices. Statistical significance was set at $p < 0.05$ and all statistical analyses were carried out using SPSS 15.0 (SPSS Inc., Chicago, Ill., USA).

Results

Among the 114 eligible patients (mean age 63.5 ± 17.5 years, 30 females), 25 patients had LV systolic dysfunction, 29 had LV diastolic dysfunction, and 60 had normal LV function. Their baseline characteristics are shown in table 1. More patients with LV systolic dysfunction appeared to have prevalent diabetes and coronary artery disease, and more patients with

Table 1. Clinical characteristics, cardiovascular measurements, and mechanical properties of CCA in the study population with and without LV systolic and diastolic dysfunction

Variable	Systolic dysfunction (n = 25)	Diastolic dysfunction (n = 29)	Normal LV function (n = 60)	p value
Age, years	62.9±16.6	69.7±12.2	60.8±19.5	0.081
Male gender, % (n)	84 (21)	69 (20)	72 (43)	0.400
Past medical history, % (n)				
Hypertension	64 (16)	66 (19)	50 (30)	0.278
Diabetes	48 (12)	28 (8)	12 (7)	0.001
CAD	88 (22)	45 (13)	12 (7)	<0.001
Smoking	68 (17)	45 (13)	38 (23)	0.043
eGFR, ml/min/1.73 m ²	76.4±28.1	73.0±28.0	85.2±33.6	0.183
Medications				
ACEI/ARB, % (n)	84 (21)	48.3 (14)	35 (21)	<0.001
β-Blockers, % (n)	84 (21)	58.6 (17)	25 (15)	<0.001
CCB, % (n)	20 (5)	27.6 (8)	31.7 (19)	0.550
Diuretics, % (n)	68 (17)	37.9 (11)	16.7 (10)	<0.001
α-Blockers, % (n)	8 (2)	31 (9)	15 (9)	0.064
Brachial and central blood pressures				
Brachial SBP, mm Hg	117±19 ^b	133±20	126±18	0.013
Brachial DBP, mm Hg	70±9 ^b	78±13	74±11	0.025
Brachial PP, mm Hg	48±13	55±13	52±13	0.149
Brachial MBP, mm Hg	86±12 ^b	96±14	91±12	0.010
Heart rate, beats/min	76±16 ^{a, b}	64±13	65±9	<0.001
Carotid SBP, mm Hg	110±16 ^b	122±18	114±17	0.039
Carotid PP, mm Hg	38±12	44±12	39±11	0.128
Cardiac structure and function				
LVM index, g/m ²	159±56 ^a	147±70 ^a	94±25	<0.001
LV RWT	0.33±0.09 ^{a, b}	0.50±0.26	0.46±0.17	0.002
LVEDV index, ml/m ²	95±35 ^{a, b}	55±17 ^a	43±12	<0.001
LV EF, %	31±7 ^{a, b}	60±10 ^a	65±8	<0.001
E/A	1.5±0.6 ^{a, b}	0.9±0.3 ^a	1.1±0.4	<0.001
E/E'	22.6±9.7 ^{a, b}	17.4±8.5 ^a	10.0±2.7	<0.001
Deceleration time, ms	169±56 ^{a, b}	241±71	226±50	<0.001
Arterial stiffness and wave reflections				
cf-PWV, m/s	12.2±4.9	12.7±3.9 ^a	10.3±4.0	0.027
cAI, %	10.4±31.9 ^{a, b}	25.5±13.9	22.3±16.2	0.017
Mechanical properties of CCA				
Carotid Einc, kPa	1,295±496 ^{a, b}	1,017±503 ^a	719±322	<0.001
β Stiffness index	10.7±4.9 ^{a, b}	7.7±3.8 ^a	5.5±1.9	<0.001
CD, kPa ⁻¹ ×10 ⁻³	15.0±6.9 ^a	19.0±8.9 ^a	24.4±9.3	<0.001
Carotid CS, %	1.3±0.9 ^{a, b}	2.0±0.8	2.2±0.9	<0.001

Figures are means ± SD unless indicated otherwise. CAD = Coronary artery disease; ACEI/ARB = angiotensin-converting enzyme inhibitor or angiotensin receptor blocker; CCB = calcium channel blocker; eGFR = estimated glomerular filtration rate; RWT = relative wall thickness. ^a p < 0.05, compared to the normal LV function group. ^b p < 0.05, compared to the diastolic dysfunction group.

normal LV function were smokers. In addition, patients with LV systolic dysfunction were more likely to take angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, β-blockers, and diuretics, indicating that these patients had been well treated. Patients with LV systolic dysfunction had significantly lower brachial SBP, DBP and MBP, and carotid SBP than patients with LV diastolic dysfunction. Heart rate was significantly greater

Table 2. Correlates of arterial stiffness with cardiac structure and function by multiple linear regression analyses

	LVM index (g/m ²)		LVEDV index (ml/m ²)		LV EF (%)		E/A		E/E'	
	model 1	model 2	model 1	model 2	model 1	model 2	model 1	model 2	model 1	model 2
cf-PWV (m/s)	0.092	–	0.328*	–	–0.471**	–	0.124	–	0.210	–
Carotid Einc (kPa)	0.184*	0.179	0.426**	0.398**	–0.398**	–0.351**	0.134	0.122	0.310**	0.294**
β Stiffness index	0.195*	0.190	0.454**	0.431**	–0.431**	–0.394**	0.086	0.076	0.285**	0.271**
CD (kPa ^{–1} ×10 ^{–3})	–0.258**	–0.254*	–0.410**	–0.381**	0.384**	0.336**	–0.195*	–0.185*	–0.299**	–0.282**
Carotid CS (%)	–0.089	–0.084	–0.231*	–0.212**	0.277**	0.249**	0.134	0.143	–0.223*	–0.211*

Model 1: accounting for age and brachial MBP. Model 2: accounting for age, brachial MBP, and cf-PWV. * p < 0.05; ** p < 0.01.

Table 3. Association of arterial stiffness with impaired LV function: logistic regression analysis

	Model 1		Model 2		Model 3	
	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
cf-PWV (1 SD = 4.3 m/s)	1.70 (1.13–2.54)	0.010	1.97 (1.07–3.65)	0.030	–	–
Carotid Einc (1 SD = 473 kPa)	3.19 (1.89–5.38)	<0.001	3.33 (1.92–5.76)	<0.001	3.19 (1.84–5.54)	<0.001
β Stiffness index (1 SD = 3.8)	2.88 (1.74–4.79)	<0.001	3.05 (1.80–5.18)	<0.001	2.97 (1.74–5.05)	<0.001
CD (1 SD = 9.5 kPa ^{–1} ×10 ^{–3})	0.37 (0.22–0.62)	<0.001	0.35 (0.20–0.62)	<0.001	0.38 (0.21–0.66)	0.001
Carotid CS (1 SD = 0.96%)	0.52 (0.33–0.80)	0.003	0.54 (0.35–0.83)	0.006	0.55 (0.36–0.86)	0.008

Model 1: crude ratio. Model 2: accounting for age, sex, and brachial MBP. Model 3: accounting for age, sex, brachial MBP and cf-PWV.

in patients with LV systolic dysfunction than in other groups. LV EF increased significantly, and the LVEDV index and E/E' decreased significantly, in the order of LV systolic dysfunction, diastolic dysfunction, and normal function. Patients with LV systolic or diastolic dysfunction had a significantly greater LVM index than patients with normal LV function. Patients with LV systolic dysfunction had a significantly greater E/A ratio, a shorter deceleration time, and smaller relative wall thickness than patients with LV diastolic dysfunction or normal LV function.

Patients with LV systolic dysfunction were characterized by a low cAI when compared with the other groups. On the other hand, patients with LV diastolic dysfunction had significantly greater cf-PWV than patients with normal LV function. CCA stiffness tended to increase in the order of normal LV function, LV diastolic dysfunction, and LV systolic dysfunction. All measures of CCA stiffness were significantly greater in patients with LV systolic dysfunction than those in patients with normal LV function.

Coupling of Arterial Stiffness with LV Structure and Function

In the whole study population, cf-PWV significantly correlated with LVEDV index and LV EF but not LVM index, E/A or E/E', when age and brachial MBP were accounted for (table 2). In contrast, CCA stiffness was apparently coupled with LV structure and systolic and diastolic function. All measures of CCA stiffness correlated significantly with LVEDV index, LV EF, and E/E' with adjustments for age and brachial MBP (table 2, model 1). In addition, CCA Einc, β stiffness index, and CD significantly correlated with LVM index, and CCA CD significantly correlated with E/A. With further adjustment for cf-PWV (table 2, model 2), all measures of CCA stiffness remained significantly correlated with LV EF, LVEDV index, and E/E'. In addition, CCA CD remained significantly correlated with LVM index and E/A.

Table 4. Prediction of first hospitalization for AHF by the highest or lowest quartile of an individual parameter

Variable	Quartile cutoff value	Hazard ratio (95% CI)	p value
E/E'	17.5	26.20 (3.28–209.56)	0.002
LV EF ^a , %	47	11.44 (2.37–55.14)	0.002
LVM index, g/m ²	138	11.06 (2.30–53.29)	0.003
Carotid CS ^a , %	1.2	6.82 (1.70–27.35)	0.007
LVEDV index, ml/m ²	67	6.57 (1.64–26.32)	0.008
Carotid Einc, kPa	1,200	6.56 (1.64–26.26)	0.008
β Stiffness index	11.1	3.91 (1.05–14.57)	0.042
eGFR ^a , ml/min/1.73 m ²	53.8	2.70 (0.72–10.08)	0.140
CD ^a , kPa ⁻¹ ×10 ⁻³	14.1	2.51 (0.67–9.34)	0.171
Age, years	81	1.94 (0.48–7.76)	0.351
Brachial PP, mm Hg	59	1.82 (0.45–7.33)	0.397
Carotid SBP, mm Hg	128	1.70 (0.43–6.82)	0.452
cf-PWV, m/s	13.9	1.62 (0.41–6.51)	0.494
Carotid PP, mm Hg	47	1.47 (0.37–5.88)	0.586
E/A	1.4	1.47 (0.37–5.88)	0.586
Brachial SBP, mm Hg	139	0.95 (0.29–4.59)	0.952
cAI, %	33.2	0.89 (0.19–4.30)	0.887

eGFR = Estimated glomerular filtration rate. ^a Hazard ratio of the lowest quartile. **Fig. 2.** Kaplan-Meier survival analysis of the development of AHF for subjects with high or low carotid Einc (75-percentile value, 1,200 kPa) (a), carotid β stiffness index (median value, 7.7) (b), and carotid CS (25-percentile value, 1.21%) (c).

Association of Arterial Stiffness with Impaired LV Function

All measures of arterial stiffness, including cf-PWV, CCA Einc, β stiffness index, CD, and CS, were significantly associated with the presence of either systolic or diastolic LV dysfunction (table 3, model 1). After adjustments for age, sex, and brachial MBP, the associations remained significant (table 3, model 2). With further adjustment for cf-PWV, all measures of CCA stiffness remained significant predictors of impaired LV function (table 3, model 3).

Prediction of the Development of AHF

During a mean follow-up of 265 ± 106 days, 9 patients (6 patients with LV systolic dysfunction and 3 with LV diastolic dysfunction at baseline) had AHF. N-terminal pro-brain natriuretic peptide levels were available in 5 patients (average $4,011 \pm 2,711$ pg/ml). Major

predictors of AHF were measures of cardiac function and structure (table 4). In addition, the simple Cox proportional regression analyses also identified the highest quartiles of CCA Einc (75-percentile value, 1,200 kPa) and β stiffness index (75-percentile value, 11.1), and the lowest quartile of CCA CS (25-percentile value, 1.2%) as significant predictors of AHF (table 4). In contrast, neither cf-PWV nor cAI was associated with the incidence of AHF. The Kaplan-Meier survival curve analysis also showed that high CCA Einc, high β stiffness index, and low CCA CS were significantly associated with a higher event rate of AHF (fig. 2).

Discussions

Pulsatile hemodynamics may play an important role in the pathogenesis of heart failure with reduced [3] and preserved EF [29], and cf-PWV in particular may complement the diagnosis of heart failure with preserved EF [30]. cf-PWV is the most widely accepted indicator of arterial stiffness, covering the territory of CCA but excluding the ascending aorta. However, the present study found that measures of CCA stiffness consistently increased in patients with LV systolic and diastolic dysfunction and were significantly coupled with measures of LV structure and systolic and diastolic function, over and above cf-PWV. Moreover, measures of CCA stiffness but not cf-PWV predicted the development of first hospitalization due to AHF. Given that the CCA stiffness is not the major afterload of the left ventricle, it may be considered as a surrogate for proximal aortic stiffness, which may be more important than cf-PWV in the pathogenesis of heart failure. The results complement the recent findings that carotid artery stiffness is associated with exercise intolerance in patients with preserved EF heart failure [9, 20], and may suggest that an increase in CCA stiffness beyond the changes attributed to normal aging is involved in the pathogenesis of heart failure [20].

The proximal aortic root may be crucial to the development of heart failure [3, 5, 6]. It has been shown that elderly patients with preserved or reduced EF heart failure have reduced proximal thoracic aortic distensibility that may contribute to their severe exercise intolerance [5, 31]. In patients with heart failure with reduced EF, the central pulsatile load (characteristic impedance) but not cf-PWV was elevated in comparison to the subjects without heart failure [3]. This may imply that normal vascular aging may not be sufficient to cause heart failure and cf-PWV may underestimate, and thus is inappropriate in the assessment of the proximal aortic stiffness.

The impedance mismatch between the proximal aorta and CCA may disappear with a disproportionate increase in aortic impedance [14], so the proximal aorta and CCA may become a common conduit with remarkably reduced wave reflection at the interface [14]. On the one hand, the impedance matching may facilitate the transmission of the excessive pulsatile energy and damage the cerebral microcirculation [14]. On the other hand, the CCA may become a 'window' to access the mechanical properties of the proximal aorta. In patients with heart failure and preserved EF, the carotid SBP, PP, PP amplification, and CCA Peterson's modulus but not brachial blood pressures, total peripheral resistance or cf-PWV were substantially elevated at rest and dramatically increased when compared with controls [9]. The study further demonstrated that CCA stiffness rather than cf-PWV was the determinant of exercise intolerance, further emphasizing the importance of proximal aortic stiffness in patients with heart failure and preserved EF [9].

Previous studies have demonstrated the usefulness of CCA stiffness as a risk factor for cardiovascular disease [32–35]. The present study expanded the usefulness of CCA stiffness in the risk stratification of patients at risk of developing heart failure. Moreover, the present study also showed that CCA stiffness can be easily and effectively assessed using the speckle-tracking semi-automatically derived CCA CS, which may be superior to Einc or β stiffness

index in the assessment of vascular aging [36]. However, the results of the present study do not suggest that CCA stiffness may effectively replace cf-PWV as the gold standard for the assessment of arterial stiffness in the general population [37].

Study Limitations

Firstly, cf-PWV and CD were significantly related to cardiac structure and functions but could not predict the development of AHF, which might also be the result of insufficient power to detect significance due to the limited sample size and number of events in the present study. For the same reason, we did not compare the LV systolic versus diastolic dysfunction subgroups concerning the risk of development of AHF. While the CCA stiffness parameters demonstrated identical and constant associations with LV functions, the independency of their prognostic value should be tested in future studies with larger populations. Secondly, the study was a secondary analysis for subjects participating in another hemodynamic study. Therefore, the study may be subject to selection bias, despite its prospective nature. Thirdly, we did not measure the pulsatile hemodynamics during exercise. Because arterial stiffness may be underestimated at rest in patients with preserved EF heart failure [9], the true impact of CCA stiffness on LV structure and function and the development of AHF may have been underestimated in the present study.

Conclusions

In patients at risk of developing heart failure, mechanical properties of CCA may be associated with LV structure and function and predict the first AHF independently of arterial stiffness indexed by cf-PWV. The usefulness of CCA stiffness in the risk stratification of patients at risk of developing heart failure needs to be confirmed in future studies with larger study populations.

Disclosure Statement

The authors have no conflicts of interest to declare.

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