CHAPTER 5

Relationship between left ventricular diastolic function and arterial stiffness in asymptomatic patients with diabetes mellitus

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Abstract

Left ventricular (LV) diastolic dysfunction and increased arterial stiffness are common in patients with diabetes mellitus (DM). However, the relation between these two pathophysiological factors remains unclear. The aim of this study was to investigate the relationship between LV diastolic function and arterial stiffness as assessed with applanation tonometry.

In 142 asymptomatic patients with DM (mean age 48 years, 75 (53 %) men, 72 (51 %) patients with type 2 DM) LV diastolic function was assessed with echocardiography. Arterial stiffness was evaluated measuring the aortic pulse wave velocity (PWV) whereas wave reflection was assessed measuring central systolic blood pressure (cSBP), central pulse pressure (cPP), and augmentation index (AIx) with applanation tonometry.

Mean E/A ratio, E' and E/E' ratio were 1.1 ± 0.3, 8.1 ± 2.3 cm/s and 9.2 ± 3.3, respectively. Mean PWV, mean cSBP, median cPP and mean AIx were 7.9 ± 2.4 m/s, 122 ± 17 mmHg, 40 [35-51] mmHg and 17.9 ± 12.1 %, respectively. PWV was independently associated with LV diastolic dysfunction grade ($\beta = 0.76$, $p = 0.03$). In contrast, measures of wave reflection, cPP , cSBP and AIx were independently related with E/A ratio, but not with the LV diastolic dysfunction grade.

Parameters of arterial stiffness and wave reflection are associated with echocardiographic indices of LV diastolic function in asymptomatic patients with DM. Therapies that prevent progression of arterial stiffness and reduce late-systolic pressure overload may help to reduce the prevalence of LV diastolic dysfunction in this population.

Introduction

Patients with diabetes mellitus (DM) have a two- to fourfold higher risk of cardiovascular events than nondiabetic patients.[1] Endothelial dysfunction, micro- and macrovascular remodeling, increased deposition of collagen and advanced glycation end products are well known pathophysiologic mechanisms that lead to accelerated arterial and myocardial stiffness in diabetic patients.[2] Left ventricular (LV) diastolic dysfunction is one of the first consequences of increased myocardial stiffness, contributes to 50 % of the incidence of heart failure with preserved LV ejection fraction and is associated with poor outcome.[3-5] In addition, increased arterial stiffness has been associated with LV diastolic dysfunction and is an independent predictor of cardiovascular events.[6, 7] Therefore, early detection of LV diastolic dysfunction and increased arterial stiffness in patients with DM may help to identify the patients at increased risk for cardiovascular events and allow for early initiation of preventive therapeutic strategies.

So far, evaluation of the relation between LV diastolic function and arterial stiffness in patients with DM has provided conflicting results.[8-10] Whereas LV diastolic function is consistently assessed by standardized parameters obtained with echocardiography according to current recommendations of the American Society of Echocardiography (ASE) and European Association of Echocardiography (EAE),[11] there is no uniformity in the noninvasive assessment of arterial stiffness. Based upon the methodology used to evaluate arterial stiffness, the results of previous studies investigating the relation between LV diastolic function and arterial stiffness may significantly vary.[8-10] Applanation tonometry may be the preferred technique since it provides the aortic pulse wave velocity (PWV), considered the gold standard measure of arterial stiffness and is an established end-point of target-organ damage in patients with hypertension.[12-14] Thus, the aim of the current study was to investigate the relation between LV diastolic function measured with echocardiography and tissue Doppler imaging and arterial stiffness assessed with applanation tonometry in asymptomatic patients with DM.

Methods

Patient population

The patient population was derived from an ongoing registry including asymptomatic patients with DM. DM was diagnosed and classified according the American Diabetes Association criteria.[15] Patients with demonstrable auto-antibodies to islet cells, insulin and glutamic acid decarboxylase or low levels of plasma c-peptide in laboratory analysis were considered as having type 1 DM. Otherwise, patients were considered to have type 2 DM. Comprehensive evaluation of asymptomatic DM patients was routinely performed at the outpatient clinic of the Leiden University Medical Center.[16] This evaluation included a cardiovascular risk assessment performed at the cardiology outpatient clinic consisting of structured clinical history, physical examination and blood and urine

laboratory testing. LV function and dimensions and valvular function were assessed with transthoracic echocardiography. Noninvasive assessment of arterial stiffness was performed with applanation tonometry. Clinical and echocardiographic data were prospectively collected in the departmental cardiology information system (EPD-Vision®) and echocardiographic database and were retrospectively analyzed.
Asymptomatic status was confirmed with a self-completed questionnaire on chest pain.[17] Patients with significant coronary artery disease, impaired systolic function defined as LV ejection fraction (LVEF) <50 % and moderate and severe valvular heart dysfunction were excluded.
The independent associations between parameters of LV diastolic function and indices of arterial stiffness by applanation tonometry were assessed.

Cardiovascular risk factors evaluation

Overweight defined by a body mass index (BMI) ≥25 kg/m^2, family history of coronary artery disease (in first degree family members; male <55 years and/or female <65 years), smoking status (current smoking or smoking in the last 2 years), hypertension (blood pressure >140/90 mmHg or use of antihypertensive medication) and hypercholesterolemia (total cholesterol level >5.0 mmol/L or use of cholesterol lowering medication) were recorded as cardiovascular risk factors. In addition, diabetes related risk factors were defined by DM duration in years, levels of hemoglobin A1c, renal dysfunction based on glomerular filtration rate and presence of microalbuminuria (urine albumin/creatinine ratio ≥3.5 mg/mmol).

Echocardiography

Two-dimensional transthoracic echocardiography was performed in all patients using a commercially available system (Vivid 7 and E9, General-Electric Vingmed, Horton, Norway). ECG-gated images were obtained at rest in the left lateral decubitus position using 3.5-MHz and M5S transducers in the parasternal, apical and subcostal views. Standard M-mode and two-dimensional, color, continuous and pulsed wave Doppler images were acquired during breath hold and saved in cine-loop format. The obtained images were analyzed offline, using dedicated software (EchoPac version 110.0.0 General-Electric Vingmed).
LV end-systolic volume (LVESV), end-diastolic volume (LVEDV) and LVEF were assessed using the biplane Simpson method in the apical 4- and 2-chamber views.[18] LV systolic dysfunction was defined as LVEF <50 %. In addition, left atrial (LA) volume was determined with the biplane Simpson method in the apical 4- and 2-chamber views according to the ASE and the EAE guidelines.[18] The LA volume index was calculated by dividing the LA volume by the body surface area. Enlarged left atrium was defined by a LA volume index ≥34 mL/m^2.[11]
LV diastolic function assessment included the measurement of peak velocities of the

early (E) and late (A) mitral inflow and the deceleration time (DT) of the E-wave at the apical 4-chamber view, using the pulsed wave Doppler. The E/A ratio was calculated. Isovolumic relaxation time was measured from pulsed wave Doppler spectral recordings obtained in the apical 5-chamber view placing the sample volume between the aortic valve and the anterior mitral leaflet. Furthermore, systolic and diastolic pulmonary vein velocities (PVs and PVd) were measured from pulsed wave Doppler recordings at the right superior pulmonary vein in the apical 4-chamber view. Thereafter, the pulmonary vein PVs/PVd ratio was calculated. Additionally, high frame rate tissue Doppler imaging data were obtained in the apical 4-chamber view and the early peak mitral annular velocity (E') at the lateral and septal mitral annulus were measured offline. The mean E' value was obtained by averaging these measurements. Subsequently, the E/E' ratio was calculated.[11] Finally, patients were classified in grades of LV diastolic dysfunction, according criteria derived from the ASE guidelines.[11] Patients with E' ≥9 cm/s and LA volume ≤34 mL/m^2 were defined as having a normal diastolic function. In the remaining patients, mild diastolic dysfunction (grade I) was defined as E/A ratio <0.8, DT >200 ms and E/E' ratio ≤8; moderate diastolic dysfunction (grade II) as E/A ratio 0.8-1.5, DT between 160-200 ms and E/E' ratio between 9 and 12 and severe diastolic dysfunction (grade III) as E/A ratio ≥2, DT <160 ms and E/E' ratio ≥13.[11]

Applanation tonometry

All patients underwent noninvasive evaluation of arterial stiffness with applanation tonometry using a SphygmoCor system (SphygmoCor, Atcor Medical, Sydney, Australia) with a hand-held high fidelity tonometer (Millar Instruments, Houston, TX, USA). Measurements were performed by a specially trained technologist, blinded to patient's clinical characteristics and echocardiographic results, under standardized conditions (during the morning in a quiet, temperature-controlled clinical research laboratory). Patients were instructed to abstain from their morning medication and remain fasting until the end of the test. Measurements were performed after 10-minute rest in supine position, when a state of constant heart rate and blood pressure was reached.

Pulse wave velocity

Aortic pulse wave velocity (PWV) was determined with arterial tonometry of the carotid and femoral arteries with simultaneous ECG-gating.[6, 19] The aortic PWV was defined as the distance traveled by the pulse wave, between recording sites on the carotid and femoral artery, divided by transit time (averaged from 10 consecutive beats) and was determined semi-automatically as previously described.[6, 19] To correct for measurement variability, three consecutive beats were measured and the average was calculated. The reference value of PWV for a healthy population aged between 40 and 49 years is 7.5 ± 2.5 m/s.[20]

Pulse wave analysis

Central systolic blood pressure (cSBP), central pulse pressure (cPP) and augmentation index (AIx), measures of wave reflection, were derived from pulse wave analysis. Peripheral pressure wave forms were recorded on the radial artery at the level of the wrist and calibrated by peripheral blood pressures measured at the brachial artery with a cuff-sphygmomanometer. Central aortic pressure waveforms were generated from these recorded pressure waveforms with a validated generalized transfer function and used to calculate cSBP, cPP and AIx (Figure 1).[12, 19]

cSBP was defined as the peak pressure of the aortic pressure waveform (Figure 1). cPP was calculated as the difference between central systolic and diastolic pressure (Figure 1). The aortic pressure waveform is formed by the forward pressure wave of ventricular contraction and a backward pressure wave from reflection on the peripheral arterial system.[12] With increasing arterial stiffness, the reflected wave shifts from diastole to systole and increases systolic blood pressure, which is identified on the central aortic pressure waveform by the merging point of the initial forward wave and the reflected wave (Figure 1). The AIx was defined and calculated as the percentage that the reflected wave contributes to the pulse pressure (maximum systolic pressure minus pressure at the merging point). Thereafter, AIx was normalized to a heart rate of 75 beats/min.[12, 21] AIx was measured on 3 consecutive recordings and the average was calculated. Reference values were derived from a substudy of the Anglo-Cardiff Collaborative Trial (ACCT) on vascular aging, including 559 healthy subjects (258 men and 301 women) in the age category of 40 and 49 years.[22] In this study, the observed mean cSBP, CPP and AIx in men were 113 ± 9 mmHg, 34 ± 6 mmHg and 19 ± 10 % and in women 109 ± 11 mmHg, 33 ± 8 mmHg and 28 ± 10 %, respectively.

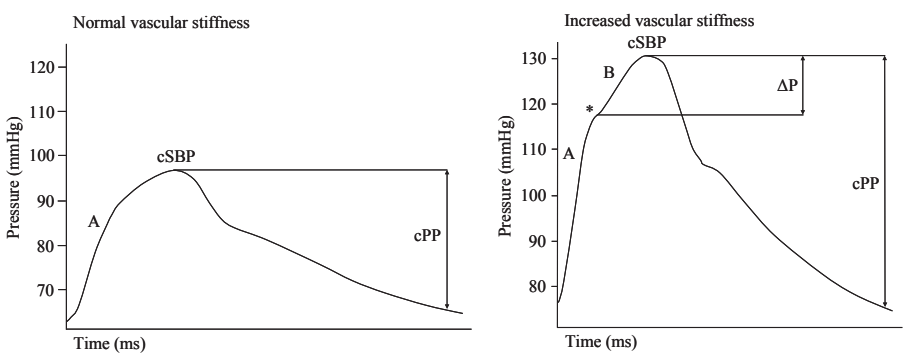

Figure 1 *Central aortic pressure waveform of an individual with normal arterial stiffness (a) and an individual with increased arterial stiffness (b). Central systolic blood pressure was defined as the peak pressure of the central aortic pressure waveform. Central pulse pressure (cPP) was calculated as the pressure difference of the aortic pressure waveform. The augmentation index is calculated as the percentage pressure augmentation from the reflected wave (ΔP) to the cPP.*

**: merging point of incident wave and reflected wave, ΔP: pressure augmentation from the reflected wave, A: incident wave, B: reflected wave, cPP: central pulse pressure, cSBP: central systolic blood pressure.*

Statistical analysis

Normal distributed continuous variables were expressed as mean ± standard deviation, non-normal distributed variables as median (25^{th} and 75^{th} percentiles), and categorical variables as numbers (percentages). The Pearson's and Spearman's correlation coefficients were used to assess univariate associations between the indices of arterial stiffness and wave reflection and baseline clinical variables and echocardiographic parameters of LV diastolic function.

Multivariate linear regression analyses were performed to assess independent relations between the indices of arterial stiffness and wave reflection and parameters of LV diastolic function. These associations were assessed for each LV diastolic function echocardiographic parameter and corrected for age, gender, type and duration of DM, heart rate and BMI. All statistical analyses were performed using SPSS software (version 16.0, SPSS Inc., Chicago, Illinois). P-values <0.05 were considered statistically significant.

Results

A total of 142 asymptomatic patients with DM were evaluated. The baseline clinical variables are presented in Table 1. The mean age was 48 ± 11 years and 75 (53 %) were men. Fifty-one percent of patients had DM type 2. The mean DM duration was 15 ± 12 years and mean BMI was 28 ± 6 kg/m^2. Sixty-eight (48 %) patients had hypertension.

Table 1 Baseline clinical variables

Clinical variables	n=142
Age (years)	48 ± 11
Male gender, n (%)	75 (53%)
DM type 2, n (%)	72 (51%)
DM duration (years)	15 ± 12
Hemoglobin A1c (%)	7.9 ± 1.5
BMI (kg/m^2)	28 ± 6
Family history of CAD, n (%)	52 (37%)
Smoking, n (%)	35 (25%)
Diastolic blood pressure (mmHg)	80 ± 9
Systolic blood pressure (mmHg)	131 ± 16
Heart rate (beats/min)	70 ± 10
Hypertension, n (%)	68 (48%)
Hypercholesterolemia, n (%)	102 (72%)
Glomerular filtration ratio (mL/min/1.73m^2)	92 ± 21
Microalbuminuria ≥3.5 mg/mmol, n (%)	21 (15%)

Abbreviations: BMI: body mass index; CAD: coronary artery disease; DM: diabetes mellitus

Echocardiography

The mean LVEF and LA volume index were normal, 65 ± 9 % and 16 ± 4 mL/m^2, respectively (Table 2). The mean E/A ratio, E' and E/E' ratio were 1.1 ± 0.3, 8.1 ± 2.3 cm/s and 9.2 ± 3.3, respectively. In 15 patients an increased left ventricular filling pressure was identified by E/E' ratio ≥13. Normal LV diastolic filling pattern, mild (grade I) and moderate (grade II) diastolic dysfunction were observed in 72 (51 %), 54 (38 %) and 16 (11 %) patients, respectively. Grade III diastolic dysfunction was not recorded in any patient.

Table 2 Echocardiographic parameters of left ventricular function and indices of arterial stiffness measured with applanation tonometry

Variable	n=142
Echocardiographic parameters	
LVEDV (mL)	114 ± 29
LVESV (mL)	41 ± 16
LVEF (%)	65 ± 9
LA volume index (mL/m^2)	16 ± 4
E (cm/s)	70 ± 16
A (cm/s)	65 ± 18
E/A ratio	1.1 ± 0.3
DT (ms)	226 ± 68
Isovolumic relaxation time (ms)	84 ± 12
E' (cm/s)	8.1 ± 2.3
E/E' ratio	9.2 ± 3.3
PV_s (cm/s)	50 ± 11
PV_d (cm/s)	42 ± 10
PV_s/PV_d ratio	1.2 ± 0.3
Indices of arterial stiffness	
PWV (m/s)	7.9 ± 2.4
cSBP (mmHg)	122 ± 17
cPP (mmHg)*	40 [35, 51]
AIx (%)	17.9 ± 12.1

Abbreviations: A: peak transmitral late diastolic inflow velocity, AIx: augmentation index, cPP: central pulse pressure, cSBP: central systolic blood pressure, DT: deceleration time of the E-wave velocity, E: peak transmitral early diastolic inflow velocity, E': peak early mitral annular velocity averaged from measurement in septal and lateral mitral annulus, LA volume index: left atrial volume index, LVEDV: left ventricular end-diastolic volume, LVEF: left ventricular ejection fraction, LVESV: left ventricular end-systolic volume, PVd: diastolic pulmonary vein velocity, PVs: systolic pulmonary vein velocity, PWV: pulse wave velocity.
**expressed as median (25th and 75th percentiles).*

Arterial stiffness assessed with applanation tonometry

The mean PWV was 7.9 ± 2.4 m/s, similar as the reference value established in a healthy study population (Table 2).[20] The mean cSBP and median cPP were both slightly increased (122 ± 17 mmHg and 40 [35-51] mmHg, respectively). However, the mean AIx was within the normal range (17.9 ± 12.1 %).[22]

Clinical and echocardiographic correlates of arterial stiffness

Table 3 presents the univariate correlation coefficients between indices of arterial stiffness and wave reflection and baseline clinical variables as well as echocardiographic parameters of LV diastolic function. Age was significantly correlated with all indices of arterial stiffness and wave reflection, whereas male gender was only significantly related with AIx. Hypertension and systolic blood pressure were significantly related with all indices of arterial stiffness and wave reflection. In contrast, other well-known cardiovascular risk factors or specific diabetes-related variables were not consistently related with indices of arterial stiffness or wave reflection. Importantly, echocardiographic parameters of LV diastolic function were significantly associated with all indices of arterial stiffness and wave reflection. Similarly, LV diastolic dysfunction grade was significantly associated with all indices of arterial stiffness and wave reflection.

Table 3 Correlation coefficients between indices of arterial stiffness and baseline clinical variables as well as parameters of LV diastolic function

	PWV	cSBP	cPP	AIx
Age (years)	0.34**	0.36**	0.45**	0.43**
Male gender	-0.05	-0.07	-0.07	-0.47**
DM type 2	0.11	0.23**	0.11	0.24**
DM duration (years)	0.24**	0.07	0.15	0.07
BMI (kg/m^2)	0.17*	0.19*	0.07	0.22**
Heart rate (beats/min)	0.17*	0.03*	-0.15	0.24**
Systolic blood pressure (mmHg)	0.22**	0.47**	0.31**	0.26**
Hypertension	0.39**	0.39**	0.31**	0.29**
Hypercholesterolemia	0.15	0.12	0.17*	0.22**
Microalbuminuria	0.25**	0.23**	0.13	0.14
E/A ratio	-0.35**	-0.44**	-0.39**	-0.52**
E' (cm/s)	0.32**	-0.40**	-0.38**	-0.44**
E/E' ratio	0.26**	0.30**	0.29**	0.31**
LV diastolic dysfunction	0.38**	0.37**	0.32**	0.29**

Abbreviations: A: peak transmitral late diastolic inflow velocity, AIx: augmentation index, BMI: body mass index, cPP: central pulse pressure, cSBP: central systolic blood pressure, DM: diabetes mellitus, E: peak transmitral early diastolic inflow velocity, E': peak early mitral annular velocity averaged from measurement in septal and lateral mitral annulus, PWV: pulse wave velocity.
** p-value <0.05, ** p-value <0.01*

Independent associations between LV diastolic function and arterial stiffness

Independent significant associations between echocardiographic parameters of LV diastolic function and arterial indices were identified with multivariate linear regression

Table 4 *Associations between echocardiographic parameters of LV diastolic function and indices of arterial stiffness.*
Multivariate linear regression analysis with adjustment for age, gender, diabetes mellitus (DM) type 2, DM duration, body mass index and heart rate.

Dependent variable	Independent variable	β	95% CI	*p*-value
PWV	E/A ratio	-1.36	-2.86 to 0.14	0.07
	E'	-0.13	-0.36 to 0.09	0.25
	E/E' ratio	0.04	-0.10 to 0.18	0.56
	LV diastolic dysfunction	0.76	0.05 to 1.46	0.03
cSBP	E/A ratio	-18.30	-28.91 to -7.68	0.001
	E'	-2.10	-3.74 to -0.47	0.01
	E/E' ratio	0.86	-0.14 to 1.85	0.09
	LV diastolic dysfunction	4.05	-0.99 to 9.08	0.11
cPP	E/A ratio	-9.93	-17.78 to -2.07	0.01
	E'	-1.08	-2.28 to 0.12	0.08
	E/E' ratio	0.56	-0.16 to 1.29	0.13
	LV diastolic dysfunction	2.40	-1.27 to 6.07	0.20
AIx	E/A ratio	-10.38	-16.62 to -4.15	0.001
	E'	-1.05	-2.01 to -0.08	0.03
	E/E' ratio	0.04	-0.54 to 0.63	0.88
	LV diastolic dysfunction	-0.79	-3.75 to 2.19	0.60

Abbreviations: A: peak transmitral late diastolic inflow velocity, AIx: augmentation index, cPP: central pulse pressure, cSBP: central systolic blood pressure, E: peak transmitral early diastolic inflow velocity, E': peak early mitral annular velocity averaged from measurement in septal and lateral mitral annulus, PWV: pulse wave velocity.

analysis (Table 4). The multivariate linear regression models were corrected for age, gender, DM type 2, DM duration, body mass index and heart rate. PWV was independently associated with LV diastolic dysfunction grade and tended to be significantly correlated with E/A ratio. In contrast, cPP was significantly correlated with E/A ratio but not with LV diastolic dysfunction grade. Furthermore, cSBP and AIx were associated with E/A ratio and E'.

Discussion

The present evaluation demonstrated the independent associations between arterial stiffness and wave reflection parameters and LV diastolic function indices in asymptomatic patients with DM. PWV, a parameter of arterial stiffness, was independently associated with LV diastolic dysfunction grade, whereas cPP, cSBP and AIx, parameters of wave reflection, were significantly associated with E/A ratio. cSBP and AIx were also independently correlated with E'.

LV diastolic dysfunction and arterial stiffness in asymptomatic DM patients

In patients with DM, endothelial dysfunction, increased extracellular deposition of collagen and advanced glycation end products, and activation of the renin-angiotensin-aldosterone system and cytokines lead to increased arterial and myocardial stiffness.[2] Increased arterial stiffness has been reported in asymptomatic DM patients with LV diastolic dysfunction and preserved LVEF.[10, 23] In addition, arterial stiffness and LV diastolic dysfunction are considered important pathophysiologic determinants of overt heart failure development and coronary heart disease events in patients with DM.[24, 25] In a population-based study including 1,760 DM patients, the presence of LV diastolic dysfunction and increased LV filling pressures (increased E/E' ratio) was independently associated with the subsequent development of heart failure.[24] In addition, data from The Cardiff Diabetes Database, including 2,911 patients with type 2 DM showed that peripheral pulse pressure was the best predictor of coronary heart disease events.[25] This evidence suggests that parameters of LV diastolic function and arterial stiffness can be used as markers of cardiovascular disease for the identification of patients with DM at increased risk of cardiovascular events. Progressive arterial stiffening causes an accelerated systolic return of the arterial wave reflection from the peripheral arterial tree, leading to increased systolic blood pressure and reduced coronary perfusion.[26] These changes result in an increased systolic workload and mismatch in the myocardial supply/oxygen demand ratio, which cause LV diastolic dysfunction and at a later stage systolic dysfunction. However, the association between arterial stiffness and LV diastolic dysfunction in DM patients remains debated.

In 49 patients with new onset type 2 DM, Loimaala et al. measured arterial stiffness with whole body impedance cardiography and LV diastolic function with conventional echocardiography and tissue Doppler imaging.[27] PWV was only independently associated with E'. Furthermore, in 42 patients with DM, Eren and coworkers demonstrated significant correlations between aortic distensibility measured with M-mode echocardiography and E/A ratio, isovolumic relaxation time and DT.[28] Using magnetic resonance imaging, van der Meer et al. demonstrated a significant correlation between aortic distensibility and LV diastolic function in asymptomatic patients with type 2 DM.[23] The use of different techniques to evaluate arterial stiffness may have led to inconsistent correlations with several parameters of LV diastolic function.

Assessment of arterial stiffness with applanation tonometry and correlates of LV diastolic dysfunction

Applanation tonometry is a validated and reproducible method for the noninvasive assessment of arterial stiffness.[19, 29] The friendly use and low costs are some of the advantages of this method. PWV measured at the carotid and femoral arteries is considered the gold standard measure of arterial stiffness.[12]

Recently, Sharman et al. evaluated wave reflection parameters (AIx and cPP) with ap-

planation tonometry in 172 patients with type 2 DM.[10] cPP was independently associated with E/E' ratio and A as assessed with echocardiography. However, PWV was not evaluated. As previously described, wave reflection parameters (such as cPP and AIx) and arterial stiffness parameters (such as PWV) may reflect different aspects of arterial properties and, therefore, may correlate differently with LV diastolic function parameters. Indeed, wave reflection parameters have demonstrated to be less affected by the aging process as compared to parameters of arterial stiffness.[30] In addition, previous studies have reported stronger associations between PWV and LV diastolic function as compared to parameters of wave reflection.[31, 32] The present evaluation confirms previous results by demonstrating independent associations between LV diastolic dysfunction and PWV and between E/A ratio and several indices of wave reflection. The indices derived by pulse wave analysis, cSBP, cPP and AIx, depend on the reflected wave and are also determined by LVEF. [12] This dependency of wave reflection parameters on LV function might explain their independent association with E/A ratio.

Limitations

Some limitations need to be mentioned. The cross-sectional design precluded the detection of a cause-effect relation between LV diastolic dysfunction and arterial stiffness. To confirm the causal link between these two entities, longitudinal studies are needed. The prevalence of LV diastolic dysfunction was relatively low in the present patient population including only asymptomatic DM patients. The present results may not apply to cohorts of patients with more advanced disease.

Conclusions

Indices of arterial stiffness and wave reflection are independently associated with echocardiographic parameters of LV diastolic function in asymptomatic patients with DM. PWV, parameter of arterial stiffness, was independently associated with LV diastolic dysfunction grade, whereas cPP, cSBP and AIx, parameters of wave reflection, were significantly associated with E/A ratio. Therapies that prevent progression of arterial stiffness and reduce late-systolic pressure overload may reduce the prevalence of LV diastolic dysfunction in this population.

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