Association of albuminuria with impaired aortic elasticity and left ventricular diastolic dysfunction in type 2 diabetes

Tip 2 diyabetes mellitusta albüminürinin, aortik elastisite ve sol ventrikül diyastolik fonksiyonu ile ilişkisi

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ABSTRACT

Objective: Albuminuria is a predictor of cardiovascular morbidity and mortality in patients with diabetes (DM). In this study, we tested the hypothesis suggesting that the presence of albuminuria reflects impaired aortic elastic properties in type 2 DM.
Methods: Overall 140 patients with type 2 DM without obvious renal impairment (serum creatinine <1.5 mg/dl) were included in this cross-sectional study. Patients were divided into 3 groups based on amount of albuminuria: Group 1 - patients with no signs of albuminuria (16 men, 34 women, mean age 51±11 years); Group 2 - patients with microalbuminuria (15 men, 35 women, mean age 52±9 years); Group 3 - patients with macroalbuminuria (14 men, 26 women, mean age 56±8 years). Each patient underwent transthoracic two-dimensional and Doppler echocardiography with assessment of diastolic function, aortic strain and aortic root distensibility. Statistical analysis was performed using ANOVA analysis for comparison of variables between 3 groups. The relationship of albuminuria with clinical variables, parameters of left ventricular mass, diastolic function, aortic strain and distensibility was assessed using multivariate regression analysis.
Results: A significant stepwise decrease in the aortic strain and distensibility was seen across Group 1 to Group 3. Similar findings were noted in left ventricular diastolic functions with longer deceleration time (DT) and lower peak early to late transmitral filling velocity ratios (E/A) in groups with albuminuria. Aortic distensibility significantly correlated with DT (r=-0.35, p<0.001), isovolumic relaxation time (r=-0.31, p<0.005) and left ventricular mass/ height$^{2.7}$ (r =-0.26, P<0.005). In multivariate analysis, the amount of albumin was significantly associated with aortic distensibility (standardized β coefficient -0.23, p<0.01) and DT (standardized β coefficient 0.26, p<0.005).
Conclusion: Our results suggest increased urinary albumin excretion is significantly correlated with impaired aortic elastic properties and left ventricular diastolic dysfunction in type 2 diabetes, which may contribute to the relation of albuminuria and increased rate of cardiovascular events among diabetics. *(Anadolu Kardiyol Derg 2008; 8: 10-5)*
Key words: Aortic stiffness, diabetes mellitus, albuminuria, left ventricular diastolic function

ÖZET

Amaç: Albüminüri diyabetes mellitus (DM)'lu hastalarda kardiyovasküler mortalite ve morbiditenin öngördürücüsüdür. Bu çalışmada, Tip 2 diyabetes mellitusta albüminüri gelişmesinin aortik elastisitede bozulmayı yansıtabileceği hipotezini test ettik.
Yöntemler: Çalışmaya aşikar böbrek yetersizliği olmayan (serum kreatinin <1.5 mg/dl) 140 tip 2 diyabetes mellituslu hasta dahil edildi. Hastalar albüminüri düzeyine göre 3 gruba ayrıldı: Grup 1- albüminüri olmayan hastalar (16 erkek, 34 kadın, ortalama yaş 51±11 yıl); Grup 2 - mikroalbüminüri tespit edilen hastalar (15 erkek, 35 kadın, ortalama yaş 52±9 yıl); Grup 3 - makroalbüminüri tespit edilen hastalar (14 erkek, 26 kadın, ortalama yaş 56±8 yıl). Hastaların tamamında 2-boyutlu ve Doppler ekokardiyografi kullanılarak, diyastolik fonksiyon, aortik gerilme ve aort kökü esnekliği ölçüldü. Üç grupta yer alan değişkenleri birbiriyle karşılaştırmak için ANOVA testi kullanıldı. Albüminüri ile klinik değişkenler, sol ventrikül kitlesi, diyastolik fonksiyon, aortik sertlik ve esnekliği arasındaki ilişki, çok değişkenli regresyon analizi kullanılarak değerlendirildi.
Bulgular: Üç grup birbiriyle karşılaştırıldığında, aortik gerilme ve esnekliğin, Grup 1'den Grup 3'e doğru azaldığı gözlendi. Benzer şekilde, albüminüri gelişen gruplarda sol ventrikül diyastolik fonksiyonlarda bozulmayı yansıtan akım hızı yavaşlama zamanının arttığı, en yüksek transmitral erken doluş hızının en yüksek transmitral geç doluş hızına oranının ise azaldığı belirlendi. Aortik esnekliğin, akım hızı yavaşlama zamanı (r=-0.35, p<0.001), izovolümetrik gevşeme zamanı (r=-0.31, p<0.005) ve sol ventrikül kitlesi/boy$^{2.7}$ (r=-0.26, P<0.005) ile önemli ölçüde korelasyon gösterdiği saptandı. Çok değişkenli çözümlemede ise, albüminüri miktarı önemli ölçüde aortik esneklik (standardize edilmiş, β katsayısı -0.20, p<0.05) ve akım hızı yavaşlama zamanı (standardize edilmiş, β katsayısı 0.27, p<0.001) ile ilişkili bulundu.
Sonuç: Bu çalışma, tip 2 diyabetes mellituslu hastalarda albüminüri miktarının aortik elastisitede azalma ve sol ventrikül diyastolik fonksiyon bozukluğu ile önemli korelasyon gösterdiğini desteklemektedir. Bu korelasyon, diyabetik populasyonda albüminürinin kardiyovasküler risk artışı ile olan ilişkisini açıklamada önemli katkı sağlayabilir. *(Anadolu Kardiyol Derg 2008; 8: 10-5)*
Anahtar kelimeler: Aortik sertleşme, albüminüri, diyabetes mellitus, sol ventrikül diyastolik fonksiyon bozukluğu

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Introduction

Albuminuria is an early marker of diabetic nephropathy and has been shown to strongly predict future cardiovascular morbidity and mortality in patients with type 2 diabetes mellitus (DM). (1-4). Although the pathophysiologic mechanism underlying this relationship has not been elucidated (3-6), it was suggested that generalized vascular damage might serve as a common pathogenetic mechanism linking albuminuria and premature atherosclerosis (7, 8). This is supported by the findings of higher incidence of coronary and peripheral vascular disease in diabetic patients with microalbuminuria compared with those without microalbuminuria (9-11). In addition, existence of distinct diabetic cardiomyopathy, characterized by diastolic and systolic dysfunction, may also contribute to the increased cardiovascular events seen in patients with type 2 DM (12). Increased arterial stiffness has been consistently demonstrated in type 2 DM and has also been proposed as a powerful and independent risk factor for early mortality (13-15). The mechanism of the increased arterial stiffness in diabetes may be explained by the changes in elastin and collagen content of the vessel walls; the elastin fibers become fractured and collagen deposition is increased (16). In the aorta, this process leads to gradual increase in the diameter of the aortic arch with a consequent decrease in aortic distensibility (17). Other possible contributors to increased arterial stiffness in type 2 DM include impaired glycemic control and the formation of advanced glycation end-products (AGEs) which lead to structural changes in the vessel walls (18-19).

Left ventricular (LV) diastolic dysfunction has been described as an early sign of diabetic cardiomyopathy preceding the systolic dysfunction (13). Diastolic dysfunction was observed in patients free of diabetic complications, hypertension and symptomatic coronary heart disease (13).

The present study tested the hypothesis suggesting that the microalbuminuria reflects the impaired aortic elastic properties and also is associated with diastolic dysfunction in type 2 DM.

Methods

Patients: Overall, 140 Caucasian diabetic outpatients subjects diagnosed as having type 2 DM based on the criteria of the American Diabetes Association (20) were included in this cross-sectional study. We excluded patients with coronary heart disease, moderate-severe valvular disease, left ventricular (LV) ejection fraction≤55 % on echocardiography, atrial fibrillation, or other severe arrhythmias (eg, atrial flutter, atrioventricular block), hyperthyroidism; hypothyroidism; familial hypercholesterolemia, chronic renal disease according to Kidney Disease Outcome Quality Initiative (K/DOQI) guidelines (20) (glomerular filtration rate<60 mL/min/1.73 m^2), diagnosis of diabetes before the age of 35 years, and presence of connective tissue diseases and pregnancy. The 140 patients were divided into 3 groups based on albuminuria status: Group 1 - 50 diabetic patients without albuminuria (16 men, 34 women, mean age 51±11 years); Group 2 - 50 diabetic patients with microalbuminuria (15 men, 35 women, mean age 52±9 years); Group 3 - 40 diabetic patients with macroalbuminuria (14 men, 26 women, mean age 56±8 years).

The study was approved by the local Ethics committee, and patients gave informed written consent. All measurements and procedures were taken with the patients in the fasted state. Height and weight were recorded, and body mass index (BMI) was calculated as weight/height^2 ratio and expressed in kg/m^2. Hypertension at baseline was defined as resting systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg, or if participants were on antihypertensive medications. Patients were categorized as having coronary heart disease on the basis of clinical and electrocardiographic evidence of coronary artery disease or myocardial infarction.

Echocardiographic parameters

Each patient underwent standard transthoracic two-dimensional and Doppler echocardiography. All echo-Doppler assessments were performed by a single operator who was unaware the clinical and laboratory variables of the patients in the left decubitus position with commercially available equipment (SIM 7000 CFM Challenge; ESAOTE Ultrasound, Florence, Italy). Aortic root diameters were measured 3 cm above the aortic valve by two-dimensional guided M-mode transthoracic echocardiography of the aortic root at left parasternal long-axis view (22-24). Aortic systolic diameter (AoS) was measured at the time of full opening of the aortic valve, and diastolic (AoD) diameter at the peak of the QRS complex at the simultaneous electrocardiogram recording. Ten consecutive beats were measured routinely and averaged. The percentage change of the aortic root was calculated as %ΔAo=100x(AoS-AoD)/AoD to obtain the aortic strain (22-24). The aortic root distensibility was calculated from the pulsatile changes of the echocardiographic aortic diameters and pulse pressure (PP), using the formula: distensibility=2x(AoS-AoD)/(AoDxPP) (cm^2xdyn$^{(-1)}$x10$^{(-6)}$). All patients had blood pressure measured manually in the left arm while they were in the supine position by use of a mercury sphygmomanometer. Korotkoff phases I and V were used to determine the systolic and diastolic pressures, respectively and the average of 3 readings were regarded as the clinical blood pressure.

Left ventricular diastolic filling patterns were determined by the mitral inflow pulsed wave Doppler examination. Peak early (E) and late (A) transmitral filling velocities, their ratio (E/A ratio), and the deceleration time of the E wave velocity (DT) were calculated. The isovolumic relaxation time (IVRT) was measured from closure of the aortic valve to opening of the mitral valve. The IVRT was assessed by simultaneously measuring the flow into the LV outflow tract and mitral inflow by Doppler echocardiography. Diastolic dysfunction was defined as E/A ratios of <0.6 (compatible with impaired early diastolic relaxation pattern) and >1.5 (compatible with restrictive LV filling pattern).

The LV diameters and wall thicknesses were measured with 2-dimensional targeted M-mode echocardiography, using the criteria of the American Society of Echocardiography (25). End-diastolic LV dimensions were used to calculate LV mass by a formula that yields values closely correlated with necropsy LV weight (26). The LV mass was normalized for body height$^{2.7}$, where 2.7 is the power of the allometric or growth relation between LV mass and body height (27). Each representative value was obtained from the average of 3 consecutive measurements. All measurements were performed by a single operator who was unaware of the categorization of subjects as cases or controls.

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Biochemical parameters

The 24-hour urine albumin content was measured by immunoturbidometric technique (SENTINEL, Milan, Italy). The other routine chemical variables were measured by standardized methods on auto analyzers. Microalbuminuria was defined as an albumin excretion rate of 30 to 300 mg/day. Macroalbuminuria was recognized as an albumin excretion rate ≥300 mg/day (28).

Statistical analysis

A power analysis was performed according to results of previous studies (15, 22-24). We used ∆-3.0 and total SD of 2.7 for aortic distensibility value, setting the power (beta error) at 95%, β=0.05 and α=0.01. Therefore, we calculated the minimum number of patients that would need to be enrolled as twenty-nine in each study group.

Statistical analysis was performed using the SPSS for Windows Verison 11.5 software (Chicago, IL, USA). Data are expressed as mean ± SD. Differences in baseline patient characteristics and echocardiographic variables (including aortic strain and distensibility) among the 3 diabetic groups were analyzed by 1-way ANOVA test. If ANOVA test indicated significant difference, post-hoc Scheffe's multiple comparison procedure was used to determine between groups differences. Pearson correlation for the normal variables or Spearman correlation for the skewed variables was used to asses associations between the study parameters. The association of amount of secreted albumin into urine with echocardiographic parameters (aortic distensibility, ejection fraction, DT, IVRT, E/A LV mass indexed to height$^{2.7}$) and clinical parameters (age, sex, systolic and diastolic blood pressure, body mass index, duration of diabetes and serum creatinine) was evaluated by multiple regression analysis. Aortic distensibility was the only parameter of aortic stiffness that was entered in the multivariate model. P< 0.05 was taken as statistically significant.

Results

The clinical and laboratory characteristics of the study population are shown in Table 1. Patients with macroalbuminuria were slightly older than those with microalbuminuria and without albuminuria, however differences were not significant. The three groups of patients were similar with regard to sex and body mass index. Stepwise increase, though not significant was seen in Hemoglobin A1C levels, while significant trends for stepwise increase were found for systolic and diastolic blood pressure levels (p=0.001 and p=0.01) and prevalence of hypertension (p<0.05) from the Group 1 to Group 3. The prevalence of insulin therapy (p<0.05), duration of diabetes (p=0.005) and serum creatinine levels (p=0.001) also increased in stepwise fashion from Group 1 to Group 3. There were no differences in total cholesterol, low-density

Table 1. Clinical characteristics

Parameters	Group 1 (n = 50)	Group 2 (n= 50)	Group 3 (n= 40)	F**	p**
Age, years	51±11	52±9	56±8	2.96	0.09
Sex, % Female	68	70	65	-	-
BMI, kg/m²	29.8±2.9	30.4±2.6	29.6±2.7	1.03	0.36
Systolic BP, mm Hg	127±13*	132±15*	144±20†‡	7.37	0.001
Diastolic BP, mm Hg	77±10*	81±11	84±12‡	4.61	0.012
HT, %	46	52	72ᵃ	-	-
Smoking, %	24	18	29	-	-
TC, mg/dL	192±37	202±40	194±51	0.79	0.45
LDL-C, mg/dL	117±30	124±33	119±47	0.54	0.58
HDL-C, mg/dL	40±8	40±11	36±9	2.61	0.09
Triglycerides, mg/dL	174±61	186±75	193±76	0.93	0.40
Hb A1C	7.7±2.8	8.1±2.6	8.3±1.8	2.52	0.08
Uric acid, mg/dL	4.5±1.9	4.7±1.6	5.3±1.9	2.45	1.0
Serum creatinine, mg/dL	0.8±0.1*	0.9±0.2*	1.2±0.2†,‡	12.57	0.001
Duration of DM, years	7.4±3.3*	8.2±3.6	9.7±3.0‡	9.98	0.005
Statin treatment, %	39	40	54	-	-
Antidiabetic drugs, % Insulin Oral antidiabetics	 24 77	 44 54	 92ᵃ 7ᵃ	 - -	 - -
Antihypertensive drugs, % ACEI and/or ARB Beta-blockers Ca⁺⁺ antagonists Diuretics	 38 4 6 10	 44 6 4 10	 56ᵃ 8 7 15	 - - - -	 - - - -

Values are given as mean ± SD and percentages
** F and p values for one-way ANOVA test
a - p<0.05 for Chi square test
*p < 0.05 - Scheffé post-hoc test compared to macroalbuminuria
†p < 0.05 Scheffé post-hoc test compared to microalbuminuria
‡p < 0.05 Scheffé post-hoc test compared to no albuminuria
ACEI- angiotensin converting enzyme inhibitor, ARB- angiotensin receptor blocker, BMI- body mass index, BP- blood pressure, DM- diabetes mellitus, HDL-C- high-density lipoprotein cholesterol, HT- hypertension, LDL-C- low-density lipoprotein cholesterol, TC- total cholesterol

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lipoprotein cholesterol, triglycerides and high-density lipoprotein, serum uric acid levels and the prevalence of smoking among the three groups. The use of angiotensin-converting enzyme inhibitor and/or angiotensin receptor blockers was significantly higher in Group 3 than in Group 1 (p<0.05).

Echocardiographic parameters including aortic elasticity indexes are listed in Table 2. The values of LV mass indexed to height$^{2.7}$, systolic and diastolic aortic diameters were highest in Group 3 and lowest in Group 1 (p=0.03, p=0.001 and p=0.001, respectively). Isovolumetric relaxation time was longer (p=0.01) in patients with microalbuminuria than in those without albuminuria. Thicknesses of posterior wall were higher (p=0.001 and p=0.02) in the two groups of patients with albuminuria as compared with no albuminuria group, while LV end-diastolic diameter, thicknesses of interventricular septum and DT in patients without albuminuria were significantly lower (p=0.02, p=0.004, and p=0.001, respectively) than in patients with macroalbuminuria. The prevalence of abnormal diastolic function showed stepwise increases from no albuminuria to macroalbuminuria (p<0.05). Left ventricular ejection fraction decreased in stepwise fashion from no albuminuria to macroalbuminuria but it was not significant (p>0.05).

The mean value of aortic strain and distensibility in all patients with diabetes were 7.0±2.9% and 2.8±1.4 cm^2/dyn/10^3 respectively. A significant stepwise increase in the aortic strain and distensibility was seen through Group 1 to Group 3 (p=0.001 and p=0.001, respectively).

Aortic distensibility was inversely and significantly correlated with IVRT (r =-0.31, p=0.005), DT (r=-0.35, p=0.001) and LV Mass/ height$^{2.7}$ (r =-0.26, p=0.005).

Multiple regression analysis was used to evaluate the association of the amount of secreted albumin into the urine with echocardiographic and clinical parameters (aortic distensibility, ejection fraction, DT, IVRT, E/A LV mass indexed to height$^{2.7}$, age, sex, systolic and diastolic blood pressure, body mass index, duration of diabetes and serum creatinine). It was observed that amount of albumin in urine was significantly correlated with aortic distensibility (standardized β coefficient -0.23, p=0.01, overall R^2=0.05) and DT (standardized β coefficient -0.26, p=0.005, overall R^2= 0.07) (Table 3).

Discussion

The present study provides the first data on echocardiographically-derived aortic elastic properties in type 2 diabetic patients without albuminuria as compared with microalbuminuria and macroalbuminuria. We demonstrated a significant stepwise decrease in aortic strain and distensibility through groups of patients with no albuminuria to macroalbuminuria. In addition, it was shown that only aortic distensibility and DT were significantly associated with the amount of albuminuria. This study provides potentially important findings, identifying associations of albuminuria with aortic stiffness and LV diastolic dysfunction and may explain the high cardiovascular mortality in type 2 diabetic patients.

Albuminuria has been proposed as a marker of generalized vascular involvement associated with nephropathy, retinopathy and cardiovascular disease in diabetic patients (28). Studies support the opinion that increased urinary albumin excretion reflects renal and generalized transvascular albumin leakage that

Table 2. Echocardiographic findings

Parameters	Group 1 (n=50)	Group 2 (n=50)	Group 3 (n=40)	F	p**	p*	p†	p‡
LVDD, cm	4.2±0.4	4.3±0.6	4.6±0.7	4.36	0.02	0.02	0.88	0.07
LVSD, cm	2.7±0.3	2.6±0.3	2.8±0.5	0.54	0.96	0.92	0.93	0.64
EF, %	67±9	66±7	63±6	1.44	0.81	0.44	0.90	0.66
LV Mass/ heigh$^{2.7}$	37±7	38±7	43±11	6.20	0.03	0.005	0.87	0.02
LA, cm	3.34±0.41	3.24±0.28	3.41±0.18	1.62	0.32	0.52	0.86	0.24
PW thickness, cm	0.93±0.14	1.04±0.13	1.07±0.14	12.63	0.001	0.001	0.02	0.07
IVS thickness, cm	1.07±0.16	1.12±0.17	1.19±0.19	5.68	0.004	0.004	0.36	0.14
E/A ratio	0.83±0.26	0.70±0.27	0.67±0.25	5.33	0.006	0.01	0.04	0.85
DT, ms	185±43	199±29	217±45	7.73	0.001	0.001	0.21	0.08
Diastolic dysfunction, %	14[a]	29[a]	50[a]	-	-	-	-	-
IVRT, ms	106±19	117±23	112±23	4.48	0.03	0.31	0.01	0.44
ASD, cm	3.30±0.34	3.23±0.29	3.57±0.39	11.71	0.001	0.002	0.60	0.001
ADD, cm	3.05±0.27	3.02±0.33	3.39±0.40	14.74	0.001	0.001	0.96	0.001
Aortic strain, %	8.4±2.8	6.8±2.6	5.4±2.4	15.03	0.001	0.001	0.009	0.047
Distensibility, cm^2/dyn/10^3	3.4±1.3	2.8±1.4	1.9±1.0	17.98	0.001	0.001	0.039	0.002

Values are given as mean ± SD and percentages
** F and p values for one-way ANOVA test
a - p<0.05 for Chi square test
* Scheffé post-hoc test - Group 1 compared to Group 3
† Scheffé post-hoc test - Group 1 compared to Group 2 ‡ Scheffé post-hoc test - Group 2 compared to Group 3
ADD- aortic diastolic diameter, ASD- aortic systolic diameter, DT- deceleration time of the E wave velocity, E/A ratio- ratio of peak early transmitral filling to peak late transmitral filling velocity, EF- ejection fraction, IVRT- isovolumic relaxation time, IVS- interventricular septum, LA- left atrium, LV- left ventricle, LVDD- left ventricular diastolic dimension, LVSD- left ventricular systolic dimension, PW- posterior wall

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is possibly due to low vessel wall content of heparan sulfate (7). It was reported that heparan sulfate has not been only present in the glomerular basement membrane but also in the atherosclerotic aorta and coronary arteries (29). This generalized increase of vascular permeability can also cause leakage of collagen, cholesterol, and advanced glycated end-products that have been reported in the myocardium of human hearts (30). These tissue alterations can increase end-diastolic myocardial stiffness as well as LV mass, and alter normal systolic function. Furthermore, a strong negative correlation between the accumulation of lipids and concentration of the heparan sulfate in the arterial walls has been reported (31). The change in permeability causing insudation of lipoproteins into the intima of large vessels can lead to atherosclerosis of the epicardial coronary arteries as well as small arterioles of the heart. In addition, heparan sulfate proteoglycan in plasma membranes of endothelial cells has important antithrombogenic properties (32) Loss of normal sulfated heparan sulfate might therefore, contribute to the formation of microthrombi and occlusion of the small vessels of the heart. Small vessel disease can lead to subendocardial ischemia causing systolic and diastolic myocardial dysfunction.

In a prospective study, Smith et al. showed that aortic stiffness was significantly increased in patients with type 2 diabetes and raised albuminuria (33). They assessed albuminuria by albumin creatinine ratio which from the median of three non consecutive overnight urine samples. However, it was reported that the use of one albumin creatinine ratio value to define microalbuminuria may underestimate microalbuminuria in subjects with higher muscle mass (men) and possibly members of certain racial/ethnic groups (34). However, we used 24 hours urine collection, which was recommended as a gold standard for the measurement of urinary albumin excretion according to the American Diabetes Association (35) and we confirmed that albuminuria was significantly associated with impaired aortic elasticity.

The relationship between albuminuria and aortic stiffness was also investigated in nondiabetic hypertensive patients (36-37). In these studies, it was showed that patients with hypertension, those with microalbuminuria had significantly impaired elastic properties compared with their normoalbuminuric counterparts, whereas

urinary albumin excretion was a significant predictor of aortic mechanics in the entire population (36-37).

We showed a significant correlation between aortic distensibility and LV diastolic function parameters and LV mass/ height[2.7]. The affected aortic elastic properties can be contributing factors in increased LV mass index and impaired LV diastolic functions.

Present study demonstrated a significant association between LV diastolic dysfunction and amount of albuminuria in type 2 diabetic patients. A population-based study also showed that albuminuria is independently associated with LV diastolic dysfunction (38). Our results are in agreement with this study although the latter study was performed in a Native-American Indian population, present study consisted of Caucasian population. These findings suggest that increased urinary albumin excretion is associated with severity of diabetes and diabetes itself is associated with "a distinct diabetic cardiomyopathy", LV diastolic impairment in the albuminuria groups may be partially associated with a greater severity of diabetes.

In the present study, we used echocardiographically-derived method for evaluation of aortic elastic properties. However, there are different techniques including invasive and noninvasive methods for the assessment of aortic elastic properties. Angiographic and high-fidelity intravascular catheter tip micromanometer techniques are invasive (24,39). Invasive methods, especially radial artery waveforms recorded with a high-fidelity micromanometer, have been shown to be valid techniques to assess aortic elasticity (40). In contrast, aortic elastic properties were evaluated noninvasively in the present study. The most readily available noninvasive technique able to detect these changes is echocardiography. Good quality, high-resolution images can accurately determine the systolic and diastolic dimensions of the aorta. Using pressure measurements, one can calculate parameters that reflect the distensibility or stiffness of the aorta (41). Noninvasive aortic elasticity parameters demonstrate a strong relationship with age and correlate well with other parameters of vascular stiffness such as the pulse wave velocity. On the other hand, Stefanadis et al. showed that distensibility of the aorta determined by the echocardiographic method was closely related to that obtained by directly invasive measurements and reported that aortic distensibility could be obtained noninvasively with a high degree of accuracy (39).

Limitations of the study

The medication history, including antihypertensive and antidiabetic treatments, among the patients with DM was different, which could possibly have influenced our results. A second limitation of this study is that the presence of coronary heart disease cannot be ruled out because a stress test or coronary angiography was not performed in study population. However, it seems unlikely that a major ischemic contribution was present, because of absence of clinical, echocardiographic and electrocardiographic evidence.

Conclusion

In conclusion, our results suggest increased urinary albumin excretion is significantly correlated with impaired aortic elastic properties and LV diastolic dysfunction in type 2 diabetes, which may contribute to the relation of albuminuria and increased rate of cardiovascular events among diabetics.

Table 3. Multiple regression analysis of the variables associated with amount of secreted albumin into urine

Variables	ß	p	95% Confidence interval
Age, years	0.23	0.18	1.59-4.89
Sex	-0.095	0.18	-337.40-330.96
BMI, kg/m²	-0.098	0.17	-60.22-10.65
Duration of DM, years	0.72	0.32	-14.17-42.72
Serum creatinine, mg/dL	0.158	0.09	418.45-1448.11
Systolic BP, mm Hg	0.106	0.18	-1.99-10.43
Diastolic BP, mm Hg	-0.046	0.71	-17.96-12.20
EF, %	-0.03	0.68	-16.71-10.98
LV Mass/ height[2.7]	0.054	0.50	-8.19-16.83
IVRT, ms	0.083	0.28	-2.08-7.19
E/A ratio	-0.05	0.48	-506.56-240
DT, ms	0.26	0.001	1.81-6.62
Distensibility, cm²/dyn/10³	-0.23	0.009	-175.06-(-22.4)

BMI- Body mass index, BP- blood pressure, DM- diabetes mellitus, DT- deceleration time of the E wave velocity, E/A ratio- ratio of peak early transmitral filling to peak late transmitral filling velocity, EF- ejection fraction, IVRT- isovolumic relaxation time, LV- left ventricle

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