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ScienceDirect
Metabolism Clinical and Experimental 57 (2008) 448 – 452
Metabolism
Clinical and Experimental
www.elsevier.com/locate/metabol

Is albuminuria an indicator of myocardial dysfunction in diabetic patients without overt heart disease? A study with Doppler strain and strain rate imaging

Chi Young Shim[a], Sungha Park[a], Eui-Young Choi[a], Seok-Min Kang[a], Bong-Soo Cha[b], Jong-Won Ha[a], Se-Joong Rim[a], Hyun-Chul Lee[b], Namsik Chung[a,*]

[a]*Cardiology Division, Yonsei Cardiovascular Center and Research Institute, Yonsei University College of Medicine, Seoul 120-752, Korea*
[b]*Endocrinology Division, Department of Internal Medicine, Yonsei University College of Medicine, Seoul 120-752, Korea*

Received 8 June 2007; accepted 20 November 2007

Abstract

The aim of this study was to address whether albuminuria could predict myocardial dysfunction in diabetic patients without overt heart disease. We studied 67 patients with normal left ventricular (LV) ejection fraction and no evidence of LV hypertrophy or coronary artery disease (47 patients with type 2 diabetes mellitus and hypertension and 20 patients with hypertension only). Diabetes patients were divided into 3 groups based on albuminuria status: group II = no albuminuria (n = 20, <30 mg/d), group III = microalbuminuria (n = 13, 30-300 mg/d), and group IV = macroalbuminuria (n = 14, >300 mg/d). Twenty patients with hypertension only served as a control group (group I). Conventional 2-dimensional and Doppler echocardiography was done. Peak strain, peak systolic strain rate (SR), and peak diastolic SR of 6 LV segments in the apical views were measured and averaged in each patient. Conventional 2-dimensional parameters such as LV ejection fraction; left atrium volume index; LV mass; deceleration time; and mitral early peak, mitral late peak, myocardial early peak diastolic, and myocardial peak systolic velocities were not different among the 4 groups. However, peak strains were significantly lower in group III ($P = .002$) and group IV ($P < .001$) than in group I; and the absolute value of peak systolic SR was lower in group III ($P = .033$) and group IV ($P < .001$) than in group I. Furthermore, the value of peak diastolic SR was lower in group IV than in group I ($P = .014$). In diabetic patients with albuminuria, Doppler strain and SR imaging detected subclinical LV systolic and diastolic dysfunction; and albuminuria was associated with myocardial dysfunction in diabetic patients without overt heart disease.

1. Introduction

Patients with diabetes mellitus are characterized by an increased likelihood of heart failure, largely through its association with coronary artery disease and hypertension [1]. Diabetic patients have myocardial dysfunction independent of coronary artery disease, hypertension, and other heart diseases. The underlying mechanisms of myocardial dysfunction are proposed to be multifactorial such as metabolic disturbances, myocardial fibrosis, microangiopathy, autonomic dysfunction, and insulin resistance [2].

Albuminuria is a predictor of cardiovascular morbidity and mortality in diabetic patients. This is independent of conventional cardiovascular risk factors including age, arterial hypertension, and hypercholesterolemia [3,4]. Albuminuria reflects renal and systemic transvascular albumin leakage and has been considered a marker of microangiopathy [5], but the mechanism of albuminuria on myocardial dysfunction is not yet clearly understood.

The aim of this study was to examine the relationship between albuminuria and myocardial dysfunction in diabetes mellitus without overt heart diseases using Doppler strain and strain rate imaging (SRI).

2. Materials and methods

2.1. Study subjects

Sixty-seven patients (28 men; mean age, 59 ± 8 years; 47 patients with type 2 diabetes mellitus and hypertension and 20 patients with hypertension only) were consecutively

* Corresponding author. Tel.: +82 2 2228 8444; fax: 82 2 393 2041.
E-mail address: namsikc@yumc.yonsei.ac.kr (N. Chung).

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doi:10.1016/j.metabol.2007.11.003

recruited at Yonsei Diabetes Clinic and Yonsei Cardiovascular Center in Seoul, Korea.

All patients had well-controlled arterial blood pressure (<140/90 mm Hg) and underwent stress electrocardiogram (ECG) or sestamibi scan to exclude the possibility of significant coronary artery disease. The blood pressure was measured with the dominant arm after being seated for 5 minutes using a mercury sphygmomanometer. The blood pressure was measured twice at 5-minute intervals, and the average value was used for analysis. The subjects who were on medication with angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers were excluded, and any antihypertensive drug was not withdrawn for this study. All patients were in sinus rhythm without signs of ischemia or bundle-branch block on resting 12-lead ECG. All patients had normal left ventricular ejection fraction (LVEF) >55%, as measured by the Simpson method. Patients with LV hypertrophy on 2-dimensional (2D) echocardiography, evidence of inducible ischemia on treadmill ECG or sestamibi scan, *uncontrolled hypertension* defined as seated office blood pressure ≥140/90 mm Hg, moderate-to-severe valvular disease, atrial fibrillation or other severe arrhythmia, and congenital heart disease were excluded. Diabetes patients were divided into 3 groups based on albuminuria status of 24-hour urine analysis. *Normoalbuminuria* was defined as an albumin excretion of less than 30 mg within 24 hours. *Microalbuminuria* was defined as an albumin excretion of 30 to 300 mg/d and *macroalbuminuria* as an albumin excretion of greater than 300 mg/d (group II = no albuminuria [n = 20], group III = microalbuminuria [n = 13], and group IV = macroalbuminuria [n = 14]). Twenty patients with hypertension only served as a control group (group I). This study received prior approval from the institutional ethics committee, and the procedures followed were in accordance with the institutional guidelines. All patients gave informed consent before being enrolled.

2.2. Conventional 2D echocardiography

All echocardiography examinations were performed on a GE Vivid Seven ultrasound machine (General Electric, Milwaukee, WI) with a 2.5-MHz transducer and stored digitally and analyzed. Left ventricular diameters and wall thickness were measured by 2D M-mode echocardiography using the criteria of the American Society of Echocardiography [6]. Left ventricular mass was determined by the formula of Devereux et al [7]. *Left ventricular hypertrophy* was defined as LV mass index >131 g/m^2 in men and >100 g/m^2 in women [8]. Left ventricular volumes and ejection fraction were estimated using a modified Simpson biplane method. Each representative value was obtained from the average of the 3 measurements.

2.3. Doppler echocardiography

Pulsed wave Doppler measurements were obtained with the transducer in the apical 4-chamber view with the Doppler beam aligned perpendicular to the plane of the mitral annulus. The sample volume was placed between the tips to the mitral leaflets. Peak early mitral inflow (E) velocity, peak atrial filling (A) velocity, and deceleration time (DT) were measured.

Tissue Doppler imaging (TDI) was obtained from the apical 4-chamber view. Peak myocardial early diastolic (Em) velocity, peak myocardial late diastolic velocity, and peak myocardial systolic (Sm) velocity were obtained by placing a tissue Doppler sample volume at the septal annulus.

2.4. Doppler strain and SRI

Strain is produced by application of a stress, a dimensionless quantity; and the resulting deformation of the material is expressed as either fractional or the percentage change from the original dimension [9]. Strain rate is the change of strain over time (t) [9]. Peak strain is a marker of regional systolic function, and peak systolic SR is an index of the speed of regional myocardial contraction [10]. Peak diastolic SR is an index of the speed of regional myocardial relaxation.

Doppler strain and SR curves were extracted from an average of 3 cycles of TDI data. Strain and SR were derived from strain and SR curves obtained by placing a bar (7 mm) on 6 LV segments in the 3 apical views. Sampling in the midmyocardial layer was performed in each segment and maintained by tracking wall motion.

Peak strain was defined as the most negative value on the strain curve. *Peak systolic SR* was determined as the most negative value in the SR curve preceding the peak systolic strain, and *peak diastolic SR* as the most positive value in the early diastolic portion of the SR curve [11]. In this study, we measured peak strain, peak systolic SR, and peak diastolic SR on 6 LV segments and averaged the values.

2.5. Statistical analysis

Values were expressed as mean ± SD. Comparisons of the discrete variables were performed using the χ^2 analysis, and comparisons of continuous variables between the 4 study groups were performed using analysis of variance. Post hoc analysis was performed using the Bonferroni method. Independent predictors of peak strain, peak systolic SR, and peak diastolic SR were determined using multiple linear regression analysis. Statistical analysis was done using SPSS 11.0 software (SPSS, Chicago, IL).

3. Results

3.1. Clinical and biochemical characteristics

There were no significant differences among the 4 groups in age, heart rate, systolic blood pressure, diastolic blood pressure, and body mass index. Most of the subjects enrolled in this study were relatively well-controlled hypertensive patients. There were no significant differences in the antihypertensive treatments. The proportion of patients

Table 1
Clinical characteristics

	Group I (n = 20)	Group II (n = 20)	Group III (n = 13)	Group IV (n = 14)
Age (y)	57 ± 9	60 ± 11	60 ± 7	60 ± 10
Sex (male/female)	8:12	9:11	5:8	6:8
HR (beats/min)	71 ± 8	67 ± 7	75 ± 7	68 ± 8
SBP (mm Hg)	130 ± 9	130 ± 7	123 ± 9	134 ± 4
DBP (mm Hg)	83 ± 7	82 ± 6	75 ± 6	80 ± 7
BMI (kg/m^2)	23.2 ± 1.7	23.7 ± 2.9	23.8 ± 2.9	24.7 ± 4.4
Smoker, n (%)	5 (25.0)	5 (25.0)	2 (15.4) *, †	2 (14.3) *, ‡
Dyslipidemia, n (%)	3 (15.0)	4 (25.0) *	4 (30.0) *	4 (28.0) *
LVEF (%)	68 ± 6	66 ± 5	72 ± 5	66 ± 10
LA vol index (mL/m^2)	18 ± 6	17 ± 4	17 ± 3	21 ± 6
LV mass index (g/m^2)	77 ± 12	75 ± 15	78 ± 10	80 ± 12
Antihypertensives, n (%)				
CCBs	7 (35.0)	8 (40.0)	6 (46.2)	6 (42.9)
β-Blockers	3 (15.0)	4 (20.0)	2 (15.4)	3 (21.4)
Diuretics	5 (25.0)	4 (20.0)	3 (23.1)	4 (28.6)

HR indicates heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; LA vol index, left atrium volume index; CCBs, calcium channel blockers.

* Significant difference vs group I.

† Significant difference between groups II and III.

‡ Significant difference between groups II and IV.

taking each major class of antihypertensives are specified in Table 1. Patients with diabetes mellitus (groups II, III, and IV) showed a greater prevalence of dyslipidemia than group I, but there were no significant differences among the diabetic groups. There were also no significant differences in LVEF, left atrium volume index, and LV mass index among the 4 groups. Table 2 summarizes the clinical and biochemical characteristics of the diabetic patients. The duration of diabetes mellitus was longer in group IV than in the other groups, but there were no significant differences in the hemoglobin A_{1c} and fasting glucose among the 3 groups. Serum creatinine was higher in group IV than in groups II and III; but there were no differences in the level of electrolytes such as sodium, potassium, calcium, and magnesium. In the treatment of diabetes mellitus, insulin and sulfonylurea were used more frequently in group IV.

Table 2
Clinical and biochemical characteristics in diabetic patients

	Group II (n = 20)	Group III (n = 13)	Group IV (n = 14)
DM duration (mo)	45 ± 34	37 ± 20	168 ± 127 †, ‡
Blood chemistry			
Hemoglobin A_{1c} (%)	7.5 ± 2.2	8.0 ± 2.0	7.9 ± 1.5
Fasting glucose (g/dL)	166 ± 44	177 ± 26	180 ± 50
Creatinine (mg/dL)	1.0 ± 0.2	1.0 ± 0.2	1.6 ± 0.6 †, ‡
Sodium (mmol/dL)	140 ± 4	139 ± 3	138 ± 4
Potassium (mmol/dL)	4.1 ± 0.6	4.0 ± 0.5	4.0 ± 0.6
Calcium (mg/dL)	9.1 ± 0.7	9.0 ± 0.8	9.2 ± 0.6
Magnesium (mmol/dL)	1.8 ± 0.2	1.9 ± 0.4	1.9 ± 0.3
24-h urine albumin (mg/d)	24.3 ± 22.4	46.0 ± 37.7 *	2164.7 ± 1221.0 †, ‡
Diabetic treatment, n (%)			
Insulin	2/15 (13%)	2/12 (17%)	4/10 (40%) †, ‡
Diet treatment only	7/15 (47%)	5/12 (42%)	3/10 (30%)
Metformin	4/15 (29%)	4/12 (33%)	4/10 (28%)
Sulfonylurea	4/15 (27%)	2/12 (17%)	4/10 (40%) †, ‡

* Significant difference between groups II and III.

† Significant difference between groups II and IV.

‡ Significant difference between groups III and IV.

3.2. Doppler echocardiography data

There were no significant differences in E velocity, A velocity, DT, and Em velocity among the 4 groups. Stepwise decreases were seen in Sm velocity in TDI, but there was no statistical significance (Table 3).

3.3. Strain and SRI analysis

The absolute value of peak strain was significantly lower in group III (−19.6% ± 1.2%, $P = .002$) and group IV (−17.4% ± 1.9%, $P < .001$) than in group I (−23.2% ± 1.9%), but time to peak strain did not differ among the 4 groups. The absolute value of peak systolic SR was lower in group III (−1.44 ± 0.27/s, $P = .033$) and group IV (−1.11 ± 1.19/s, $P < .001$) than in group I (−1.58 ± 0.30/s). The value of peak diastolic SR was lower in group IV (1.83 ± 0.60/s, $P = .014$) than in group I (2.32 ± 0.29/s) (Table 4). Multiple linear regression analysis showed significant negative correlation of 24-hour urine albumin with peak strain ($\beta = -.32$, $P = .042$), peak systolic SR ($\beta = -.303$, $P = .045$), and peak diastolic SR ($\beta = -.325$, $P = .042$) when controlled for age, diabetes duration, and LV mass index (Table 5).

3.4. Comparison of TDI and SRI parameters on the prediction of myocardial dysfunction

3.4.1. LV systolic function

There were no significant differences among the 4 groups in Sm velocity on TDI, but the absolute values of peak systolic strain and peak systolic SR were significantly lower in groups III and IV than in group I (Tables 3 and 4).

3.4.2. LV diastolic function

There were no statistically significant differences among the 4 groups in Em velocity on TDI, but peak

Table 3
Doppler echocardiography data

	Group I (n = 20)	Group II (n = 20)	Group III (n = 13)	Group IV (n = 14)
E velocity (m/s)	0.6 ± 0.1	0.6 ± 0.1	0.7 ± 0.2	0.7 ± 0.2
A velocity (m/s)	0.7 ± 0.2	0.7 ± 0.1	0.8 ± 0.2	0.8 ± 0.2
E/A	0.85 ± 0.15	0.87 ± 0.20	0.87 ± 0.18	0.84 ± 0.25
DT (ms)	210 ± 132	216 ± 39	199 ± 38	200 ± 28
Em velocity (cm/s)	5.8 ± 1.1	6.3 ± 1.4	5.9 ± 1.4	6.0 ± 2.0
Sm velocity (cm/s)	6.8 ± 0.8	6.7 ± 1.1	6.3 ± 0.5	6.4 ± 0.8
E/Em	10.2 ± 2.5	9.9 ± 3.2	11.1 ± 2.7	11.0 ± 3.4

E/A indicates ratio of the early to the late peak diastolic transmitral flow velocity; E/Em, ratio of the mitral early peak velocity to the myocardial early peak diastolic velocity.

Table 4
Doppler strain and SRI data

	Group I (n = 20)	Group II (n = 20)	Group III (n = 13)	Group IV (n = 14)
Peak strain (%)	−23.2 ± 1.9	−21.3 ± 3.3	−19.6 ± 1.2 *	−17.4 ± 1.9 *,‡
Time to peak strain (ms)	310 ± 40	300 ± 30	300 ± 40	310 ± 30
Peak systolic SR (/s)	−1.58 ± 0.30	−1.50 ± 0.29	−1.44 ± 0.27 *	−1.11 ± 1.19 *,‡
Peak diastolic SR (/s)	2.32 ± 0.29	2.46 ± 0.77	2.09 ± 0.33	1.83 ± 0.60 *,‡

†Significant difference between groups II and III.
* Significant difference vs group I.
‡ Significant difference between groups II and IV.

diastolic SR was significantly lower in group IV than in group I (Tables 3 and 4).

4. Discussion

The development of myocardial dysfunction represents a major complication of diabetes. This condition is characterized by defects of contractile and relaxation function in the absence of significant coronary artery disease or systemic hypertension. In the past 3 decades, a number of experimental, pathological, epidemiological, and clinical data were reported that confirmed the association of diabetes with myocardial dysfunction [2,12-19]. The pathogenesis of myocardial dysfunction in diabetes remains unclear, although several mechanisms, including metabolic disturbances, myocardial fibrosis, microangiopathy, autonomic dysfunction, and insulin resistance, have been proposed [2]. In these mechanisms, the alteration of microvascular structure and function is considered to be an important mechanism.

Albuminuria has been considered to be a marker of a generalized vascular dysfunction [20]. It has been shown to predict cardiovascular morbidity and mortality in diabetic patients independent of conventional cardiovascular risk factors including age, arterial hypertension, and hypercholesterolemia [3,4]. Although the mechanism of the association of albuminuria with cardiac events is not clear, it is possible that the vascular changes leading to renal dysfunction may also be present in the vasculature of the heart and thus contribute to cardiac dysfunction [5,20]. In diabetic hearts, morphological changes of small vessels characterized by microangiopathy vessel disease were seen in several animal and autopsy studies [21-23].

Table 5
Independent determinants of parameters of systolic and diastolic function

Dependent variable	Independent variables	Standardized β coefficients	P*
Peak strain	24-h urine albumin	−.32	.042
(R = 0.57)	Age	.14	.312
	DM duration	−.35	.039
	LV mass index	−.07	.607
Peak systolic	24-h urine albumin	−.30	.045
SR (R = 0.62)	Age	.02	.883
	DM duration	−.29	.066
	LV mass index	−.31	.026
Peak diastolic	24-h urine albumin	−.33	.042
SR (R = 0.55)	Age	.22	.133
	DM duration	−.17	.316
	LV mass index	−.31	.031

DM indicates diabetes mellitus.
* $P < .05$ is considered significant.

Our study provides important findings, identifying association of albuminuria with myocardial systolic and diastolic dysfunction in diabetic patients without overt heart disease.

Hypertension and LV hypertrophy frequently coexist with diabetes. In previous studies, the association of albuminuria with myocardial dysfunction has been described [24-26]; but in these previous studies, the patients with LV hypertrophy were not excluded. It is unclear whether myocardial dysfunction is due to LV hypertrophy secondary to combined hypertension or microangiopathy secondary to diabetes itself. In our study, all subjects were hypertensive diabetic patients; but we excluded patients with LV hypertrophy on echocardiography. Therefore, we could precisely examine the association of microangiopathy with myocardial dysfunction.

Tissue Doppler imaging of the mitral annulus is potentially a simple and reliable method of assessment of overall longitudinal LV systolic function [27]. Strain rate imaging is a newly developed echocardiographic modality based on TDI that allows quantitative assessment of regional myocardial wall motion. *Strain rate* is defined as the difference of tissue velocities between 2 distinct points [9,28]. Several studies have suggested that strain and SR are good indicators for evaluation of regional LV systolic and diastolic function [10,28-30]. Our study revealed that SRI data were significantly correlated with the albuminuria status but TDI data were not. These results show that subclinical myocardial dysfunction can be detected by SRI more sensitively than by TDI. It may be due to regional myocardial dysfunction preceding global myocardial dysfunction.

Our study provides the first data on LV systolic and diastolic function in diabetic patients without overt heart disease including LV hypertrophy by using Doppler strain and SRI.

4.1. Study limitations

All patients included in this study were diagnosed with hypertension. Although many subjects were on medication, the influence of antihypertensive drugs cannot account for our results. We only excluded the subjects on medication with angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker because they could influence the albuminuria status.

Because coronary angiography was not performed, the possibility of coronary artery disease cannot be completely excluded. However, we attempted to rule out ischemia by performing noninvasive tests, such as treadmill exercise ECG and sestamibi scanning.

5. Conclusions

In diabetes patients without overt heart disease, albuminuria is associated with myocardial dysfunction assessed by strain and SRI. Unlike conventional 2D and Doppler parameters, strain and SRI detected subclinical LV systolic and diastolic dysfunction in diabetic patients.

References

[1] Grundy SM, Benjamin IJ, Burke GL. Diabetes and cardiovascular disease: a statement for healthcare professionals from the American Heart Association. Circulation 1999;100:1134-46.
[2] Fang ZY, Prins JB, Marwick TH. Diabetic cardiomyopathy. Endocr Rev 2004;25:543-67.
[3] Mattock MB, Morrish NJ, Viberti G, Keen H, Fitzgerald AP, Jackson G. Prospective study of microalbuminuria as predictor of mortality in NIDDM. Diabetes 1992;42:736-41.
[4] Morgensen CE. Microalbuminuria predicts clinical proteinuria and early mortality in maturity-onset diabetes. N Engl J Med 1984;310:356-60.
[5] Deckert T, Feldt-Rasmussen B, Borch-Johnsen K, Jensen T, Kofoed-Enevoldsen A. Albuminuria reflects widespread vascular damage. The Steno hypothesis. Diabetologia 1989;32:219-26.
[6] Sahn DJ, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978;58:1072-83.
[7] Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, et al. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. Am J Cardiol 1986;57:450-8.
[8] Levy D, Savage DD, Garrison RJ. Echocardiographic criteria for left ventricular hypertrophy: the Framingham Heart Study. Am J Cardiol 1987;59:956-60.
[9] Pislaru C, Abraham TP, Belohlavek M. Strain and strain rate echocardiography. Curr Opin Cardiol 2002;17:443-54.
[10] Greenberg NL, Firstenberg MS, Castro PL. Doppler-derived myocardial systolic strain rate is a strong index of left ventricular contractility. Circulation 2002;105:99-105.
[11] Azevedo CF, Amado LC, Kraitchman DL, Gerber BL, Osman NF, Rochitte CE, et al. Persistent diastolic dysfunction despite complete systolic functional recovery after reperfused acute myocardial infarction demonstrated by tagged magnetic resonance imaging. Eur Heart J 2004;25:1419-27.
[12] Kannel WB, Hjortland M, Castelli WP. Role of diabetes in congestive heart failure: the Framingham study. Am J Cardiol 1974;34:29-34.
[13] Zarich SW, Arbuckle BE, Cohen LR, Roberts M, Nesto RW. Diastolic abnormalities in young asymptomatic diabetic patients assessed by pulsed Doppler echocardiography. J Am Coll Cardiol 1988;12:114-20.
[14] Joffe II, Travers KE, Perreault-Micale CL, Hampton T, Katz SE, Morgan JP, et al. Abnormal cardiac function in the streptozocin-induced non–insulin-dependent diabetic rat: noninvasive assessment with Doppler echocardiography and contribution of the nitric oxide pathway. J Am Coll Cardiol 1999;34:2111-9.
[15] Dent CL, Bowman AW, Scott MJ, Allen JS, Lisauskas JB, Janif M, et al. Echocardiographic characterization of fundamental mechanisms of abnormal diastolic filling in diabetic rats with a parameterized diastolic filling formalism. J Am Soc Echo 2001;14:1166-72.
[16] Poirier P, Bogaty P, Garneau C, Marois L, Dumesnil JG. Diastolic dysfunction in normotensive men with well-controlled type 2 diabetes: importance of maneuvers in echocardiographic screening for preclinical diabetic cardiomyopathy. Diabetes care 2001;23:5-10.
[17] Fang ZY, Najos-Valencia O, Leano R, Marwick TH. Patients with early diabetic heart disease demonstrate a normal myocardial response to dobutamine. J Am Coll Cardiol 2003;42:446-53.
[18] Fang ZY, Yuda S, Anderson V, Short L, Case C, Marwick TH. Echocardiographic detection on early diabetic myocardial disease. J Am Coll Cardiol 2003;41:611-7.
[19] Di Bello V, Talarico L, Picano E, Di Muro C, Landini L, Paterni M, et al. Increased echodensity of myocardial wall in the diabetic heart: an ultrasound tissue characterization study. J Am Coll Cardiol 1995;25:1408-15.
[20] Van Hoeven KV, Factor SM. A comparison of the pathological spectrum of hypertensive, diabetic, and hypertensive-diabetic heart disease. Circulation 1990;82:848-55.
[21] Kawaguchi M, Techigawara M, Ishihata T, Asakura T, Saito F, Maehara K, et al. A comparison of ultrastructural changes on endomyocardial biopsy specimens obtained from patients with diabetes mellitus with and without hypertension. Heart and vessels 1997;12:267-74.
[22] Factor SM, Minase T, Cho S, Fein F, Capasso JM, Sonnenblick EH. Coronary microvascular abnormalities in the hypertensive-diabetic rat. A primary cause of cardiomyopathy? Am J Pathol 1984;118:9-20.
[23] Fischer VW, Barner HB, Leskiw ML. Capillary basal laminar thickness in diabetic human myocardium. Diabetes 1979;28:713-9.
[24] Liu JE, Robbins DC, Palmieri V, Bella JN, Roman MJ, Fabsitz R, et al. Association of albuminuria with systolic and diastolic left ventricular dysfunction in type 2 diabetes: the Strong Heart Study. J Am Coll Cardiol 2003;41:2022-8.
[25] Salmasi AM, Jepson E, Grenfell A, Kirollos C, Dancy M. The degree of albuminuria is related to left ventricular hypertrophy in hypertensive diabetic and is associated with abnormal left ventricular filling: a pilot study. Angiology 2003;54:671-8.
[26] Picca M, Agozzino F, Pelosi G. Influence of microalbuminuria on left ventricular geometry and function in hypertensive patients with type 2 diabetes mellitus. Ital Heart J 2003;4:48-52.
[27] Sanderson JE, Wang M, Yu CM. Tissue Doppler imaging for predicting outcome in patients with cardiovascular disease. Curr Opin Cardiol 2004;119:458-63.
[28] Urheim S, Edvardsen T, Torp H, Angelsen B, Smiseth OA. Myocardial strain by Doppler echocardiography. Validation of a new method to quantify regional myocardial function. Circulation 2000;102:1158-64.
[29] Heimdal A, Stoylen A, Torp H, Skjaerpe T. Real-time strain rate imaging of the left ventricle by ultrasound. J Am Soc Echo 1998;11:1013-9.
[30] Hashimoto I, Li X, Bhat AH, Jones M, Zetts A, Sahn DJ. Myocardial strain rate is a superior method for evaluation of left ventricular subendocardial function compared with tissue Doppler imaging. J Am Coll Cardiol 2003;42:1574-83.