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ORIGINAL ARTICLE

Early Diagnosis Of Right Ventricular Dysfunction In Type 2 Diabetes Mellitus:Value Of 3 Dimensional Strain/Strain Rate

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Background right ventricular dysfunction is relevant in a variety of disease states affecting both the course and prognosis of diabetes mellitus and therefore assessment of right ventricular performance is also an important issue in diabetic patients.

Aim to diagnose early right ventricular systolic and diasolic dysfunction in type 2 diabetics by 3D and strain/strain rate imaging.

Methods Groups studied consisted of 30 patients with type 2 diabetes only, no coexisting hypertension (DM; aged 56.6±12.4years). In all patients with diabetes, coronary artery disease and pulmonary hypertension were excluded. Thirty healthy age-matched persons served as control subjects. In each patient an 3D echocardiographic study with strain/strain rate imaging was performed. Analysis of RV deformation data included assessment of systolic strain, peak systolic strain rate and peak early diastolic strain rate obtained from the basal and apical segments of the RV free wall.

Results Deterioration of right ventricular diastolic function was shown in type 2 diabetic group, which was indicated by TDI parameters (Significantly lower values of Em and Em-to-Am ratio in the basal and apical segments) and by significantly longer right ventricular IRT estimated from conventional Doppler.
Systolic strain, peak systolic strain rate and early diastolic SR of basal (−12±3% vs −24±5%, -1.28±0.3/s vs −1.9±0.4/s; 5.4±1.4 vs 8.6±1.7 respectively) and apical (−16±3% vs −26±4%, -1.2±0.3/s vs −2.1±0.3/s, 5.7±1.5 vs 8.4±1.8 respectively) segments of right ventricle were significantly lower in patients with type 2 diabetes than in controls.

Conclusions type 2 diabetis mellitus is commonly associated with right ventricular systolic and diastolic dysfunction which should be screened in each diabetic patient.

Keywords Right ventricle, Diabetes mellitus, 3 dimensional.
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INTRODUCTION

The pathogenesis of diabetic cardiomyopathy is likely to be multifactorial, including microvascular disease, altered myocardial metabolism and structural changes in myocardium with increased fibrosis. Increasingly, evidence is emerging on the role of myocardial lipotoxic injury from lipid oversupply, visceral adipose tissue insulin resistance leads to increased myocardial fatty acids delivery and uptake with associated myocardial triglyceride accumulation (1).

It has been assumed that the subsequent accumulation of fatty acids intermediates is associated with mitochondrial dysfunction, leading to cell damage, apoptosis replacement with fibrosis and myocardial contractile dysfunction. Recent studies have evaluated the relation between increased myocardial steatosis and LV dysfunction in patients with type 2 diabetes mellitus (2, 3). While left ventricular dysfunction has been recognized to be a common complication of diabetes mellitus, data regarding right ventricular (RV) performance in patients with diabetes are incomplete (4).

In the past decade, numerous studies have been published addressing the feasibility and potential clinical applicability of tissue Doppler imaging (TDI) and its derived parameters strain and strain rate (SR). The data reported in these studies strongly support that the different

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Abbreviations and Acronyms

RV	: Right ventricle
DM	: Diabetes mellitus
3D	: Three dimensional

methods are attractive in regards to their underlying theory as well as for the information revealed about cardiac function, that can be obtained by analyzing the motion of the diverse structural components of the heart (Myocardial walls, valvular rings); at the same time all these methods strive to eliminate everything subjective in the assessment of an echocardiogram. Thus, a large volume of scientific evidence has been produced in favor of clinical use of these methods and various parameters have been proposed with the ambitious goal to contribute towards additional diagnostic value with respect to various pathologies (5).

AIM

To diagnose early right ventricular systolic and diasolic dysfunction in type 2 diabetics by 3D and strain/strain rate imaging.

PATIENTS AND METHODS

The study group encompassed 30 asymptomatic type 2 diabetic, normotensive patients (DM group) aged 56.6±12.4 years and control group included 30 healthy volunteers. Coronary artery disease was excluded in diabetic group according to negative dobutamine stress echocardiography, treadmill exercise electrocardiographic test. Other exclusion criteria included valvular or congenital heart disease, decreased left ventricular ejection fraction endocrine and systemic diseases other than diabetes, absence of stable sinus rhythm, conduction or rhythm disturbances, pulmonary diseases ,pulmonary hypertension and tricuspid insufficiency exceeding 1/4. Clinical and demographic data are shown in (Table 1).

Each patient participating in the study underwent echocardiographic examination using GE Vivid 7 equipment with a 2.5-MHz multifrequency transducer. The evaluation included measurements of left and right ventricular dimensions, left ventricular ejection fraction by modified Simpson's biplane method, tricuspid plane systolic excursion, reflecting the global right ventricular systolic function (6), right ventricular conventional Doppler parameters of diastolic function (Peak early and peak late diastolic flow velocity and isovolumic relaxation time [IRT]); and TDI to assess right ventricular longitudinal myocardial function in the basal and apical segments.

TDI was performed in the apical four chamber view. Color TDI was superimposed on three-dimensional images, with the depth of imaging and the sector angle adjusted to obtain a color Doppler frame scanning rate 140 Hz. Myocardial regional velocity curves were reconstituted from digitized images and analyzed offline. The following TDI variables were evaluated (7): peak systolic velocity (Sm), peak early diastolic velocity (Em), peak late diastolic velocity (Am), and regional IRT (IRT).

The strain (Change in length per unit length) in each segment was defined as the relative magnitude of segmental deformation. From tissue Doppler data, strain rate (SR; velocity of segmental deformation) can be estimated by calculating the velocity gradient. the velocity gradient was estimated between two points with a distance of 12 mm. This spatial offset was selected as a compromise between acceptable signal-to-noise ratio and longitudinal spatial resolution. SR was determined during systole (S), early diastole (E). Systolic Strain was measured from the same wall site in the same views. To minimize the effect of respiration on variability, all calculations were performed using the mean of six or seven clearly observed consecutive beats.

Statistical Analysis

Are expressed as means±SD and percentages. Student's two-tailed t-test, ANOVA, and Pearson rank correlation test were used where appropriate .P values of <0.05 were considered statistically significant.

RESULTS

No statistically significant differences were found among two groups regarding age, sex, BMI, and plasma creatinine (Table 1). All of the groups investigated did not differ in right ventricular systolic function as expressed by tricuspid plane systolic excursion and Sm in the basal and apical-segments of the right ventricle. Deterioration of right ventricular diastolic function was shown in type 2 diabetic group, which was indicated by TDI parameters (Significantly lower values of Em and Em-to-Am ratio in the basal and apical segments) and by longer right ventricular IRT estimated from conventional Doppler (Table 2).

Systolic strain, peak systolic strain rate and early diastolic SR of basal (−12±3% vs−24±5%, -1.28±0.3/s vs −1.9±0.4/s; 5.4±1.4 vs 8.6±1.7 respectively) and apical (−16±3% vs −26±4%, -1.2±0.3/s vs −2.1±0.3/s, 5.7±1.5 vs 8.4±1.8 respectively) segments of right ventricle were significantly lower in patients with type 2 diabetes than in control (Table 3).

Table 1: Demographic characteristics of studied groups:

	Diabetic Group	Control group	P Value
Number	30	30	
Age	56.6±12.4	57.2±10.8	p >0.05
Male sex	17	16	p >0.05
Duration of diabetes	12±5	-----------	
Type of diabetes	Type 2	-----------	
Systolic Bl pressure	129±11	127±13	p >0.05
Diastolic Bl pressure	76±8	75±7	p >0.05
BMI (kg/m2)	30.4±3.1	29.1±3.2	p >0.05
Fasting plasma glucose (mmoml/l)	7.9±2.1	4.5±0.4	P <0.05*
HbA1c (%)	7.4±1.3	-----------	
Creatinine	0.8±0.5	0.9±0.4	p >0.05
Diabetic retinopathy	8	-----------	
Periphreal vascular disease	4	-----------	
Microalbuminurea /proteinurea	5	-----------	
Insulin	12	-----------	
Metformin	4	-----------	
Sulphonylurea	14	-----------	

P <0.05= significant, p >0.05= non significant

Table 2: Echocardiographic and TDI data of studied groups:

	Diabetic Group	Control group	P Value
LVEF%	64.3±6.5	64.4±5.9	p >0.05
Right ventricular end diastolic dimension (mm)	21.4±2.9	18.9±2.7	p >0.05
TPSE (mm)	18.6±3.0	18.9±2.7	p >0.05
Right ventricular Eto A ratio	1.18±0.21	1.17±0.18	p >0.05
Right ventricular IRT (ms)	53.3±16.3	42.0±15.4	P <0.05*
Right ventricular basal segment Sm.(cm/s)	11.9±1.1	12.1±1.5	p >0.05
Right ventricular basal segment Em (cm/s)	7.2±1.8	10.4±1.8	P <0.05*
Right ventricle basal segment Em to Am ratio	0.60±0.20	0.89±0.20	P <0.05*
Right ventricle basal segment IRTm (ms)	39.5±12.9	36.9±12.8	p >0.05
Right ventricle apical Sm (cm/s)	9.7±1.7	9.6±1.6	p >0.05
Right ventricle apical Em (cm/s)	7.7±1.3	9.1±1.9	P <0.05*
Right ventricle apical Em to Am ratio	0.85±0.22	0.97±0.18	P <0.05*
Right ventricle apical IRT (ms)	51.7±14.3	41.9±9.8	P <0.05*

P <0.05= significant, p >0.05= non significant, IRT= isovolumic relaxation time, TSPE= tricuspid plane systolic excursion.

Table 3: RV free wall basal & apical systolic strain, peak systolic strain rate & early diastolic strain rate:

RV BASAL	Diabetic Group	Control group	P Value
Systolic strain	-12±3	-24±5	P <0.05*
Peak systolic strain rate	-1.28±0.3/s	-1.9±0.4/s	P <0.05*
Early diastolic strain rate	5.4±1.4	8.6±1.7	P <0.05*
RV FW apical			
Systolic strain	-16±3	-26±4	P <0.05*
Peak systolic strain rate	-1.2±0.3	-2.1±0.3	P <0.05*
Early diastolic strain rate	5.7±1.5	8.4±1.8	P <0.05*

RV= right ventricle, RVFW= right ventricle free wall, P <0.05= significant .

DISCUSSION

Diabetes is thoroughly evidenced to increase the risk of development of heart failure even in the absence of frequently coexisting comorbidities such as coronary artery disease and hypertension (8). Cardiac adverse effects influenced by diabetes have been demonstrated thus far for the left ventricle, particularly systolic and diastolic dysfunction identified at rest and/or during exercise (9, 10). To date, no information is available regarding the possible involvement of the right ventricle in the pathological process evoked by diabetes. In clinical practice, right ventricular dysfunction is relevant in a variety of disease states affecting both the course and prognosis (11–15), and therefore one may assume that right ventricular performance is also an important issue in diabetic patients (16).

The main clinical findings of the present study are that in diabetic patients without clinically evident heart disease, not only left ventricular but also right ventricular function is impaired and the deterioration of right ventricular performance implicates diastolic & systolic abnormalities. Impairment in right ventricular diastolic function was evidenced mainly by TDI-derived indexes (Decreased Em and Em-to-Am ratio in both the basal and apical -segments of the right ventricular free wall) and by only one conventional Doppler parameter, right ventricular IRT. Significantly lower values of systolic strain and SRs in the basal and apical segment of the RV free wall in the DM group as compared with controls indicated impairment of RV systolic function. Similarly, decreased SRe in patients with diabetes in both RV segments examined reflected abnormalities of RV diastolic performance.

Ng ACT, et al. studied left Ventricular strain and strain rate imaging in asymptomatic patients With type 2 diabetes mellitus, their study included one hundred male subjects (47 with and 53 without DM). Exclusion criteria for DM patients included HbA1c >8.5%, known cardiovascular disease or DM related complications, blood pressure >150/85 mmHg. Myocardial ischemia was excluded by a negative dobutamine stress test. Healthy controls were matched for age, body mass index and body surface area. Their results showed that there were no differences in LV end-diastolic volume index (41±9 vs 44±8 mL/m2, p= ns), end-systolic volume index (16±5 vs 18±4 mL/m2, p= ns) and ejection fractions (61±6 vs 60±5%, p= ns). Transmitral E/A (0.95±0.21 vs 1.12±0.32, p= 0.007) and pulmonary S/D ratios (1.45±0.28 vs 1.25±0.27, p= 0.001) were more impaired in diabetics. Diabetic patients had impaired longitudinal but preserved circumferential and radial functions. Presence of DM was an independent predictor for longitudinal strain, systolic SR and early diastolic SR on multiple linear regressions (All p <0.001). So they concluded that LV longitudinal systolic and diastolic functions were impaired but circumferential and radial functions were preserved in uncomplicated type 2 diabetic patients (1).

In agreement with the present study, Kosmala, et al. evaluated right ventricular dysfunction in diabetes mellitus by 2D strain/strain rate imaging, Groups studied consisted of 33 subjects with diabetes only and 40 subjects with coexisting diabetes and hypertension. In all patients with diabetes, coronary artery disease and pulmonary hypertension were excluded. Thirty-six healthy age-matched persons served as control subjects. In each patient an echocardiographic study with strain/strain rate imaging was performed. Analysis of RV deformation data included assessment of systolic strain, peak systolic strain rate (SRs) and peak early diastolic strain rate (SRe) obtained from the basal and apical segments of the RV free wall. Their results showed that, lower values of systolic strain and SRs in the basal and apical segment of the RV free wall in the DM and DMHT groups as compared with control subjects indicated impairment of RV systolic function and decreased SRe in patients with diabetes in both RV segments examined reflected abnormalities of RV diastolic performance. All measured parameters were similar in the two groups with diabetes. They concluded that diabetes mellitus is associated with right ventricular systolic & diastolic dysfunction (4).

Moreover. Karamitsos, et al. previously studied right ventricle diastolic impairment in diabetic patients, 66 type 1 diabetic patients and 66 age and sex-matched normal subjects evaluated by conventional and tissue Doppler echocardiography. A possible correlation was examined for age, diabetes duration, echocardiographic measurements of left ventricular and right ventricular functions with univariate analysis. Diabetic patients were found to have impaired diastolic function in both ventricles with either conventional or tissue Doppler echocardiography. Systolic function in both ventricles was preserved in diabetic population. The measured indexes showed a correlation with age and diabetes duration except from systolic velocity in tricuspid annulus determined by color tissue Doppler. Significant correlations were found among parameters of left and right ventricular function. So they suggested that Patients with type 1 diabetes mellitus have impaired diastolic function, and particularly relaxation, in both ventricles before the development of myocardial systolic dysfunction and these alterations in myocardial function may be attributed to ventricular interdependence as well as to the uniform effect of diabetes to cardiac function (17).

CONCLUSION AND RECOMMENDATIONS

Type 2 diabetes mellitus is a commonly associated with right ventricular systolic and diastolic dysfunction and every diabetic patient should be screened for right venticular function (Systolic and diastolic).

Strain and strain rate are new, sensitive noninvasive tissue Doppler diagnostic modalities for right ventricular systolic and diastolic function evaluation.

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