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Left Ventricular Changes in Patients with Type 2 Diabetes

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Abstract: ***Heart failure is a common and serious co-morbidity of diabetes mellitus (DM). Data from clinical studies confirm the association of DM with left ventricular (LV) dysfunction independent of hypertension, coronary atheromatosis, or any other known heart disease. The aim of this study was to investigate the impact of DM without HTA or CAD on LV phenotype, its systolic and diastolic function. One hundred patients with type 2 DM presenting the Endocrinology Department at Regional Hospital, Durres, Albania, from 2010 to 2013 and one hundred age and gender-matched non-diabetic controls, as evidenced by a normal oral glucose tolerance test were included in the study. .Age and gender, and smoking status were comparable in the two groups. However, several significant differences were noticed. The diabetic patients when compared with the controls had significantly higher BMI, heart rate, arterial pressure, and hyperlipidaemia. Also conventional and tissue Doppler parameters were significantly higher among diabetic patients.***

Keywords: diabetic cardiomyopathy, left ventricular hypertrophy, dysfunction

1. Introduction

The prevalence of heart failure among diabetic patients was as high as 19% to 26% in various clinical trials (1,2). These two disease entities tend to coexist, and the impact of each condition on the other has bidirectional influences in terms of causation and outcome (93). The Framingham Heart Study reported that 19% of patients with heart failure have type 2 diabetes mellitus (T2DM) and that the risk of heart failure increases 2- to 8-fold in the presence of T2DM (4). Furthermore, an increase of 1% in hemoglobin A1c (HbA1c) levels is related to an 8% increase in the risk of heart failure, independently of age, body mass index, blood pressure, and the presence of CAD. This suggests that the risk of heart failure is controlled by factors unique to T2DM, such as hyperglycemia and insulin resistance (5). Conversely, a 1% reduction in HbA1c levels is related to a 16% reduced risk of developing heart failure and poor outcomes (6). This bidirectional interaction has provided evidence to support the existence of DCM as a distinct clinical condition, and suggests that the presence of diabetes mellitus might independently increase the risk of heart failure (7). The prevalence of DCM is not yet clear because of a lack of large study outcomes from different populations with diabetes mellitus. The prevalence of diastolic dysfunction in patients with T2DM was up to 30% in some studies (8). However, there are other studies that reported a prevalence rate as high as 40% to 60% (9). A recent major prospective study examining the prevalence of heart failure and MD in patients with chronic (≥ 10 years) type 1 diabetes mellitus (T1DM) showed a prevalence of 3.7% and 14.5%, respectively, at the end of a 7-year follow-up (10). The annual incidence of heart failure and MD were 0.02% and 0.1%, respectively. Diastolic heart failure accounted for 85% of the cases of heart failure (11).

Pathophysiological Mechanisms Of Diabetic Cardiomyopathy: The pathophysiological mechanisms of DCM have not yet been sufficiently elucidated. The occurrence of DCM is multifactorial, and there are various proposed mechanisms including insulin resistance, microvascular impairment, subcellular component abnormalities, metabolic disturbances, cardiac autonomic dysfunction, alterations in the renin-angiotensin-aldosterone system (RAAS), and maladaptive immune responses (12).

A long-standing hypothesis is that hyperglycemia plays a pivotal role in the development of DCM, although multiple complex mechanisms and the interplay of many metabolic and molecular events within the myocardium and plasma contribute to its pathogenesis. The main metabolic abnormalities in diabetes mellitus are hyperglycemia, inflammation, and hyperlipidemia, all of which induce the production of the nitrogen species or reactive oxygen species (ROS) that cause most diabetic complications, including DCM and diabetic nephropathy. The aim of this study was to investigate the impact of DM without HTA or CAD on LV phenotype, its systolic and diastolic function.

2. Material and Methods

One hundred patients with type 2 DM presenting the Endocrinology Department at Regional Hospital, Durres, Albania, from 2010 to 2013 and one hundred age and gender-matched non-diabetic controls, as evidenced by a normal oral glucose tolerance test were included in the study. Participants were stratified into three distinct age-groups: <46 yr, 46–60yr and >60 years and underwent full biochemical and echocardiographic examination. Definitions and laboratory tests: The diagnosis of DM was established by WHO criteria (13). Hypercholesterolaemia and hypertriglyceridaemia were defined as the use of either cholesterol or triglyceride-lowering therapy or total cholesterol levels of .200 mg/dL or triglycerides levels of 150 mg/dL. Total cholesterol, triglycerides, HDL-cholesterol, creatinine, and glycated haemoglobin (HbA1C) were estimated in all subjects within 1 week of the echocardiographic study. All patints and controls underwent conventional and tissue Doppler ecographic examination.

Statistical analysis

Continuous data are expressed as mean+SD. Inter-group comparisons for continuous variables were performed with the use of ANOVA, Student's unpaired t-test and Wilcoxon

rank-sum test as appropriate. Categorical variables were compared by x2 test or Fisher's exact test as appropriate. Univariate correlations using Pearson's correlation coefficient (r) were performed to assess potential relations between various clinical variables. Stepwise linear regression analysis was performed using all variables of potential significance identified in the univariate correlation test. A two tailed P-value of ,0.05 was used for entering variables of potential significance into the model.

3. Results and Discussion

The main clinical parameters of the study population are shown in Table 1. Age and gender, and smoking status were comparable in the two groups.

However, several significant differences were noticed. The diabetic patients when compared with the controls had significantly higher BMI, heart rate, arterial pressure, and hyperlipidaemia. Also, possibly due to specific indications in diabetic state, diabetic patients received more frequently inhibitors of the renin–angiotensin system, with a trend towards higher statin and lower b-blocker therapy. Data derived from conventional echocardiography revealed several differences between groups (table 2). Left ventricular mass-index, left atrial volume and other parameters were significantly higher in the DM group and within each age-group.

It was shown that diabetic patients have in general increased LV mass with impaired performance and systolic longitudinal myocardial dysfunction. The association of diastolic dysfunction with either DM or hypertension in adults has been well known and reported previously. In one study, DM and hypertension were found to exert independent and similar adverse impact on LV diastolic function. In addition, the coexistence of hypertension and DM showed the more severely abnormal LV filling. However, it has to be stated that variations in the severity of the diabetic and hypertension state influence the results of relevant studies.

The surprising finding of the comparable diastolic function in the two groups, as evidenced by conventional Doppler, is not unique in literature. Several previous studies reported contrasting data regarding the assessment of diastolic function in diabetic and non-diabetic subjects mainly due to the lack of uniformity in the selection criteria in terms of prevalence and severity of hypertension in the groups under evaluation (14–16) One of the main findings of this study is the observation that in the early course of cardiac disease systolic dysfunction starts to develop earlier in diabetic vs. non-diabetic individuals. Although it is generally believed that diastolic dysfunction may occur solely and earlier than systolic dysfunction, our results illustrated that systolic abnormalities probably coexist in diabetic patients. This interesting finding could be attributed to a diabetes-specific myocardial disease resulting in an increased susceptibility of DM patients to develop myocardial dysfunction. Previous studies demonstrated that long-axis LV dysfunction is established in the earliest stages of diabetic cardiomyopathy (17–20). However, some studies did not detect any impairment in LV systolic function at rest in diabetic patients with either conventional echocardiography. Our study demonstrate using new Doppler techniques the earlier induction of systolic dysfunction in type 2 asymptomatic diabetic subjects when compared with age- and sex-matched non-diabetic controls. Furthermore, based on our data, systolic and diastolic dysfunction probably coexist in diabetic subjects, whereas the underlying mechanism is doubtless multifactorial and is generally augmented by the presence of hypertension and glycaemic control. The impact of DM on LV mass has been extensively investigated. Santra et al. in 135 normotensive individuals, half with DM and half healthy, reported higher LV mass in DM patients compared to controls (21). In the Framingham Heart Study, increased LV mass and wall thickness was independently associated with DM, although in multivariable analysis, significance was reached only in females (22). In the Cardiovascular Health Study, both in male and females, increased LV mass was independently linked with DM after adjustment for body weight, blood pressure, heart rate and coronary disease (23). Similar data came from even larger trail, The Strong Heart Study (24). Our results are in concordance with the results showing concentric remodeling and LV hypertrophy associated with DM, independently from age, obesity, HTA and CAD. Although none of our patients with lone DM (i.e. without HTA and CAD) had LV hypertrophy (i.e. LV mass index above reference points), LV mass and LV mass index were increased compared to matched control. Increased LV mass is negative prognostic marker, an independent risk factor for sudden death and ventricular arrhythmias and might contribute to increased cardiovascular risk among DM patients. Left atrial size is often referred to as HbA1c of diastolic dysfunction and LV filling pressure. Our results support the observation of Atas et al. who found among normotensive DM patients without symptomatic cardiovascular disease higher volume, impaired compliance and contractility of the left atrium, even when LV geometry and LV systolic function were within normal limits (25).

4. Conclusion

Patients with type 2 diabetes demonstrate early induction of systolic and diastolic dysfunction of the myocardium as a preclinical manifestation of diabetic cardiomyopathy. Through echocardiographic techniques that evaluate the speed of myocardial movement, we can detect myocardial DM damage at an early stage. Diagnosing early heart disease changes helps us to prevent the advancement of diabetic cardiopathy and clinical signs of cardiac failure. Through new echocardiographic techniques, we can detect myocardial injury from DM at an early stage.

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Table 1: Clinical characteristics of patients and controls

Variables	Diabetics	Controls	P
Age (years)	56.4 (±13)	57 (+14)	0.8
Gender			0.9
Female	43 (43.0)	40 (40.0)	
Male	57 (57.0)	60 (60.0)	
Diabetes duration (years)	9.4 (±7)	0	
BMI (kg/m^2)	31(± 4)	28 (±4)	<0.001
P. Systolic (mmHg)	144 (±19)	138 (±20)	0.03
P. Diastolic (mmHg)	87 (±11)	83 (±13)	0.002
Mean arterial pa (mmHg)	106 (±13)	101(±15)	0.004
Heart rate (bpm)	77 (±11)	74(±9)	0.01
Smoking	49 (49.0)	34 (34.0)	0.04
Alcohol consumption	28 (28.0)	19 (19.0)	0.03
Insulin use	35 (35.0)	0	
Statin	30 (30.0)	19 (19.0)	0.05
Total cholesterol (mg/dL)	218 (±50)	208 (±52)	0.1
LDL-cholesterol (mg/dL)	137 (±43)	129 (±47)	0.8
HDL-cholesterol (mg/dL)	41 (±11)	46 (±8)	0.3
Triglycerides (mg/dL)	205 (±195)	128 (±58)	<0.001
Creatinine (mg/dL)	0.96 (±0.18)	0.87 (±0.12)	<0.001
Fibrinogen	465.1 (±50.1	443.2 (±62.3)	<0.01
Fasting glucose	151.2 ± (9.7)	99.5 (±10.4)	<0.01
Uricemia	17.7 (±4.2)	15.3 (±3.6)	<0.01
PCR	10.1 (2±.22)	7.45 (±1.61)	<0.01

HbA1C (%)	8.9 (±1.6)	4.6 (±0.4)	<0.001
TSH	2.16 (±0.79)	1.67 (±0.84)	<0.01

Table 2: Conventional echographic data

Echographic Parameters	Diabetes	Controls	
	M (SD)	MSD	P
LV & LA geometry and mass			
VM-DTD (mm)	52.06 (2.30)	49.30 (1.68)	0.03
VM-TD (ml)	121.68 (12.6)	100.20 (6.24)	<0.01
VM-TSp (mm)	11.2 (1.72)	9.37 (1.97)	<0.01
VM-TMP (mm).	10.62 (4.77)	8.30 (1.23)	<0.01
VM-DTS (mm)	35.19 (2.95)	26.70 (3.83)	<0.01
VMvolTS (ml)	42.97 (9.63)	34.38 (5.03)	<0.01
Volumi i AM (ml)	29.57 (1.59)	23.76 (1.15)	<0.01
LV systolic function			
MVM I (g/m^2)	267.19 (54.59)	169.08 (23.09)	<0.01
FE (%)	56.35 (3.25)	61.68 (2.44)	<0.01
FS (%)	29.6 (3.4)	32 (3.7)	<0.01