Left Ventricular Function in Nigerians With Type 2 Diabetes Mellitus With and Without Hypertension

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Abstract

Background. Diabetes mellitus is an established risk factor for cardiovascular events and has been found to be independently associated with abnormal left ventricular function. We therefore decided to embark on this study to assess the left ventricular function in our diabetic patients.

Method. The study design was cross-sectional and conducted among patients attending out patient clinic of the Obafemi Awolowo University Teaching Hospitals complex (OAUTHC) Ile Ife, Osun State south western Nigeria. It comprised 75 consecutive patients with type 2 diabetes mellitus with or without hypertension and 50 apparently healthy age- and sex- comparable controls. Using a structured pre-evaluated questionnaire, the demographic and clinical data were obtained. All subjects had two-dimensional (2D) M-mode, and Doppler echocardiography using Sonoline G60s Ultrasound imaging system with 4.2 MHZ transducer equipped with simultaneous ECG tracing.

Results. A total of 125 consecutive subjects were recruited comprising 75 patients with type 2 diabetes mellitus with or without hypertension and 50 apparently healthy age-and-sex comparable controls. There were no significant difference in left ventricular ejection fraction and fractional shortening between the patients and controls. The ratio of early trans-mitral flow to late atrial filling of the left ventricle (E/A ratio), isovolumic left ventricular relaxation time, and left ventricular deceleration time were predominantly prolonged among the study patients compared to the controls.

Conclusion. This study showed that left ventricular systolic function was preserved among patients with type 2 diabetes mellitus. The abnormal diastolic function noted was predominantly that of impaired relaxation compared with controls. This is particularly more in hypertensive-diabetics than normotensive-diabetics.

Keywards Diabetes mellitus, Left ventricular function.

Introduction

Diabetes mellitus is an established risk factor for cardiovascular events, [1, 2] and several population studies have shown that diabetes is associated with left ventricular structural and functional abnormalities.[3,4]. Diabetes mellitus is independently associated with abnormal left ventricular relaxation pattern which is more severe in those who are also hypertensive than in patients with either disease alone (hypertension or diabetes mellitus).[5] Study of left ventricular function in type 2 diabetes patients without cardiac symptoms in Zaria-Nigeria by Danbauchi et`al showed lower a ejection fraction and fractional shortening indicating a reduction in systolic function while diastolic dysfunction of impaired were observed among the study patients compared to the

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controls[6].

It has been documented that impairment of left ventricular function in diabetics is due to concomitant risk factors such as systemic hypertension and/or coronary artery disease[7], autonomic dysfunction, metabolic derangements, and cardiac interstitial fibrosis.[8] Many factors at the cellular level have been implicated, but myopathy, independent of micro-vascular and macro-vascular disease, is proposed to be the final common Pathway.[9,10]

Literatures on diabetic left ventricular function in Nigerian diabetics are few. We therefore decided to embark on this study to assess the left ventricular function in our diabetic patients.

Materials and Methods

The study design was cross-sectional and conducted among patients attending the Out Patient Clinic of the Obafemi Awolowo University Teaching Hospitals complex (OAUTHC) Ile Ife, Osun State south western Nigeria. It comprised 75 consecutive patients with type II diabetes mellitus with and without hypertension, as well as 50 apparently healthy age- and sex- comparable controls including hospital staff and relatives of other patients besides those being studied. Using a structured pre-evaluated questionnaire, the demographic and clinical data, were explored. Diagnosis of diabetes mellitus was made on the basis of the reported history and medical records. People with diabetes mellitus who had chronic kidney disease or congestive cardiac failure and those that did not consent were excluded from the study. Ethical clearance was obtained from the ethics and research Committee of the Obafemi Awolowo University Teaching Hospitals Complex, and all participating subjects signed the informed consent form after being clearly explained to them.

All subjects had two dimensional (2D) M-mode Doppler echocardiography using Sonoline G60s Ultrasound imaging system with 4.2 MHZ transducer equipped with simultaneous ECG tracing. Measurements were based on the American Society of Echocardiography guidelines.[11] A simultaneous ECG tracing was recorded in each patient to determine the diastolic and systolic phases of the cardiac cycle. The following measurements were taken: interventricular septum in diastole (IVSTd); left ventricular internal diameter in diastole (LVIDd); left ventricular posterior wall thickness in diastole (PWTd); interventricular septum in systole (IVSTs); left ventricular internal diameter in systole (LVIDs); left ventricular posterior wall thickness in systole (PWTs); left atrial diameter (LAD). The presence or absence of wall motion abnormalities were also looked for.

The Pulse Wave mode was used to determine flow across the mitral and tricuspid valves while the aortic and pulmonary valves were assessed using Continuous Wave mode. The following measurements were recorded: early transmitral mitral peak flow velocity (E); transmitral flow velocity during atrial systole (A); Mitral E:A ratio (E/A); transmitral flow deceleration time (DCT); isovolumic ventricular relaxation time (IVRT). The Doppler colour flow was used to assess the presence and severity of valvular regurgitation.

Statistical Analysis

Data was presented as mean ± standard deviation (SD). Student t-test was used to determine the significance of differences between mean values of continuous variables. Fisher's exact and chi square tests were used to test for significance of categorical variables where necessary, with statistical significance set at p (probability) value less than 0.05 Tables and figures were used to present data, Statistical Package for Social Sciences version 11.0 (SPSS Chicago Ill. USA) was used for all statistical analysis.

Results

Demographic and clinical characteristics of the study population

A total of 125 consecutive subjects were recruited comprising 75 with type II diabetes mellitus with or without hypertension and 50 apparently healthy age-and-sex comparable controls. Forty-five (60.0%) patients and 31 (62.0%) controls were females with mean ages ± SD of 57.15 ± 9.39 years and 56.64 ± 7.84 years, respectively (p = 0.804). Thirty (40.0%) patients and 19 (38.0%)

controls were male with mean ages of 58.31 ± 10.26 years and 58.31 ± 7.34 years, respectively (p = 0.995). Fifty-two (69.3%) patients were hypertensive-diabetic and 23 (30.7%) were normotensive-diabetic. Thirty-four (65.38%) of the hypertensive-diabetic were females, while the remaining 18 (34.61%) were males. The mean systolic blood pressure of the patients and controls were 144.00 ± 12.19 mmHg and 120.20 ± 9.14 mmHg, respectively (p = 0.0001). While the mean diastolic blood pressures were 87.06 ± 8.01 mmHg and 79.80 ± 8.20 mmHg, respectively (p = 0.0001).

Echocardiographic findings in the study population

There was no significant difference in the mean left ventricular ejection fraction of the patients and controls i.e. 61.04 ± 7.76 % versus 63.40 ± 7.34 % (p = 0.092). Two patients had reduced left ventricular ejection fraction and fractional shortening, while the remaining 73 patients and all the control had normal left ventricular ejection fraction and fractional shortening with no significant difference observed between patients and controls (P = 0.9) Similarly, there was no significant difference in the mean fractional shortening between the patients and controls i.e. 27.29 ± 4.83 and 28.81 ± 4.77 % (p = 0.086). Doppler study across the mitral valve showed that the mean mitral E/A ratio of the patients and controls were 0.86 ± 0.30 and 1.23 ± 0.34, respectively (p = 0.0001). Fifty-seven (76.0%) patients and 16 (32.00%) controls had reversal of mitral E/A ratio (E/A ratio less than 1) (X^2 test, p = 0.0001). Sixteen (21.3%) patients and 34 (68.00%) controls had normal mitral E/A ratio (E/A ratio 1-1.5) (X^2 test, p = 0.0001). Two (2.7%) patient had mitral E/A ratio of greater than 1.5 and none of the controls had mitral E/A ratio greater than 1.5 (Fisher's exact test, p = 0.9).

The mean IVRT of the patients and controls were 102.87 ± 20.06 ms and 85.08 ± 18.94 ms, respectively (p = 0.0001). Fifty-one (68.0%) patients and 13 (26.0%) controls had IVRT greater than 100 ms (X^2 test p = 0.0001). Twenty-two (29.3%) patients and 37 (74.0%) controls had 60-100ms (X^2 test p = 0.0001), Two (2.7%) patient had IVRT of less than 60ms (Fisher's exact test, p = 0.9). The mean DCT of the patients and controls were 203.86 ± 26.69 ms and 186.52 ± 28.74 ms, respectively (p = 0.001). Fifty-three (70.7%) patients and 16 (32.00%) controls had a DCT greater than 200 ms (X^2 test, p = 0.0001). Twenty (26.7%) patients and 34 (68.00%) controls had a DCT between 140-200 ms (X^2 test, p = 0.0001). Two (2.7%) patient had a DCT less than 140 ms (Fishers exact, p = 0.9).

Hypertensive-diabetics had significantly reduced mitral E/A ratio, prolonged IVRT and DCT compared to normotensive-diabetic. The mean mitral E/A ratio of the hypertensive-diabetic and normotensive-diabetic were 0.77 ± 0.26 and 1.06 ± 0.30, respectively (p = 0.0001). While their mean IVRT were 107.29 ± 20.96 ms and 93.08 ± 13.88 ms, respectively, (p = 0.0001). The mean DCT were 211.90 ± 24.62 ms and 186.04 ± 22.44 ms, respectively, (p = 0.0001). Forty six (88.5%) hypertensive-diabetics in this study had reversal of mitral E/A ratio compared to 11(47.8%), in normotensive-diabetic (P = 0.0001) While 43(82.7%) hypertensive diabetics and 9(39.1%) normotensive diabetics had prolonged IVRT (P = 0.0001). Forty five (86.5%) hypertensive diabetics and 8(34.8%) had normotensive diabetics had prolonged DCT (P = 0.0001)

Discussion

In this study, we found that left ventricular systolic function was preserved among patients with type 2 diabetes mellitus although when compared with the healthy controls, diabetics had lower left ventricular systolic function. This is in keeping with the study by Attali *et al*[12] where they found that ejection fraction is less frequently affected in asymptomatic diabetic patients. Similarly, Mustonen *et al*,[13] found no significant differences among patients with insulin dependent diabetes mellitus, non-insulin dependent diabetes mellitus and control subjects regarding resting ejection fraction. Dawson *et al*[14] also reported that left ventricular systolic dysfunction is much less common than diastolic dysfunction in patients with type II diabetes mellitus. However, this is contrary to the study by Danbauchi et`al[6] where they found a significant reduction in ejection fraction and fractional shortening among their

studied subjects

However, there was a significant difference in left ventricular diastolic filling pattern between patients and controls. Transmitral flow velocity ratio (Mitral E/A) was reduced, IVRT and DCT were prolonged in patients compared to the controls. These abnormalities of diastolic filling observed in the study patients are in keeping with impaired relaxation pattern. This finding agrees with that reported by Balogun *et al*, [15] where they found abnormalities of ambulatory blood pressure and diastolic function preceded microalbuminuria in young normotensive insulin dependent diabetic. The findings of Liu *et al*[5] on the association between diabetes mellitus and abnormal left ventricular relaxation is in keeping with our study. Hypertensive-diabetics predominantly had left ventricular diastolic dysfunction of impaired relaxation pattern compared to normotensive-diabetic.

The predominance of left ventricular diastolic dysfunction of impaired relaxation pattern seen in the hypertensive-diabetic may be due to the combined effect of hypertension and diabetes on left ventricular structure. The pathophysiologic mechanism of diastolic dysfunction in diabetic is thought to be due to poor glycemic control as interstitial accumulation of advanced glycated end products (AGES) which include collagen, elastin, and other connective tissue proteins as well as fibrosis in the myocardium have been reported in human diabetic hearts; this is thought to increase end-diastolic stiffness as well as left ventricular mass.[16] The quantitation of fibrosis in hypertensives, diabetics, and hypertensive-diabetics revealed that hypertensive hearts had lowest proportion of fibrosis, hypertensive-diabetics with the highest proportion while normotensive-diabetics in the midrange.[16]

Another factor linking diabetes and abnormal left ventricular relaxation may be the presence of coronary artery disease. Although this may be the aetiology in some cases, in this study almost all the patients had normal myocardial contractility and normal ejection fraction except two. This study did not include exercise ECG and stress echocardiography to evaluate regional wall motion abnormalities, but the absence of regional wall motion abnormalities excludes a significant previous or present myocardial death or infarction but not ischaemia.

Conclusion

This study showed that left ventricular systolic function was found to be preserved among patients with type II diabetes mellitus with abnormal diastolic function predominantly of impaired relaxation pattern. This is particularly more in hypertensive-diabetic than normotensive-diabetics.

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Table 1: Comparison of demographic and clinical characteristics of the study population

Parameters	Patients	Controls	P-Value
Age			
Male	58.31±10.26	58.31±7.34	0.995
Female	57.15±9.39	56.64±7.84	0.804
Sex			
Male	30(40.0%)	19(38.0%)	0.822
Female	45(60.0%)	31(62.0%)	0.822
BMI (kg/m^2)	25.96±5.11	21.86±1.60	0.0001*
Weight (kg)	67.16±14.00	60.16±6.11	0.001*
Waist circumference (cm)			
Male	95.26±7.16	92.84±2.38	0.162
Female	92.51±9.95	81.45±2.73	0.000*
SBP (mmHg)	144.00±12.19	120.20±9.14	0.000*
DBP (mmHg)	87.06±8.01	79.80±8.20	0.000*

* = Significant at $p < 0.05$, DBP = Diastolic Blood Pressure, SBP = Systolic Blood Pressure.

Table 2: M-mode echocardiographic parameters of the study population

Parameters	Patients N=75	Controls N=50	P-value
Ejection fraction (%)	61.04±7.76	63.40±7.34	0.092
Normal	73 (97.3%)	50 (100%)	0.9
Fractional shortening (%)	27.29±4.83	28.81±4.77	0.086
Normal	73 (97.3%)	50 (100.0%)	0.9
Left atrial diameter (cm)	3.81±0.35	3.65±0.31	0.013*
Left atrial diameter (cm)			
Normal	42 (56.0%)	39 (78.0%)	0.010*
Enlarged	33 (44.0%)	11 (22.0%)	0.010*

***** = significant at $p < 0.05$

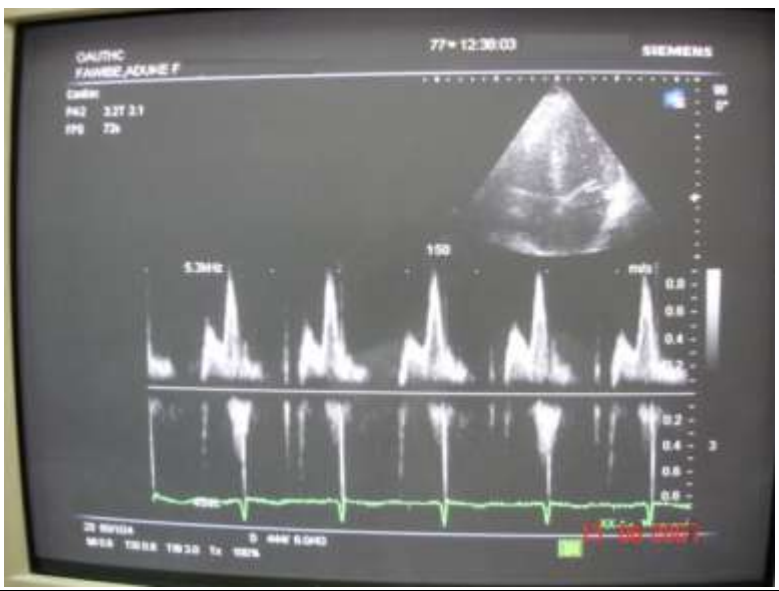

Figure 1 Doppler echocardiography showing reversed transmitral flow velocity in a study patient.

Table 3: Doppler echocardiographic parameters of the study population

Parameters	Patients N=75	Controls N=50	P-value
Mitral E/A ratio	0.86±0.30	1.23±0.34	0.0001*
IVRT (ms)	102.87±20.06	85.08±18.94	0.0001*
DCT (ms)	203.86±6.69	186.52±28.74	0.0001*
Mitral E/A ratio			
Less than 1	57 (76.0%)	16 (32.0%)	0.0001*
1-1.5	16 (21.3%)	34 (68.0%)	0.0001*
> 1.5	2(2.6%)	0 (0.0%)	0.9
IVRT (ms)			
60-100	22 (29.3%)	37 (74.0%)	0.0001*
< 60	2 (2.7%)	0 (0.0%)	0.9
> 100	51 (68.0%)	13 (26.0%)	0.0001*
DCT (ms)			
140-200	20 (26.7%)	34 (68.0%)	0.0001*
< 140	2 (2.7%)	0 (0.0%)	0.9
> 200	53 (70.7%)	16 (32.0%)	0.0001*

Mitral E/A ratio = Early transmitral flow Velocity: Late transmitral flow velocity, IVRT = Isovolumic Ventricular Contraction Time, DCT = Deceleration time, ***** = Significant at $p < 0.05$

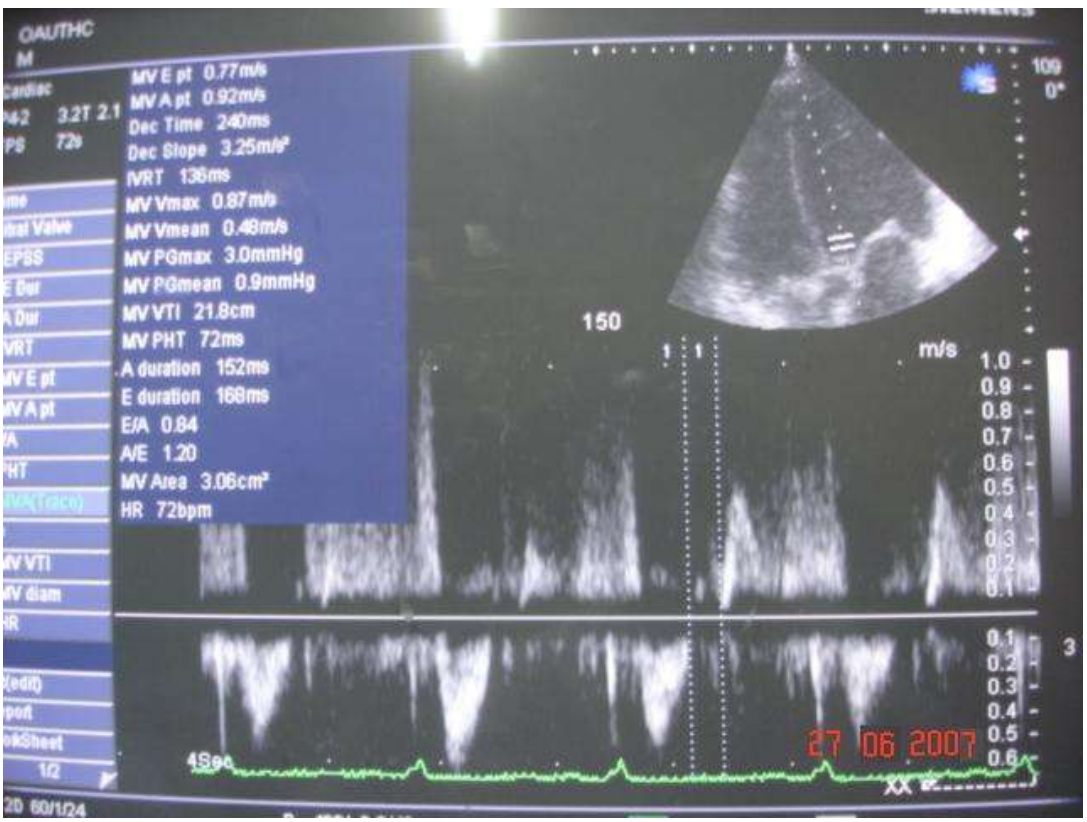

Figure 2 Doppler echocardiography showing prolonged isovolumic ventricular relaxation time in a study patient IVRT = 136ms

Table 4: Comparison of Doppler echocardiographic parameters between hypertensive-diabetic and normotensive-diabetic

Parameters	hypertensive-diabetic N = 52	Normotensive-diabetic N = 23	P-value
Mitral E/A ratio			
< 1	46(88.5%)	11(47.8%)	0.0001*
1-1.5	4(7.7%)	12(52.2%)	0.0001*
>1.5	2(3.8%)	0(0.0%)	0.9
IVRT (ms)			
60-100	8(15.4%)	14(60.9%)	0.0001*
<100	0(0.0%)	0(0.0%)	
>100	43(82.7%)	9(39.1%)	0.0001*
DCT (ms)			
140-200	5(9.6%)	15(62.5%)	0.0001*
<140	1(1.9%)	0(0.0%)	0.9
>200	45(86.5%)	8(34.8%)	0.0001*
Mitral E/A ratio			
	0.77±0.26	1.06±0.30	0.0001*
IVRT (ms)	107.29±20.96	93.08±13.88	0.0001*
DCT (ms)	211.90±24.62	186.04±22.44	0.0001*

Mitral E/A = Early transmitral flow Velocity: Late transmitral flow velocity ratio, IVRT = Isovolumic Ventricular Contraction Time, DCT = Deceleration time, * = Significant at $p < 0.05$