Original article

Cardiac Function in Uncomplicated Type 2 Diabetes Mellitus

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Abstract

Objective: Diabetic cardiomyopathy (DC) is a myocardial disease characterized by myocyte hypertrophy, interstitial fibrosis, protein glycosylation and intra-myocardial micro-angiopathy due to prolonged exposure of myocardial tissues to hyperglycemia in diabetes mellitus (DM) patients. Alteration in cardiac function can be non-invasively assessed via echocardiography. The early recognition of cardiac dysfunction can prevent the symptomatic heart failure in DM patients. The study aimed at evaluating cardiac function in uncomplicated type 2 diabetes mellitus. ***Materials And Methods:*** Sixty Type 2 DM patients without any feature of the coronary arterial disease (CAD), hypertension, nephropathy and respiratory illness were enrolled in the study and compared with the sixty age matched healthy controls. Echocardiographic assessment was done in all subjects to evaluate the cardiac function. ***Results:*** Diastolic dysfunction was more common in diabetic patients when compared with normal healthy population. Systolic dysfunction progresses with age of the diabetic patient. ***Conclusion:*** Echocardiography is a simple noninvasive cost effective test for detecting cardiac dysfunction in Type 2 DM patients and should be applied to detect early Left ventricular(LV) dysfunction so that corrective measures may be initiated early and cardiac functions may be preserved for long.

Keywords: Diabetic Cardiomyopathy; Diastolic Dysfunction; Doppler Echocardiography; Left Ventricle

Bangladesh Journal of Medical Science Vol. 18 No. 02 April'19. Page : 211-215
DOI: https://doi.org/10.3329/bjms.v18i2.40687

Introduction

Diabetes Mellitus (DM) is emerging as a massive outbreak in developed and developing countries; inflicting considerable human suffering. Worldwide, India is turning into the capital for diabetes. Currently India is one of the 6 countries of the IDF (International Diabetes Federation) South-East Asia region with 69.1 million cases of diabetes in 2015[1]

Diabetic patients are prone to various complications involving retina, kidneys, nerves and cardiovascular system that cause morbidity and premature mortality. It is an independent risk factor for cardiovascular diseases (CVD) and cardiac complications are responsible for three-fourths of all diabetic mortality.[2] Several researchers have indicated major risk factors for cardiovascular disease act as independent contributors to CVD in patients with diabetes.[3] These risk factors include smoking, high blood pressure, and dyslipidemia. This is because atherosclerosis occurs early in diabetics and it is more extensive and has multi-vessel involvement. This pathophysiological phenomenon directly or indirectly causes myocardial pathology which is a common and vital determinant of cardiovascular morbidity.[4]

Despite enormous research activities, the prevalence of diabetic related complications

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is increasing worldwide. Various researchers proposed that prolonged exposure of myocardium to hyperglycemia results in myocyte hypertrophy, interstitial fibrosis, protein glycosylation and intramyocardial microangiopathy and is termed as diabetic cardiomyopathy.[5] The hallmark of diabetic cardiomyopathy is believed to be reduced ventricular compliance and diastolic dysfunction and it may be seen without any coronary arterial disease.[6]

Material and methods

The present study was conducted in the department of Medicine in a tertiary care hospital. Sixty patients fulfilling the diagnostic criteria for diabetes mellitus with no cardiovascular symptoms were included in Group 1. Sixty age matched healthy individuals were included in Group 2 as the control. All patients were subjected to detailed history, clinical examination, biochemical evaluation, and echocardiography.

Exclusion criteria:-

1. Systemic Hypertension (SBP ≥140 mm of Hg, DBP ≥90 mm of Hg).
2. Coronary artery disease as detected by resting 12 lead ECG.
3. Diabetic nephropathy (Presence of albumin in urine with > 300 mg/24 hrs.)
4. Diabetic autonomic neuropathy as assessed by clinical examination and tests of dysautonomia.
5. Associated respiratory diseases. (Assessed by Chest X-ray and Vital Capacity by peak flowmeter.)

Echocardiographic assessment was done in 2-dimensional (2D) mode; M-mode and Doppler's mode using color flow mapping. Stress test (TMT) was performed in all subjects.

- Criteria for Systolic dysfunction was indicated by ejection fraction (EF) <50%.
- Mitral E/A ratio <1 or >2 was taken as echocardiographic Diastolic dysfunction criteria, where E wave denotes peak velocity flow in Early diastole and A wave denotes peak velocity flow in late diastole (atrial contraction).

Ethical Clearance: The approval of study was obtained from the Institutional Ethical Committee.

Results

In this study, mean age among the diabetic patients was 46.5 years which was comparable with the control group being 48.75 years. Majority of patients were females (55 %) in the diabetic group while control group consisted of predominantly males (55%). BMI and lipid profile was comparable among both groups (Table 1). Mean duration of diabetes in the study group was 5 years.

Table 1: Basic Parameters among cases and controls

Parameter	Case group: T2DM	Control group	P value
Age (years)	46.5 ± 8.83	48.75 ± 6.05	>0.05
BMI (Kg/m^2)	22.47 ± 1.7	22.26 ± 1.82	>0.05
HbA_1C (%)	7.28 ± 0.59	5.46 ± 0.79	<0.01
Total Cholesterol (mg/dL)	186.30 ± 15.81	175.88 ± 14.75	>0.05
Triglycerides (mg/dL)	120.04 ± 14.58	119.68 ± 9.36	>0.05
HDL-Cholesterol (mg/dL)	38.64 ± 3.5	40.54 ± 2.28	>0.05
FBS (mg/dL)	161.5 ± 41.8	102.6 ± 6	<0.001
PPBS (mg/dL)	219.72 ± 58.8	151 ± 9.13	<0.001

BMI: Body Mass Index; HDL: High Density Lipoprotein; FBS: Fasting Blood Sugar; PPBS: Post Prandial Blood Sugar

Mean ejection fraction in group 1 & group 2 were not statistically different but 13.33% patients i,e group 1, had decreased EF (<50%) (Table 2). Majority of these patients with decreased EF were in the age group of 51-70 years. However there was no significant difference in EF between 2-10 years of the duration of DM.

Table 2: Systolic parameters in the study population.

Parameter	Case group: T2DM	Control group	P value
LVEF (%)	56.62 ± 5.3	57.9 ± 4.48	> 0.05
LVEF ≥ 50	86.67% (n=52)	100% (n=60)	
LVEF ≤ 50	13.33% (n=8)	0	
FS (%)	29.5 ± 3.3	30.3 ± 2.1	> 0.05
FS ≥ 25	91.7% (n=55)	100% (n=60)	
FS ≤ 25	8.3% (n=5)	0	

LVEF: Left Ventricular Ejection Fraction; FS: Fractional Shortening

Mean Mitral E velocity in group 1 was comparable to group 2 but mitral A velocity and E/A ratio were significantly lower in group 1 with p <0.001. E/A ratio <1 was present in 83.3% of patients in group I indicating diastolic dysfunction (Table 3). Diastolic dysfunction (E/A ratio <l) was significantly

associated with age of the population under study (p <0.001) but was not found to be associated with the duration of diabetes (p >0.05).

Table 3: Diastolic parameters among the study group

Parameter	Case group: T2DM	Control group	P value
MITRAL E	0.76 ± 0.12	0.75 ± 0.05	>0.05
MITRAL A	0.89 ± 0.12	0.62 ± 0.06	<0.001
E/A ratio	0.84 ± 0.18	1.19 ± 0.10	<0.001
E/A <1	83.3% (n=50)	0	-

Mean Iso-volumetric relaxation time (IVRT) was significantly higher in diabetics (group 1) as compared to control (group 2). Forty one patients had IVRT of > 100ms. All these patients also had E/A ratio of <1. IVRT was within normal range in 13 patients who also had coexisting LV systolic dysfunction with an ejection fraction of <50 % (Table 3). Mean deceleration time (DT) in group 1 was significantly higher in comparison to group 2. Five patients (8.3%) had DT <150 ms indicating severe diastolic dysfunction.

Mean LVIDd, LVIDs, and LVPWd in group 1 was comparable to group 2 with p >0.05. Increase in Mean LVMI was highly significant in group 1 as compared to group 2 (Table 4).

Table 4: M-mode parameters among the study group

Parameter	Case group: T2DM	Control group	P value
LVIDd (cm)	4.15 ± 0.49	4.3 ± 0.48	> 0.05
LVIDs (cm)	2.56 ± 0.32	2.97 ± 0.44	> 0.05
LVPWd (cm)	0.97 ± 0.1	0.92 ± 0.2	> 0.05
LVMI (g/m^2)	101.3 ± 15.6	78.5 ± 22.7	<0.001

LVIDd: Left ventricular internal diameter end diastole; LVIDs: Left ventricular internal diameter end systole; LVPWd: Left Ventricular Posterior Wall end diastole; LVMI: Left ventricular Mass index

DISCUSSION

Cardiovascular related deaths are most common cause of mortality in Type 2 DM patients.[2] In Diabetic patients, apart from hypertension and coronary arterial diseases, finding of histological changes in myocardium are frequently seen. This has been attributed to damage to the myocardium by advanced glycation end products, reactive oxygen species and activation of inflammatory pathways due to prolonged hyperglycemia in uncontrolled diabetic patients.[7,8] Diabetic cardiomyopathy leads to heart failure and is characterized functionally by decreased or preserved systolic function, impaired diastolic function, ventricular dilation, hypertrophy of myocytes and myocardial fibrosis.[3]

Several researcher have shown cardiac dysfunction leading to heart failure in Type 2 DM patients in absence of coronary arterial disease and hypertension.[9,10] However, no author has been able to provide the exact pathophysiology. Sanderson et al.[11] suggested that diastolic dysfunction of the left ventricle, i.e. left ventricular filling abnormality is predominant feature in diabetic patients. This view has been further strengthen by the study of Leonardo M Shapiro.[12]

In the present study, LV Systolic function was evaluated by measuring ejection fraction and fractional shortening as vital parameters through M-mode and Doppler echocardiography. The study measured mean EF of 56.62% which was comparable to that of Poirier ct al (65%)[13], Abdul Khaliq M.H. et al(58%)[14] and John K. Boyer et al(64%).[15] In contrary to study by Uusitupa et al[16] who showed EF to be decreased more in males than in females, our study showed no difference in EF between males and females.

Doppler assessment of Mitral valve flow was taken as an indicator of filling abnormalities i.e. diastolic dysfunctions of the Left ventricle. Our study shows lower E/A ratio in diabetic patients indicating Left Ventricular diastolic dysfunction in 83.3% of these patients despite most of these having relatively normal LVEF. When our result of E/A ratio was compared with the studies of Poirier ct al (0.72 ± 0.13)[13], Abdul Khaliq M.H. et al (0.9 ± 0.2)[14] and John K. Boyer et al (0.95±0.29)[15] we observed similar results. Zarich et al[17] and Paillole et al[18] reported that diabetics with normal LVEF had decreased E/A ratio suggesting diastolic dysfunction. They also found that all diabetics with decreased E/A ratio had normal LV fractional shortening.

In the present study, When E wave and A wave were compared, we found that late atrial filling wave (A) was significantly increased. It can be attributed to elevated left ventricular filling pressure which can be secondary to delayed relaxation among diabetic patients. The reduced LV compliance in diabetic patients is responsible for diastolic abnormalities which can be secondary to metabolic derangement, infiltrative myocardial process, small vessel disease, or a combination of the three.[19]

Similar to study by Galderisi et al[20], no correlation of diastolic dysfunction found with the duration

of diabetes. They stated that the severity of diabetes mellitus is more important than duration of diabetes mellitus for the development of diastolic dysfunction. However Shrestha et al[21] and Bajraktari et al[22] found a significant correlation of duration of diabetes with the diastolic dysfunction. Significant correlation of diastolic dysfunction with the age of diabetic patients was seen in the present study which further strengthens the fact that age is an independent risk factor for the development of diastolic dysfunction.[23]

The prolongation of IVRT > 100 ms (in 68% of diabetics), prolongation of DT of E wave (in 36% of diabetics) further shows diastolic dysfunction in diabetic patients. Similarly, Hiramatsu et al[24] and Paillole et al[18] showed in their studies that diabetic patients had higher IVRT.

Conclusion

This study found diastolic ventricular dysfunction as a common finding among diabetic individuals and its correlation with increasing age needs screening among old aged patients. LV systolic dysfunction was observed in a limited number of normotensive asymptomatic Type 2 DM patients which signify the prevalence of silent myocardial disease in asymptomatic Type 2 DM patients.

Echocardiography is a simple non-invasive cost effective test for detecting cardiac dysfunction in Type 2 DM patients and should be applied to detect early Left ventricular dysfunction so that corrective measures may be initiated early and LV functions may be preserved for long.

Acknowledgement : We are grateful to the participants for their cooperation to conduct this study.

Conflict of Interest: None declared.

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