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Research Article

Impact of glycaemic control in Type 2 Diabetes Mellitus patients on left ventricular diastolic function: Two-Dimensional Echocardiography Based Study.

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Abstract

Background: Type 2 Diabetes Mellitus affects left ventricle (LV) diastolic function.
Aim of the study: This study's primary objective was assessment of the LV diastolic Functioning in asymptomatic diabetic individuals with normal blood pressure and comparing it to control group by the use of 2D echocardiography. **Patients and methods**: 80 Diabetes Mellitus (DM) type 2 patients were enrolled. We excluded hypertensive patients and Patients with valvular or coronary heart diseases. All patients got thorough clinical and cardiological examination, laboratory work up including (HbA1C, Fasting blood sugar (FBS), post prandial blood sugar (PPS), CBC, Lipid profile, S.Creatinine, albumin and liver enzymes), 12 leads ECG and echocardiographic assessment of both ventricles by tissue Doppler and conventional methods. **Results**: In the uncontrolled diabetic individuals, ratio (E/A) of peak early to peak late diastolic flow velocities across mitral were significantly lower than those with controlled diabetes. **Conclusion**: Patients with uncontrolled type II DM were associated with compromised left ventricular diastolic function compared to controlled diabetics.

Keywords: Diabetes mellitus, Echocardiography, Cardiomyopathy, Diastolic function.

Introduction

Diabetic cardiomyopathy has a complex and multifactorial pathogenesis; mitochondrial dysfunction, atherosclerosis, lipotoxicity and subclinical microinfarctions, In addition, long-standing hyperglycemia leads to accumulation of more advanced glycation end products which has been recognized and it causes ventricular stiffness.[1] fibrosis occurs by cross-linking collagen which yields from development and accumulation of more complex advanced glycation end products, thus increasing myocardial stiffness. Only limited data exist on effect of diabetes control on LV diastolic function. The most frequently used imaging technique for measuring LV size and function is Two-dimensional echocardiography due to its widespread availability.[2]

Diabetes Mellitus type 2 is a metabolic disorder in which there is hyperglycaemia and insulin resistance which are the main contributors to several cardiovascular risk factors, including obesity, hypertension and dyslipidaemia. [3] in diabetes mellitus type 2 (T2DM) there is also elevated levels of cytokines and inflammatory mediators that cause renal and vascular complications, These factors together lead to increased cardiovascular potential hazards to those with diabetes.[4]

In diabetics, diabetic DCM (cardiomyopathy) is crucial and critical cardiovascular problem, which can be defined as myocardial dysfunction among diabetic patients in the absence of other potential heart failure risk factors.[5]

Numerous hypotheses propose that having elevated blood sugar in diabetic patients plays an essential role in the emergence of cardiac dysfunction and heart failure. The different synchronized pathological events in diabetes and hyperglycaemia lead eventually to myo-cardial fibrosis, which is believed to be The most important reason of systolic and diastolic disorders in diabetic heart.[6]

Many researchers believe that diastolic dysfunction of the left ventricle (LVDD) is the initial obvious symptom of heart remodeling in diabetics. DM and heart failure (HF) have a bidirectional cause and effect relationship. In patients suffering from heart failure, nineteen percent among them are reported to have Diabetes Mellitus type 2, moreover, T2DM raises the risk of development of heart failure into 2- to 8-fold.[7]

So, we recommend careful evaluation of LV diastolic function during routine echocardio-graphic study of DM patients. In addition, the proper diabetic state control protects against this dysfunction as well.

Subjects and Methods:

Our study is cross sectional research study. 120 subjects were included, 80 diabetic individuals as cases (40 males & 40 females) with the mean age 49.65±13.1 years and 40 healthy people as control group (16 males and 24 females) and the average age was 54.30±12.4 years. Then, the diabetic patients were subdivided into two groups: Controlled diabetic state: n = 38

Uncontrolled diabetic state: n = 42

Methods: All subjects included in our study were characterized by normal Left Ventricle (LV) Ejection Fraction (EF), estimated by standard 2D Trans-Thoracic Echocardiography (TTE). We excluded Subjects who had diseases that influence the RV or LV systolic function as coronary arterial diseases, hypertension, arrhythmias, pulmonary illnesses, pulmonary hypertension and valvular diseases. Firstly informed verbal consent was taken from all studied people, then they were subjected to, recording history. full general and cardiac examinations. Then standard 12-leads Electro-cardiogram (ECG) in rest has been done to analyze and exclude arrhythmias. The echocar-diographic parameters were the conventional 2D ones; LVEF, diastolic dysfunction (DD), left atrium (LA) diameter, dimensions and systolic function of right ventricle (RV), Fractional area change (FAC), RA diameter and Systolic pressure in the pulmonary arteries (PASP). The laboratory parameters were lipid profile parameters and glycemic control by FBS, PPS and A1C, Figure (1).

Ethical consideration:

The study protocol was approved by the Ethics committee of the Faculty of Medicine, Minia University; with approval number 11:1/2021

Results

1- As regard demographic and clinical data, There was no difference of statistical importance between the two studied groups (Table 1):

Table 1: Demographic data of the studied population

Demographic data	Cases (n = 80)	Control (n = 40)	p value
Age (years):	49.65 ± 13.1	54.3 ± 12.1	**0.086**
• **Range**	20 - 71	36 - 73	
Sex:			
• **Male N (%)**	40 (50%)	16 (40%)	**0.301**
• **Female N (%)**	40 (50%)	24 (60%)	
BMI (kg/m^2):	28.7 ± 3.9	26.5 ± 4.3	**0.068**
• **Mean ± SD**	27- 35	25- 34	
• **Range**			
SBP (mmHg):	120.7 ± 9.10	116 ± 10.3	**0.117**
• **Range**	100 - 130	100 - 130	
DBP (mmHg):	74.68 ± 9.15	74.12 ± 9.12	
• **Range**	60 - 85	60 - 85	**0.747**

BMI: Body Mass Index, SBP: Systolic Blood Pressure and DBP: Diastolic Blood Pressure

2-Both groups of our study showed no statistically significant difference as regard LV ejection fraction, LV diastolic function and LA diameter (Table 2):

Table 2: conventional 2D echo Doppler study on LV

Cardiac parameters	Cases (n = 80)		Control (n = 40)		p value
	Mean ± SD	Range	Mean ± SD	Range	
LVEF (%)	59.9 ± 4.88	50 – 70	61.6 ± 5.24	55 – 70	0.179
LA (mm)	36.42 ± 3.44	28 – 45	36.5 ± 3.6	30 – 42	0.574
LVDD:					
• **Absent N (%)**	54 (67.5%)		32 (80%)		0.152
• **Present N (%)**	26 (32.5%)		8 (20%)		

LVEF; left ventricle ejection fraction, LA: left atrium and LVDD: left ventricle diastolic dysfunction

Among the controlled diabetics, only 8 (21%) had grade I LV diastolic dysfunction. On the other side, 18 (42%) of uncontrolled diabetics had grade I LV DD.

3- In terms of LV diastolic function, there was a variance that was statistically significant between the two groups (p=0.038), but Regarding LV ejection fraction and LA diameter, there was no discernible difference between the two groups. (Table 3):

Table 3: conventional 2D echo Doppler study on LV

Cardiac parameters	Controlled diabetes (n = 38)		Uncontrolled diabetes (n = 42)		p value
	Mean ± SD	Range	Mean ± SD	Range	
LVEF (%)	-60.73 ± 5.51	50 - 70	59.14 ± 4.15	50 – 67	0.208
LA (mm)	35.89 ± 2.99	32 - 45	36.90 ± 3.77	28 – 45	0.145
LVDD: • Absent N (%) • Present N (%)	 30 (78.9%) 8 (21.1%)		 24 (57.1%) 18 (42.9%)		0.038*

LVEF; left ventricle ejection fraction, LA: left atrium and LVDD: left ventricle diastolic dysfunction

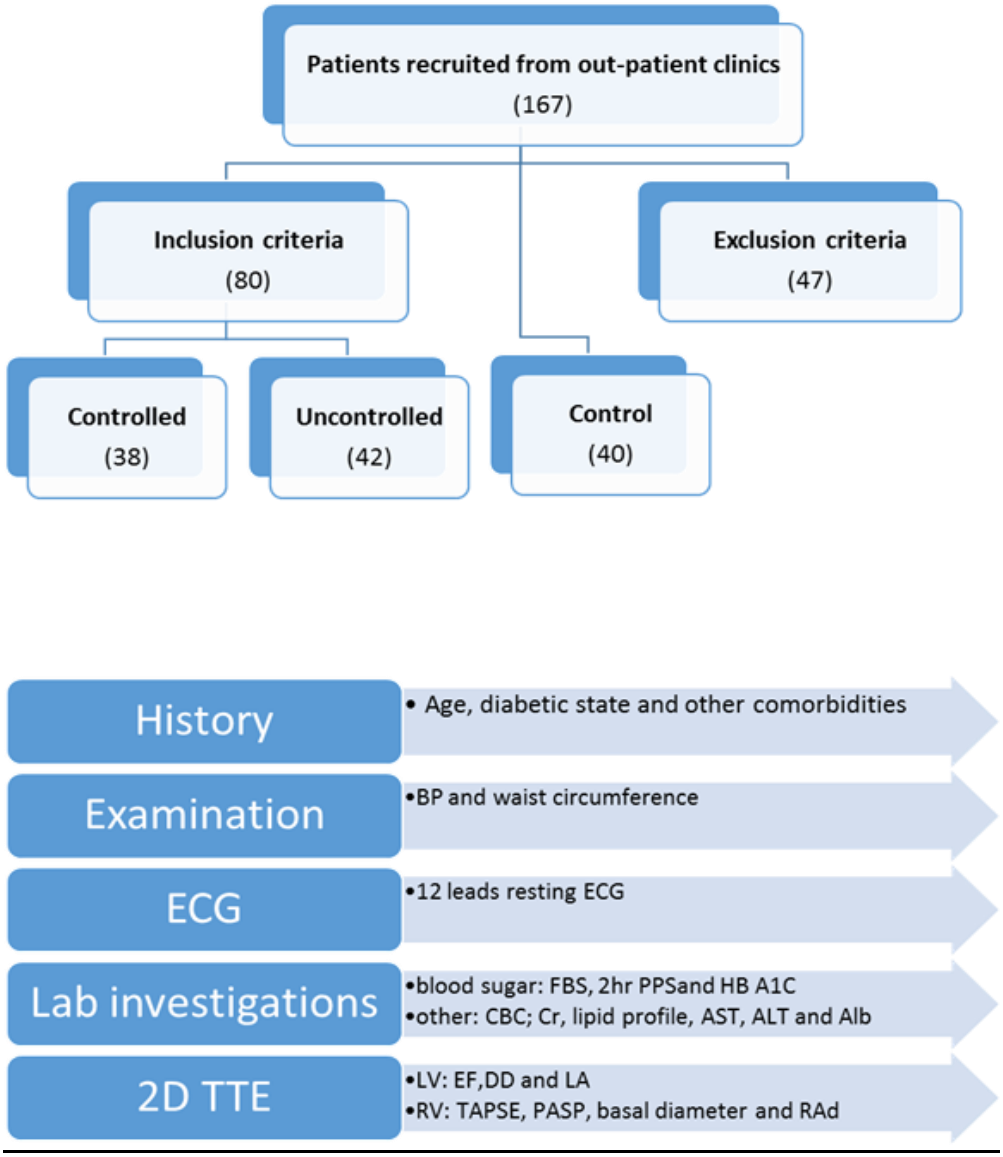

Figure 1: Flow chart of the case control study.

Discussion

The rate of incidence of diabetes mellitus (DM) is rising universally. Along the three last decades, several clinical, epidemiological and autopsy researches have suggested that diabetic heart disease being a separate and distinctive clinical entity. Diastolic heart failure (HF) can be defined as HF, with normal or preserved LV systolic function. Various studies have mentioned that occurrence of heart failure in diabetic patients is high despite having no coronary artery disease, or hypertension. In these studies, they found that DM patients have a significant prevalence of pre-clinical diastolic dysfunction. And this reveals that in diabetics, cardiac affection and the damage impacts diastolic function before systolic one.

In diabetic patients systolic heart failure occurs due to increased myocardial stiffness which is mainly associated with advanced glycation end products (AGE) deposition and then fibrosis. diastolic heart failure occurs mainly due to high cardiomyocyte resting tension and hypertrophy[8]. Interestingly, myocellular hypertrophy in diabetics occurs due to Insulin resistance and increased fasting insulin levels and not related to pressure overload.

There are more and more papers demonstrating the correlation between the degree of hyperglycaemia and diabetic cardiac dysfunction, that reduction of heart failure risk occurs by effective metabolic control, and that there is correlation between the degree of improvement in diastolic function and the degree of glucose control improvement[8].

Our study has found that uncontrolled diabetic subjects exhibit LV impairment of diastolic function in comparison with those who have to controlled diabetes ($P = 0.038$). These results are consistent with Hassan et al., who studied the relationship between glycemic control and diastolic function in individuals with preserved ejection fraction.[9] There was a considerable dyslipidemia in Patients with left ventricular diastolic dysfunction in comparison to those without LVDD. Additionally, HbA1c levels were found to be a predictor of diastolic dysfunction in individuals with newly diagnosed DM by multivariate logistic regression analysis. Additionally, Kaplan-Meier survival curves revealed a significant relationship between the Diastolic dysfunction frequency and DM duration, with a higher frequency with HbA1c ≥8.1.

Even in well controlled DM patients, LVDD is common despite absence of clinically identifiable heart disease. One of the earliest studies of correlation between DM and diastolic dysfunction was conducted by Poirier et al., they enrolled 46 diabetic men with type 2 diabetes and with no subjective or objective proof of HTN, congestive heart disease (CHD) or CHF. By using Doppler echocardiography, LVDD was assessed. 28 individuals (60%) exhibited LVDD, with 15 (32%) having poor relaxation and 13 (28%) having a pseudo-normal ventricular filling pattern. Systolic function was normal in each participant, and there was no correlation between LVDD and markers of metabolic control.[10]

To establish a sturdy association between DM and LVDD, Patil et al., developed a case control prospective study over year. To evaluate left ventricular diastolic function, echocardiography was done on 127 patients (cases) with type 2 diabetes who were diagnosed with it for more than five years. In addition, 100 healthy people were used as the control group. Diastolic dysfunction was seen in 69 (54.33%) of the case group participants and 11% of the 100 participants in the control group ($P < 0.001$). Diastolic dysfunction was more common in patients with DM who had had it for 11 to 15 years or longer ($P < 0.02$). Diastolic dysfunction was more common in individuals with HbA1c > 7.5% than in subjects with HbA1c < 7.5% ($P < 0.02$)[8]

Cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) and are inextricably linked in a vicious cycle in which the former increases the risk of the latter and the latter is a essential cause of complications, comorbidities, and mortality in the former. This is especially concerning because both are becoming increasingly prevalent globally.

Conclusion

LVDD is common in DM patients and associated with HbA1c level regardless of LV ejection fraction (preserved ejection fraction).

Data availability:

All data are included in the manuscript

Declaration and Conflict of interest:

The authors declare no conflict of interest

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Author contribution:

Authors contributed equally to the study.

Permission to publish

Each and every patient and study subject gave their permission to publish after giving their informed consent.

References

1. Kass, D. A., Bronzwaer, J. G. F. & Paulus, W. J. What mechanisms underlie diastolic dysfunction in heart failure? Circulation research (2004) **94**, 1533–1542 .
2. Aronson, D. Cross-linking of glycated collagen in the pathogenesis of arterial and myocardial stiffening of aging and diabetes. Journal of hypertension (2003)**21**, 3–12.
3. Guo, S.-X. et al., Association of Serum Free Fatty Acids with Hypertension and Insulin Resistance among Rural Uyghur Adults in Far Western China. International journal of environmental research and public health (2015).**12**, 6582–6590
4. Abate, N. et al., Resistin: an inflammatory cytokine. Role in cardiovascular diseases, diabetes and the metabolic syndrome. Current pharmaceutical design (2014).**20**, 4961–4969
5. Jia, G., DeMarco, V. G. & Sowers, J. R. Insulin resistance and hyperinsulinaemia in diabetic cardiomyopathy. Nature reviews Endocrinology(2016) **12**, 144–153.
6. Battiprolu, P. K. et al., Metabolic stress-induced activation of FoxO1 triggers diabetic cardiomyopathy in mice. The Journal of clinical investigation (2012)**122**, 1109–1118 .
7. Wang, T. J. et al., Natural history of asymptomatic left ventricular systolic dysfunction in the community. Circulation (2003)**108**, 977–982.
8. Patil, V. C., Patil, H. V, Shah, K. B., Vasani, J. D. & Shetty, P. Diastolic dysfunction in asymptomatic type 2 diabetes mellitus with normal systolic function. Journal of cardiovascular disease research (2011) **2**, 213–222.
9. Hassan Ayman, K. M. et al., Correlation between left ventricular diastolic dysfunction and dyslipidaemia in asymptomatic patients with new-onset type 2 diabetes mellitus. The Egyptian Journal of Internal Medicine (2021) **33**, 8.
10. Poirier, P., Bogaty, P., Garneau, C., Marois, L. & Dumesnil, J. G. Diastolic dysfunction in normotensive men with well-controlled type 2 diabetes: importance of maneuvers in echocardiographic screening for preclinical diabetic cardiomyopathy. Diabetes care (2001)**24**, 5–10.