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RESEARCH ARTICLE

ASYMPTOMATIC LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN DIABETES MELLITUS: IMPACT OF RISK FACTORS

Mohammad M. Sallam[1], Abdallah Nawara[1], Elsayed A. Elgohary[1], Mohamed Arab[2]

1. Internal Medicine department, Faculty of Medicine, Zagazig University,Egypt

2. Cardiology department , Faculty of Medicine, Zagazig University, Egypt

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Corresponding Author

Mohammad M. Sallam

Abstract

Introduction: Several studies have reported that the incidence of heart failure in patients with type 2 diabetes mellitus (DM) is high and that the diastolic heart failure seems to be the leading cause. Despite the association between diabetes and cardiovascular morbidity and mortality, the prevalence of left diastolic dysfunction (LVDD) in asymptomatic patients with type 2 DM is not well defined and existing data are controversial. **Aim and objective** : We conducted this study to assess the prevalence of diastolic dysfunction of the left ventricle in patients with type 2 DM and to explore its relation to other parameters, including patients' age ,the duration of diabetes and glycemic control. **Material and Methods** : 100 patients with type 2 diabetes were enrolled in the study . Diastolic function of the left ventricle was assessed by pulsed Doppler echocardiography. **Results:** This study included 100 diabetic patients comprising 52 female and 48 male , all studied patients were between the age of 30 and 70 years. (58%) had diastolic dysfunction and 48 % were having diabetes less than 5 years. Mean HbA1C level of LVDD group was found higher as compared to those without LVDD. **Conclusion:** We documented the high prevalence of asymptomatic left ventricular diastolic dysfunction in patients with type 2 diabetes without clinical evidence of structural heart disease. Left ventricular diastolic dysfunction was significantly related to the glycemic control and age of patients. Doppler echocardiography is a simple, inexpensive, widely available and sensitive method for the diagnosis and follow-up of cases with diastolic dysfunction. We recommend the use of this technique in the routine workup of diabetic patients even in early stages.

INTRODUCTION

Diabetes mellitus (DM) is a common endocrine disorder affecting 387 million people worldwide (1). DM is associated with multiple cardiovascular complications. Many studies attribute the increased occurrence of clinical congestive heart failure in diabetic patients to diabetic cardiomyopathy , which could take the form of diastolic and /or systolic left ventricular dysfunction.(2-4)

Left ventricular diastolic dysfunction (LVDD) may represent the reversible first stage of diabetic cardiomyopathy preceding changes in systolic function reinforcing the importance of early examination of diastolic ventricular dysfunction in individuals with DM.(5)

Diastolic heart failure is a distinct clinical entity that in most cases has a silent course and may be totally asymptomatic especially in early stages and almost constitute one third of all cases of heart failure (6).

The mortality rates among the patients with diastolic heart failure ranges from 5-8 % annually as compared with 10-15 % among patients with systolic heart failure. (7)

The proposed mechanisms that may be implicated in the pathogenesis of diabetic cardiomyopathy, include autonomic dysfunction, microvascular disease, interstitial fibrosis and metabolic disorders. However, the actual causes and mechanisms remain unclear. (8)

Despite the close relations between diabetes and cardiovascular morbidity and mortality, The relationship between diastolic dysfunction and glycemic control is still a matter of debate.(9)

Thus , this study was conducted with aim of determining the prevalence of asymptomatic LV diastolic dysfunction in type 2 diabetic patients and to explore its relation to other parameters, including patients' age ,the duration of diabetes and glycemic control .

Patients

This study included 100 patients (48men and 52 women) with type 2 diabetes, diagnosed according to the American Diabetes Association criteria (10),recruited over a period of one year , from the medical outpatient Clinics of the Internal Medicine department, Zagazig university hospitals.

Exclusion criteria included:

- Patient of known hypertension with or without treatment.
- Ischemic heart disease (excluded by history of angina, chest pain ,Electrocardiogram (ECG) changes and abnormal Treadmill test) .
- Cardiac arrhythmias.
- Cardiomyopathy.
- Valvular heart disease.
- Heart failure.
- Chronic pulmonary disease.
- Extreme age.
- Chronic renal failure.
- Subjects with poor transthoracic echo window.

Methods:

All participants were subjected to the following after fully informed consents:

- Medical history taking with special emphasis on smoking history, the duration of diabetes and the current medical treatment when applicable.
- Thorough clinical examination, including anthropometric measurements (weight, height, waist and hip circumferences). The waist/hip ratio and body mass index of each participant were estimated from these measurements.
- Resting 12-lead ECG .
- Chest X Ray.
- Baseline laboratory tests included fasting blood glucose, glycosylated hemoglobin (HbA1C) levels, lipid profile (total cholesterol, high density lipoproteins (HDL), low density lipoproteins (LDL), very low density lipoproteins (VLDL) and triglycerides), and serum creatinine and urea.

Echocardiographic Examinations

All the subjects were underwent resting transthoracic 2-dimensional echocardiography and Doppler imaging, to assess left ventricular diastolic function.

Echocardiographic study was done by the same operator using an echocardiographic machine (hp 5500) equipped with 2.5 MHz phased array probe.

The examinations were done with the patient in left lateral decubitus, utilizing left parasternal long axis, short axis apical 4 and 5 apical chamber views according to the recommendations of American Society of Echocardiography (10).

The measurements included:, LV systolic function (EF and Fractional Shortening) and LV diastolic function was obtained from Doppler examination of mitral valve flow pattern.

The transducer was positioned in the apical 4 chamber views; the sample volume marker was positioned at the level of mitral valve annulus.

Left ventricular overall ejection fraction (systolic function) was calculated by modified Simpson's method ; and, LVEF ≥ 50% was considered as normal.(11,12)
All patients were in sinus rhythm, the following parameters were measured:

- Maximal early filling velocity (E wave), maximal late atrial filling velocity (A wave), from which the E/A ratio was derived.
- The deceleration time of E wave (DT-E) was obtained by measuring the interval from the peak of E wave to the end of E flow.
- Isovolumic relaxation time (IVRT) was measured as the interval from the end of aortic flow to the onset of mitral inflow with the transducer in apical 5-chamber view with the sample volume marker midway between mitral valve annulus and LV outflow tract.

LV diastolic dysfunction was considered to be present if any of the following findings were seen, as previously described: (12)

- E/A ratio < 1 or > 2.
- DT < 150 or > 220 ms.
- IVRT < 60 or > 100 ms.

Statistical Analysis was performed using a computer-based program (SPSS version 11). The data are presented as mean ± standard deviation. Continuous data were compared with a two-tailed unpaired *t* test. The strength of the link between the continuous variables was tested by Pearson correlation coefficient r. *P* value less than 0.05 indicated statistical significance.

Results

This study included 100 diabetic patients comprising 52 female and 48 male , all studied patients were between the age of 30 and 70 years. Maximum patient belongs to age group 50-59 years(44)and minimum in age group 30-39 years (14 patients). (**Table 1)**
Out of a total of 100 included subjects, 58 subjects (58 %) had left ventricular diastolic dysfunction (LVDD) among them 36 were female and 22 were male.**(Table 2)**
The most of subjects were having diabetes less than 5 years comprised (48 %) of studied population and the minimum (8%) was found among those having diabetes more than 15 years.**(Table 3)**

Among the age group of 50-59 years the diastolic dysfunction was most prevalent (37.39%) and among age group of 30-39 years it was least prevalent (13.7%). **(Table 4)**

(Table 5) showing comparison between patients with diastolic dysfunction and those without diastolic dysfunction using various parameters: Age, BMI, Serum total cholesterol , Fasting blood glucose (FPG) and HB A1C.The mean Fasting blood glucose of patients with LVDD was found higher (192.07 ± 30.92) as compared to those without LVDD (173.68 ± 29.82) and this correlation was highly significant (p=0.002).The mean HbA1C of population with LVDD was higher (7.71 ±1.01) as compared to population without LVDD (7.28 ± 0.75), Correlation was significant (p-value=0.0157). This signifies that higher the HbA1C at the time of diagnosis, higher will be the incidence of LVDD **(Figure 1**).The mean age of subjects with LVDD was higher as compared to subjects without LVDD and correlation was found highly significant (p=0.0012) **(Figure2)**. BMI (p=0.0744) and serum cholesterol (p=0.1827) had no significant correlation with incidence of LVDD in our study.

Echocardiographic data are shown in **Table (6)**. There were significant differences between the two studied groups regarding left ventricle fractional shortening, left ventricle ejection fraction(despite they still within normal range), E wave, A wave, E/A ratio, the deceleration time of the E wave (DT-E) and IVRT. The differences in the other studied parameters were not statistically significant.

Table (1): Age and Sex distribution of the cases.

Age in years	**Male**	**Female**	**Total**	
30-39	6	8	14	14%
40-49	12	4	16	16%
50-59	18	26	44	44%
60-70	12	14	26	26%

Table (2): Distribution of LVDD according to sex.

Sex	With LVDD	Without LVDD	Total
Male	22	26	48
Female	36	16	52
Total	58	42	100

Table (3) : Distribution of LVDD according to Duration of DM.

Duration of DM in years	Number of cases		With LVDD	Without LVDD
0-5	48	48%	18	30
6-10	26	26%	20	6
11-15	18	18%	14	4
> 15	8	8%	6	2
Total	100		58	42

Table (4) : Distribution of LVDD according to age.

Age in years	With LVDD	Without LVDD	Total
30-39	8 (13.7%)	6	14
40-49	10 (17.24%)	6	16
50-59	18 (31%)	26	44
60-70	22 (37.39%)	4	26
Total	58	42	100

Table (5): Comparison of study parameters among prevalence of diastolic dysfunction.

parameter	LVDD	NO LVDD	P value
Age (years)	54.58±6.51	46.49 ± 7.17	0.0012
BMI (kg/m²)	27.11±2.86	26.17±2.38	0.0744
S. Cholesterol (mg/dl)	190.25 ± 22.46	184.53± 19.57	0.1827
Fasting Plasma Glucose (mg/dl)	192.07 ± 30.92	173.68 ± 29.82	0.0002
HbA1C (%)	7.71 ±1.01	7.28 ± 0.75	0.0157

Figure (1) : Relation of LVDD with HBA1C .

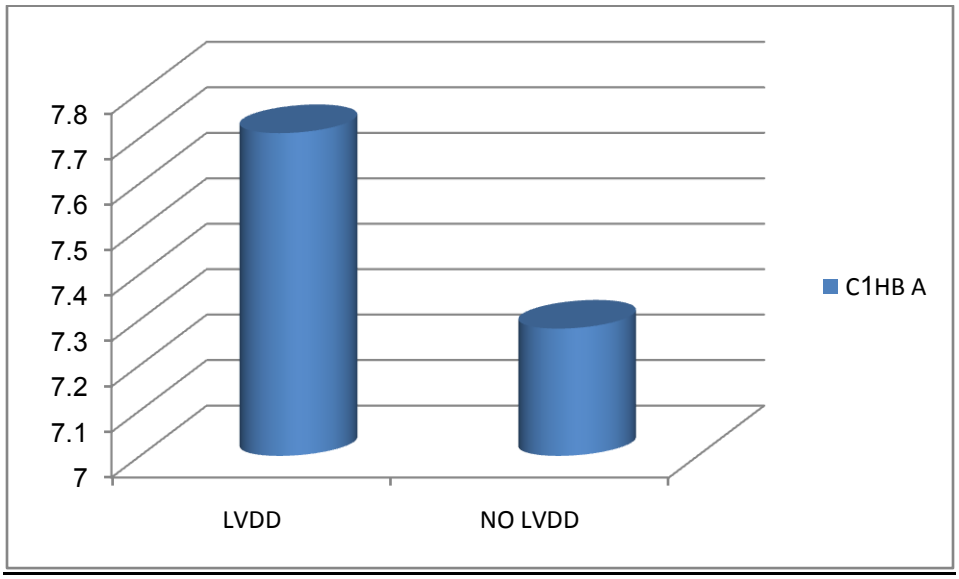

Figure (2) : Relation of LVDD with Age .

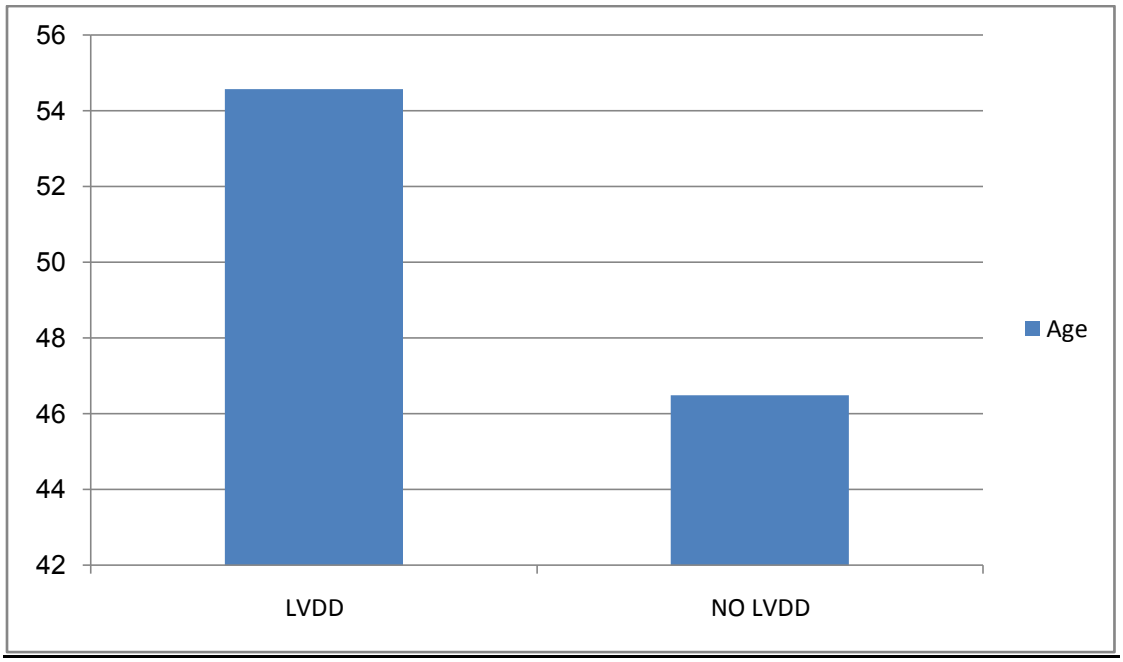

Table (6) : Distribution of LVDD according to Echocardiographic parameters.

Echocardiographic parameters	With LVDD	Without LVDD	P value
Aorta (cm)	3.22 ± 0.36	3.16 ± 0.33	NS
Left Atrium(cm)	3.63 ± 0.32	3.58 ± 0.31	NS
LV(EDD) (cm)	4.9 ±0.39	4.76 ±0.37	NS
LV(ESD)(cm)	3.39 ± 0.43	3.22 ± 0.44	NS
EF (%)	66.89 ± 8.44	69.04 ± 8.65	<0.01
Fractional shortening (%)	30.8 ± 5.29	32.3 ± 5.36	< 0.05
E (cm/s)	0.63 ± 0.18	0.71 ± 0.19	<0.01
A(cm/s)	0.76 ± 0.19	0.64 ± 0.14	<0.01
E/A ratio	0.83 ± 0.22	1.11 ± 0.34	<0.01
DT-E (ms)	244.66 ± 43.61	183.9 ± 22.09	<0.01
IVRT(ms)	108.25± 18.32	81.19± 9.43	<0.01

DISCUSSION:

Diabetes mellitus is a well-studied major risk factor for coronary heart diseases, which is one of the leading causes of death worldwide. Another distinct entity of diabetes-related cardiac affection is the diabetic cardiomyopathy. This entity of cardiac affection by diabetes still needs more and more attention, not only because it is common in diabetic patients, but also because of its easy detection by the simple, inexpensive and widely available diagnostic echocardiography**.**

In the current study most of cases having diabetes less than 5 years, this can be explained with increase the duration of diabetes there is increased incidence of cardiovascular disease as coronary heart diseases, hypertention, and arrhythmia which were excluded from our study design. Other studies dealt with the alteration in LV diastolic function in the early stage of diabetes. One important study done by Attali et al (13) noticed that LV diastolic dysfunction was present in early stage of diabetes mellitus in asymptomatic patients. Soldatos G. et al.(12) also reported similar results. Another study by Di Bonito et al. (14) showed the same findings even in the very early stage of diabetes mellitus (less than 1 year) using Doppler echocardiography.

The present study shows that diastolic dysfunction was more prevalent among females (62%) compared to males (40 %), Deverux et al, demonstrated the same, this can be attributed to hormonal disturbance that associate the period of menopause.(15)

In our study more than half of our patients (58%) showed evidence of myocardial diastolic dysfunction, taking into the consideration that those diabetic patients were free from structural heart diseases, hypertension and diabetic complications or symptomatic coronary artery diseases. Actually many studies reported similar findings (16 - 20). Karvounis et al (18) showed that the LV diastolic function was markedly impaired in asymptomatic patients with type 2 diabetes mellitus as evidenced by decreased E/A ratio, prolonged DT-E and prolonged IVRT. Patil et al., in their study, of 127 asymptomatic subjects found the prevalence of diastolic dysfunction in asymptomatic type 2 diabetics as 54.33% (19). Moreover, Braga et al (20) reported that normotensive patients with type 2 diabetes mellitus without clinical signs of cardiovascular compromising showed signs of diastolic dysfunction .

In our study there is significant correlation between impaired diastolic function and glycemic control. This relationship in diabetic patients is still a matter of debate. In concordance with our results Grandi A.M. et al. (21)

demonstrated an improvement of diastolic function in newly diagnosed diabetics, concomitantly with declining blood glucose levels evaluated after a 15-month period. Fiorina et al. (22) also demonstrated an improvement of diastolic function in every type 1 diabetic patient with uremia after kidney-pancreas transplantation. This improvement appeared to be positively associated with glycemic control. Ponată L et al. (23) found that a short term glycemic control with insulin for 6 months improved diastolic filling abnormalities on repeated doppler echocardiographic examination. On the other hand, in the study of Punzengruber C et al. (24), no correlation between glycemic control over a period of 12 months and left ventricular diastolic function in a fairly well-controlled group of young diabetics could be observed. Also other studies showed that adequate glycemic control for more than 12 months (HbA1c 7.0%), was not associated with significant improvement in the E/A ratio (25, 26).
In the present work , The mean age of subjects with LVDD was higher as compared to subjects without LVDD and correlation was found highly significant (p=0.0012).Similar results were recorded by Mamatha B and Nishkal A (27), This meaning that the older the age at the time of diagnosis, the higher the incidence of LVDD.

Conclusion*:*

We documented the high prevalence of asymptomatic left ventricular diastolic dysfunction in patients with type 2 diabetes without clinical evidence of structural heart disease. Left ventricular diastolic dysfunction was significantly related to the glycemic control and age of patients. Doppler echocardiography is a simple, inexpensive, widely available and sensitive method for the diagnosis and follow-up of cases with diastolic dysfunction. .
We recommend the use of this technique in the routine workup of diabetic patients even in early stages. Further large-scale studies are needed to address the value of early introduction of ACE inhibitors and/or ARBs in diabetic patients without cardiovascular compromising in prevention or even slowing the course of LV diastolic dysfunction.

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