Original Article

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Diastolic Dysfunction in Young Asymptomatic Diabetic Patients

N Senthil[1], K Vengadakrishnan[2], Sumanth Simha Vankineni[3], S Sujatha[2]

[1]Associate Professor, Department of General Medicine, Sri Ramachandra Medical College, Porur, Chennai, Tamil Nadu, India, [2]Professor, Department of General Medicine, Sri Ramachandra Medical College, Porur, Chennai, Tamil Nadu, India, [3]Resident, Department of General Medicine, Sri Ramachandra Medical College, Porur, Chennai, Tamil Nadu, India

Abstract

Background: Heart failure is 2-5 times more common in diabetic subjects than in non-diabetic population and can occur even in the absence of coronary artery disease. The relationship between diastolic function and glycemic control has been a matter of debate and studies have shown that they have no definite relationship. The prognostic importance of subclinical diastolic dysfunction creates the need for early intervention.

Aim and Objectives: To study the prevalence of diastolic dysfunction in young asymptomatic diabetic patients and to analyze whether its prevalence varies with glycemic control and duration of diabetes.

Materials and Methods: The study included 100 young (<40 years with 50 males and 50 females) diabetic patients in Sri Ramachandra Medical College and Hospital from the year 2011 to 2013. 50 healthy controls under 40 years (25 males and 25 females) were taken. All routine lab parameters, fasting and post-prandial sugars, hemoglobin A1c (HbA1c), chest X-ray, electrocardiogram, and two-dimensional echocardiogram were done for all patients.

Results: The overall prevalence of diastolic dysfunction was 30%. Of the 50 females 20 patients (40%) had left ventricular diastolic dysfunction (LVDD), while 10 out of 56 males had LVDD (20%). Among 70 Type II diabetes mellitus (DM) patients, 21 had LVDD (30%) while among 30 Type I DM patients 9 had LVDD (30%). Among 60 patients of <6 months duration of diabetes LVDD was found in 18 patients (30%), of patients who had DM of 6 months-3 years duration, LVDD was found in 9 (30%). Of 10 patients who had DM more than 3 years duration, LVDD was found in 3 patients (30%).60 patients had good glycemic control and 18 had LVDD. 9 patients with HbA1c between 7 and 8 had LVDD (30%) and 3 with HbA1c >8 had LVDD.

Conclusion: Diastolic dysfunction could have no definite relation to duration of diabetes.

Key words: Cardiomyopathy, Diastolic dysfunction, Diabetes mellitus, Echocardiography, Glycemic control

INTRODUCTION

Diastolic left ventricular dysfunction is now increasingly recognized as a condition leading to morbidity, hospitalizations and death. The term "diastolic dysfunction" refers to changes in ventricular diastolic properties that have an adverse effect on stroke volume. Recent studies suggest that isolated diastolic heart failure occurs in 30-60% of all patients presenting to hospitals with evidence of congestive heart failure (CHF). Diastolic heart failure in diabetes is a unique clinical entity. Several factors have been shown to be predisposing conditions associated with the development of diastolic CHF. The most common of these conditions is hypertension. Studies show that 60% of patients with diastolic CHF are hypertensive. Elevations of blood pressure alter left ventricular diastolic function via several mechanisms, some of which are not well-understood. One of these mechanisms is the development of left ventricular hypertrophy. Coronary artery disease (CAD), even in the absence of infarction, is also associated with the development of the left ventricular diastolic dysfunction (LVDD). Less common conditions associated with diastolic CHF are hypertrophic cardiomyopathy, infiltrative cardiomyopathy such as amyloidosis, and rarely restrictive cardiomyopathies. Ventricular function

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Corresponding Author: Dr. K Vengadakrishnan, Department of General Medicine, Sri Ramachandra Medical College, Porur, Chennai, Tamil Nadu, India. E-mail: drkvk1975@gmail.com

is highly dependent on pre-load as demonstrated by the Frank-Starling relationship. Therefore, if ventricular filling (pre-load) is impaired, this will lead to a decrease in stroke volume. The diagnosis of diastolic heart failure is currently based on the presence of signs or symptoms of the CHF such as dyspnea or orthopnea, documentation of normal or only minimally reduced left ventricular systolic function by cardiac imaging technique, and evidence of abnormalities of left ventricular relaxation. This last criterion is the most difficult to document. The analysis of diastolic function can be complex. Unlike systolic dysfunction, there is no single physiological parameter such as ejection fraction that reliably describes the presence and severity of diastolic problems.

Clinical, epidemiological and pathologic data support the presence of a specific cardiomyopathy related to diabetes mellitus (DM). DM is commonly associated with conditions, such as coronary atherosclerosis and hypertension, which may impair myocardial performance. The existence of a diabetic cardiomyopathy was first suggested by Rubler *et al.*[1] in 1972 on the basis of post-mortem findings in four diabetic adults who had CHF in the absence of atherosclerotic, valvular, congenital, hypertensive, or alcoholic heart disease. Diabetic women were especially vulnerable, having congestive, heart failure at twice the frequency experienced by men irrespective of CAD status. The role of severity or duration of diabetes in the development of CHF was not addressed in this study. Further support for the existence of a diabetic cardiomyopathy was provided by Hamby *et al.*, who noted an increased incidence of diabetes in patients with idiopathic cardiomyopathy. Regan[2] described the angiographic and hemodynamic findings in patients with adult-onset diabetes without hypertension or valvular disease.

Since no myocardial ischemia could be demonstrated, abnormalities of the small arteries or capillaries were thought to be responsible for a restriction in myocardial perfusion. Hemodynamic findings included a modest elevation of left ventricular end diastolic pressure and a reduction in both stroke volume and ejection fraction. Ventricular compliance was found to be significantly diminished. A similar impairment of left ventricular compliance was discovered in eight diabetic subjects without evidence of congestive failure (D'Elia *et al.*)[3]. Several mechanisms for diabetic cardiomyopathy have been proposed including small and microvascular disease, autonomic dysfunction, metabolic derangements, interstitial fibrosis and the development of fibrosis, possibly caused by the accumulation of a periodic acid-Schiff-positive glycoprotein, leading to myocardial hypertrophy and diastolic dysfunction. Growth hormone also appears to be involved in the pathogenesis of angiopathy in the diabetic patients.[4-7]

The present study was done to identify the prevalence of diastolic dysfunction in young asymptomatic diabetics and to analyze whether its prevalence varies with glycemic control and duration of diabetes.

MATERIAL AND METHODS

The study included 100 young (<40 years with 50 males and 50 females) diabetic patients in Sri Ramachandra Medical College and Hospital from the year 2011 to 2013. 50 healthy controls under 40 years (25 males and 25 females) were taken. A thorough clinical examination was done. All routine lab parameters, fasting and post-prandial sugars, hemoglobin A1c (HbA1c), Chest X-ray, electrocardiogram (ECG), and two-dimensional echocardiogram (2D ECHO) were done for all patients. Diabetic patients aged >40 years, presence of cardiovascular symptoms, hypertensive (more than 140/90 mm of Hg), abnormal resting ECG, patients with positive TMT, smokers, renal failure, signs of vascular involvement (defined as absent peripheral pulses in the lower limb, amputation because of gangrene) and patients with complications of peripheral neuropathy or retinopathy were excluded from the study.

All ECHO recordings and measurements were obtained by the same observer according to the recommendations of the "American Society of Echocardiography" and were always performed at midday to avoid the influence to the circadian rhythm on LVDD. LVDD was evaluated using well-standardized diagnostic criteria and Doppler measurements were done at end expiration. The definitions published by Canadian consensus on diastolic dysfunction by ECHO were used to classify diastolic dysfunction as normal, impaired relaxation, pseudonormal or restrictive pattern. HbA1c was measured by an affinity binding assay.

RESULTS

Out of 100 young diabetics, 50 males and 50 females were included in the study with 50 healthy controls. The mean age of patients was 29.02 (minimum age 21 years). 30 patients had Type I diabetes. 60 patients had a duration of diabetes less than 6 months (mean duration 3.2 months), 30 patients with duration 6 months-3 years (mean duration 1.33 years), and 10 had duration more than 3 years (mean duration 6.25 years). 60 patients had HbA1c <7, 30 patients with 7-8 and 10 had >8.

Among 60 patients with <6 months duration of diabetes, LVDD was found in 18 patients. Out of 30 patients who had DM of 6 months-3 years duration LVDD was found in 9. Of 10 patients who had DM more than 3 years duration, LVDD was found in 3 patients. Of these 40 patients on

whom HbA1c was done, 70 had good glycemic control and 18 of them had LVDD. 10 had poor glycemic control and 3 of them had LVDD (Table 1).

LVDD was found in 30 patients. All patients had impaired relaxation by ECHO. No patients had pseudonormal pattern or restrictive pattern (Table 2).

DISCUSSION

In the present study, the overall prevalence of LVDD in young diabetic patients is 30%. The study by Zarich *et al.*[7] revealed the prevalence of diastolic dysfunction was 30% only. The earlier studies pointed out that prevalence was more. In several of these earlier reports, many of these asymptomatic diabetic patients were older or may have had coexistent illnesses known to affect ventricular function. Subsequent studies have focused on younger patients and have excluded subjects at risk for cardiac dysfunction with other comorbids.

Of the 50 females 20 patients (40%) had LVDD, while 10 out 56 males had LVDD (20%). In the Framingham Heart study[8] also females outnumbered the males. Among 70 Type II DM patients, 21 had LVDD (30%) while among 30 Type I DM patients 9 had LVDD (30%). In a study by Raev,[9] diastolic dysfunction was present even in patients of 6 months duration of diabetes. Our results also correlate with this study. This indicates that pre-clinical cardiomyopathy in diabetes has different pathogenesis not related to the duration of DM or glycemic control. Diastolic dysfunction in diabetes must involve the same pathogenetic mechanisms as in any other etiology. This is of great interest and has given rise to many hypothetical mechanisms. Correlation of Diastolic dysfunction and autonomic neuropathy among diabetic subjects revealed that diastolic dysfunction and autonomic neuropathy are both common problems among diabetics.

In a study by Mishra *et al.*,[10] duration of diabetes correlated well with diastolic dysfunction which is in contrary to the present study. Studies by Di Bonito *et al.*[11] and Boyer *et al.*[12] had concluded that diastolic dysfunction occurs early in diabetes. From *et al.*[13] had studied the incidence of early heart failure in diabetic patients with LVDD.

The strength of the study is that it studied a specific group of young diabetics with equal males and females with matched controls, but the limitations remain. Subjects with uncomplicated diabetes are difficult to study because of the high incidence of coexistent CAD and hypertension. In this study, we attempted to rule out ischemia by performing non-invasive, tests, such as symptom-limited exercise ECG, which is shown to be reliable in excluding CAD. Although pre-clinical atherosclerosis may have present, it is highly unlikely that is an important confounding variable in explaining the observer abnormalities in left ventricular diastolic function. This study was limited to a small group of well-characterized patients to avoid too many confounding variables.

Table 1: The study group and profiles

Parameter	Number	LVDD
Sex		
Male	50	20
Female	50	10
Types		
Type I DM	30	19
Type II DM	70	21
HbA1c		
<7	60	18
7-8	30	9
>8	10	3
Duration of DM		
<6 months	60	18
6 months-3 years	30	9
>3 years	10	3

DM: Diabetes mellitus, LVDD: Left ventricular diastolic dysfunction, HbA1c: Hemoglobin A1c

Table 2: Transmitral Doppler flow velocity

Doppler parameter	Normal subjects (*N*=70)	Impaired relaxation (*N*=30)
Number of IVRT (ms)	106±17	109±11
E wave (cm/s)	69±11	56±10
A wave (cm/s)	52±9	71±3
E/A	1.34±0.17	0.79+0.07
DT (ms)	189±42	224±51
A wave duration (ms)	129±16	128±25

IVRT: Isovolumetric relaxation time

CONCLUSION

Diastolic dysfunction is present even in early stages of diabetes. The prevalence of diastolic dysfunction in diabetes has a female pre-ponderance in the ratio of 2:1. Diastolic dysfunction does not vary with glycemic control, duration of diabetes or type of diabetes. Even though LVDD has been demonstrated to occur very early in this study, routine ECHO evaluation of all DM patients cannot be recommended, but it is useful to screen all DM patients with the ECHO to detect LVDD.

REFERENCES

1. Rubler S, Dlugash J, Yuceoglu YZ, Kumral T, Branwood AW, Grishman A. New type of cardiomyopathy associated with diabetic glomerulosclerosis. Am J Cardiol 1972;30:595-602.
2. Regan TJ. Congestive heart failure in the diabetic. Ann Rev Med 1983;34:161-8.

3. D'Elia JA, Weinrauch LA, Healy RW, Libertino JA, Bradley RF, Leland OS Jr. Myocardial dysfunction without coronary artery disease in diabetic renal failure. Am J Cardiol 1979;43:193-9.
4. van Heerebeek L, Hamdani N, Handoko ML, Falcao-Pires I, Musters RJ, Kupreishvili K, *et al*. Diastolic stiffness of the failing diabetic heart: Importance of fibrosis, advanced glycation end products, and myocyte resting tension. Circulation 2008;117:43-51.
5. From AM, Scott CG, Chen HH. Changes in diastolic dysfunction in diabetes mellitus over time. Am J Cardiol 2009;103:1463-6.
6. Oh JK, Seward JB, Tajik AJ. Assessment of diastolic dysfunction and diastolic heart failure. In: Oh JK, editor. The Echo Manual. 34th ed. New Delhi: Wolters Kluwer; 2006. p. 120-41.
7. Zarich SW, Nesto RW. Diabetic cardiomyopathy. Am Heart J 1989;118:1000-12.
8. Kannel WB, Hjortland M, Castelli WP. Role of diabetes in congestive heart failure: The Framingham study. Am J Cardiol 1974;34:29-34.
9. Raev DC. Which left ventricular function is impaired earlier in the evolution of diabetic cardiomyopathy? An echocardiographic study of young type I diabetic patients. Diabetes Care 1994;17:633-9.
10. Mishra TK, Rath PK, Mohanty NK, Mishra SK. Left ventricular systolic and diastolic dysfunction and their relationship with microvascular complications in normotensive, asymptomatic patients with type 2 diabetes mellitus. Indian Heart J 2008;60:548-53.
11. Di Bonito P, Cuomo S, Moio N, Sibilio G, Sabatini D, Quattrin S, *et al*. Diastolic dysfunction in patients with non-insulin-dependent diabetes mellitus of short duration. Diabet Med 1996;13:321-4.
12. Boyer JK, Thanigaraj S, Schechtman KB, Pérez JE. Prevalence of ventricular diastolic dysfunction in asymptomatic, normotensive patients with diabetes mellitus. Am J Cardiol 2004;93:870-5.
13. From AM, Scott CG, Chen HH. The development of heart failure in patients with diabetes mellitus and pre-clinical diastolic dysfunction a population-based study. J Am Coll Cardiol 2010;55:300-5.

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