

ORIGINAL ARTICLE

FREQUENCY OF DIASTOLIC DYSFUNCTION IN ASYMPTOMATIC, NORMOTENSIVE TYPE-2 DIABETIC PATIENTS

Fawad Ahmad Randhawa, Malik Tayyab Hussnain*, Shaista Nazir, Faisal Masud

Endocrinology Unit & Diabetes Management Center, *Medical Unit-IV, Services Hospital Lahore, Pakistan

Background: Diabetes mellitus affects heart in multiple ways and can affect virtually any part of heart specifically cardiac myocardium. Hence this involvement can severely affect the cardiac contractility resulting in severely debilitating symptoms of cardiac failure and hampering life. Early diagnosis therefore is of paramount importance as it can enable early diagnoses and treatment to counter the irreversible damage to the cardiac contractility dysfunction. The objective of this study was to determine the frequency of diastolic dysfunction in asymptomatic normotensive type-2 diabetics. **Methods:** In this descriptive case series, 150 consecutive patients with type-2 diabetes mellitus having normal blood pressure and normal resting electrocardiogram and without any symptoms of heart failure were selected from diabetes management center and Doppler echocardiography was performed. Pulmonary venous flow recordings were also obtained from the four-chamber view directed at the right upper pulmonary vein. Presence or absence of diastolic dysfunction will be documented in each case. Valsalva maneuver was used to unmask pseudo-normal patterns of ventricular filling. **Results:** Of the total, 72(48%) of patients had diastolic dysfunction. **Conclusion:** Type-2 diabetes mellitus is associated with diastolic dysfunction in the absence of other causes of diastolic dysfunction.

Keywords: Diabetes Mellitus, Type-2, Diastolic dysfunction, Normotensive

J Ayub Med Coll Abbottabad 2014;26(1):35-7

INTRODUCTION

Type-2 Mellitus (T2DM) is almost reaching epidemic proportions. With tight hyperglycemic control the risk reduction is 24% for any diabetes related end-point and 32% for death related to diabetes, against only 0.9% decrease in HbA1c level.¹ The incidence of Ischemic Heart Disease (IHD) is higher in diabetic patient as compared to general population.² Diabetes is associated with increased cardiovascular complications, the most common of which are IHD and left ventricular dysfunction.³ The presence of myocardial dysfunction in diabetic patients in the absence of ischemic, valvular or hypertensive heart disease has been termed as “diabetic cardiomyopathy”.^{4,5} Diastolic dysfunction has been described as an early sign of this diabetic heart muscle disease preceding the systolic damage.⁶

Abnormalities in diastolic function may occur in the presence or absence of a clinical syndrome of heart failure and with normal or abnormal systolic function. Therefore, despite diastolic dysfunction describing an abnormal mechanical property, diastolic heart failure on the other hand describes a clinical syndrome.⁷ Cardiac catheterization with simultaneous pressure and volume measurements is the “Gold Standard” for assessing left ventricular diastolic dysfunctions. Nevertheless this diagnostic method is invasive and cannot be performed in all patients with suspected diastolic dysfunction. During the last two decades, Doppler echocardiography has emerged as an important and noninvasive diagnostic tool providing reliable data on diastolic performance.⁸ Some studies, which used Doppler assessment of transmitral flow

velocity, could have underestimated the prevalence of left ventricular diastolic dysfunctions, because they neglected to account for pseudo-normal patterns of ventricular filling, which are often noted in the evaluation of left ventricular diastolic function.⁹ Thus, the frequency of left ventricular diastolic dysfunctions in subjects with diabetes should be reassessed by using methods designed to unmask pseudo-normal ventricular filling patterns. It was previously shown that the Valsalva maneuver can be easily used for this purpose and that the results of the technique are in accordance with the results of pulmonary venous recordings, which have also been suggested as an alternate means of identifying pseudo-normal patterns.^{10,11} Left ventricular diastolic dysfunction may represent the first stage of diabetic cardiomyopathy, reinforcing the importance of early assessment and hence early treatment of diastolic function at asymptomatic stage in individuals with diabetes. Hence this study was planned to see the occurrence of diastolic dysfunction in asymptomatic, normotensive type-2 diabetic patients.

MATERIAL AND METHODS

In this descriptive case series, patients with T2DM having normal blood pressure and normal resting electrocardiogram and without any symptoms of heart failure were selected from Diabetes management center, Services Hospital Lahore. Patients having segmental wall motion defects and valvular heart disease on Doppler echocardiography, taking any antihypertensive medication, serum creatinine >1.5mg/dl, patients with T2DM diagnosed for more than 10 years and whose

fasting blood sugar level is ≥ 126 mg/dl or random blood sugar level is ≥ 200 mg/dl at the time of diagnosis were excluded. These patients were then booked for Doppler echocardiography at a later date after informed consent. Doppler echocardiography was performed on all patients in left lateral decubitus position using standard parasternal, short axis, and apical views. Pulmonary venous flow recordings were obtained from the four-chamber view directed at the right upper pulmonary vein. Presence or absence of diastolic dysfunction was documented in each case. Valsalva maneuver was used to unmask pseudo-normal patterns of ventricular filling.

RESULTS

A total of 150 consecutive patients with T2DM were selected from the Diabetes Management Centre of Services Hospital Lahore from 1st January to 30th June, 2011. Amongst them, 93 (62%) were males and 57 (38%) were females. Mean age was 46.26 ± 8.096 years. Of the total, 72 (48%) patients were found to have diastolic dysfunction and 78 (52%) patients did not have diastolic dysfunction. (Table-1) Diastolic dysfunction by gender is shown in Table-2.

Table-1: Diastolic dysfunction by Age

Age range	Diastolic dysfunction		Total (100%)
	Yes	No	
30-40	12 (36%)	21 (64%)	33 (22%)
41-50	27 (37.5%)	45 (62.5%)	72 (48%)
51-60	33 (73%)	12 (27%)	45 (30%)
Total	72 (48%)	78 (52%)	150 (100%)

Table-2: Diastolic dysfunction by Gender

Gender	Diastolic dysfunction		Total (100%)
	Yes	No	
Male	48 (52%)	45 (48%)	93 (62%)
Female	24 (42%)	33 (58%)	57 (38%)
Total	72 (48%)	78 (52%)	150 (100%)

DISCUSSION

Diabetes is associated with left ventricular diastolic and systolic dysfunction known as diabetic cardiomyopathy. Echocardiography is helpful for the detection of diastolic dysfunction and screening for asymptomatic diabetic cardiomyopathy should be performed in all asymptomatic diabetic subjects. Identification of diabetic cardiomyopathy should result in the initiation of therapies to prevent the progression of diabetic cardiomyopathy.¹² Isolated diastolic dysfunction is the cause of congestive heart failure in 50% of patients with normal systolic function. Several factors have been shown to be predisposing conditions associated with the development of diastolic dysfunction and diastolic heart failure.¹³ Doppler echocardiography is used to evaluate global myocardial performance.¹⁴

Diastolic dysfunction is an important predictor of morbidity and mortality in patients with metabolic syndrome.¹⁵ Diabetic cardiomyopathy in humans is

characterized by diastolic dysfunction, which may precede the development of systolic dysfunction. In study, echocardiography performed in 87 patients with type 1 diabetes mellitus without known coronary artery disease revealed diastolic dysfunction as indicated by reduced early diastolic filling, increased atrial filling, extended isovolumetric relaxation, and increased supraventricular premature beats.¹⁶ Similarly in individuals with uncomplicated type 1 diabetes without clinically apparent macrovascular or microvascular complications, Carugo *et al*¹⁷ reported an age-related increase in diastolic diameter. Similar well controlled T2DM patients revealed a prevalence of diastolic dysfunction in upto 30% cases.¹⁸ The use of flow and tissue Doppler techniques suggests an even greater prevalence of diastolic dysfunction (40-75%) in individuals with Type-1 and T2DM without overt coronary artery disease.¹⁹ Indeed, indices for diastolic dysfunction were impaired in patients with T2DM.^{20,21}

Many local studies also have been conducted in the past that studied various factors that could exert their effect by causing diastolic dysfunction of the heart. One them concluded that diastolic dysfunction is much more prevalent than previously suggested in patients with T2DM. Hence diastolic dysfunction is an early marker of diabetic cardiomyopathy.²² Despite the association between diabetes and cardiovascular morbidity and mortality, the prevalence of diastolic dysfunction in asymptomatic patients with NIDDM or its relation with other diabetic complications (nephropathy, retinopathy, and neuropathy) is not well defined and data are controversial.^{23,24} The main finding of this study is that 48% of patients with T2DM without evidence of structural heart disease or arterial hypertension demonstrate diastolic dysfunction of the left ventricle. So this can be inferred that T2DM is an independent marker of diastolic dysfunction.

Diabetic cardiomyopathy was described in diabetic patients who had no evidence of coronary artery disease, arterial hypertension, or valvular heart disease.^{25,26} Decreased left ventricular diastolic function in patients with T2DM found in this study is in accordance with previous studies.^{23,24,27} One case control study conducted over the course of three years also concluded that around 66% of the patients had diastolic dysfunction independent of other factors.²⁸ However this case control study had more females and they also had fasting lipid profile of their patients done which was lacking in current study.

This study has some pitfalls. Firstly there were no controls. Moreover duration of T2DM was not taken in to consideration which has considerable effect on the diastolic dysfunction. Di Carli *et al* also demonstrated that diastolic dysfunction appeared in the early stages of the disease.²⁹ Only one parameter, i.e., T2DM was studied. Other parameters like smoking and

hypercholesterolemia were not taken in to consideration which have profound effect on myocardium, were not studied.²⁸ Coronary angiography was not performed in T2DM patients in order to exclude coronary artery disease as the underlying cause of left ventricle diastolic dysfunction. Nonetheless, only patients without any clinical signs of coronary artery disease were carefully included in the study. Pulmonary venous flow to obtain comparable parameters for left ventricle diastolic function was not recorded. However, it was believed that these limitations do not invalidate the main findings of the study.

CONCLUSION

Type-2 diabetes Mellitus is associated with a higher prevalence of impaired left ventricular diastolic function. T2DM was the strongest independent predictor of asymptomatic left ventricular diastolic dysfunction in patients without structural heart disease or arterial hypertension.

REFERENCES

- Khan Z, Iqbal MA, Nadeem MA, Shoaib S. Rosiglitazone and Metformin in patients with type-2 Diabetes Mellitus who are inadequately controlled on Metformin alone. *Ann King Edward Med Uni* 2005;11:20-3.
- Nagra MH, Bilal A, Shahid M, Amin K. Incidence of Ischemic Heart Disease in patients with non insulin dependent Diabetes Mellitus. *Professional Med J* 2004;11:320-7.
- Aamir AH. Targets for treating type-2 diabetes and preventing its complications: can we achieve it? *Pak J Med Res* 2004;43:95-6.
- Boyer JK, Thanigaraj S, Schechtman KB, Perez JE. Prevalence of ventricular diastolic dysfunction in asymptomatic, normotensive patients with diabetes mellitus. *Am J Cardiol* 2004;93:870-5.
- Fang ZY, Yuda S, Anderson V, Short L, Case C, Marwick TH. Echocardiographic detection of early diabetic myocardial disease. *J Am Coll Cardiol* 2003;41:611-7.
- Ali L, Abid AR, Mohyuddin MT, Azhar M. Echocardiographic evaluation of patients with diastolic dysfunction. *Pak J Cardiol* 2005;16:143-8.
- Gull A, Rehman A, Jalil A. Changes in glycosylated proteins in type-2 diabetic patients with and without complications. *J Ayub Med Coll Abbottabad* 2005;17(3):33-7.
- Cosson S, Kevorkian JP. Left ventricular diastolic dysfunction: an early sign of diabetic cardiomyopathy? *Diabetes Metab* 2003;29:455-66.
- Cakir M, Baskal N, Güllü S, Erdogan M, Atilla E, Erol Ç, *et al.* Microalbuminuria, nondipping and diastolic dysfunction in normotensive type 2 diabetic Patients. *Turk J Endocrinol Metab* 2003;1:23-9.
- Zalgoitia M, Ismaeil MF, Anderson L, Maklady FA. Prevalence of diastolic dysfunction in normotensive, asymptomatic patients with well-controlled type 2 diabetes mellitus. *Am J Cardiol* 2001;87:320-3.
- Poirier P, Bogaty P, Garneau C, Marois L, Dumesnil JG. Diastolic dysfunction in normotensive men with well controlled type 2 diabetes. *Diabetes Care* 2001;24:5-10.
- Hameedullah, Faheem M, Bahadar S, Hafizullah M, Najeeb S. Effect of glycaemic status on left ventricular diastolic function in normotensive type 2 diabetic patients. *J Ayub Med Coll Abbottabad* 2009;21(3):139-44.
- Ali L, Abid AR, Azhar M. Risk factors of Diastolic heart failure; an epidemiological analytic study. *Professional Med J* 2006;13:410-6.
- Najafian J, Khaledian MR, Farahnaz F. A study of the relationship between myocardial performance index and left ventricular end-diastolic pressure in patients with left ventricular systolic dysfunction. *Pak J Cardiol* 2006;17:57-9.
- Khan AR, Khan MQ. Association and pattern of Diastolic dysfunction in patients of metabolic syndrome. *J Ayub Med Coll Abbottabad* 2008;20(2):70-5.
- Schannwell CM, Schneppenheim M, Perings S, Plehn G, Strauer BE. Left ventricular diastolic dysfunction as an early manifestation of diabetic cardiomyopathy. *Cardiology* 2002;98:33-9.
- Carugo S, Giannattasio C, Calchera I, Paleari F, Gorgoglione MG, Grappiolo A, *et al.* Progression of functional and structural cardiac alterations in young normotensive uncomplicated patients with type 1 diabetes mellitus. *J Hypertens* 2001;19:1675-80.
- Beljic T, Miric M. Improved metabolic control does not reverse left ventricular filling abnormalities in newly diagnosed non-insulin-dependent diabetes patients. *Acta Diabetol* 1994;31:147-50.
- 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.
- Boudina S. Clinical manifestations of diabetic cardiomyopathy. *Heart Metab* 2009;45:10-4.
- Ozasa N, Furukawa Y, Morimoto T, Tadamura E, Kita T, Kimura T. Relation among left ventricular mass, insulin resistance, and hemodynamic parameters in type 2 diabetes. *Hypertens Res* 2008;31:425-32.
- Ashraf S, Basir F. Association of hypertension and diastolic dysfunction with type-2 diabetes mellitus. *Pak J Med Sci* 2007;23(3):344-8.
- Annonu AK, Fattah AA, Mokhtar MS, Ghareeb S, Elhendy A. Left ventricular systolic and diastolic functional abnormalities in asymptomatic patients with non-insulin-dependent diabetes mellitus. *J Am Soc Echocardiogr* 2001;14:885-91.
- Poirier P, Bogaty P, Garneau C, Marois L, Dumesnil JG. 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.
- Yudkin JS. The United Kingdom Prospective Diabetes Study – everything you needed to know about diabetes but were afraid to ask? *Eur Heart J* 1999;20:781-3.
- Yudkin JS. Vascular events and diabetes: acute myocardial infarction and stroke. In: Alberti KG, Zimmet P, DeFronzo RA, Keen H, editors. *International textbook of diabetes*. Chichester (UK): Wiley; 1997.p.1255-79.
- Zalgoitia M, Ismaeil MF, Anderson L, Maklady FA. Prevalence of diastolic dysfunction in normotensive, asymptomatic patients with well-controlled type 2 diabetes mellitus. *Am J Cardiol* 2001;87:320-3.
- Bajraktari G, Qirko S, Rexhepaj N, Bakalli A, Beqiri A, Elezi S, *et al.* Non-Insulin Dependent Diabetes as an Independent Predictor of Asymptomatic Left Ventricular Diastolic Dysfunction *Croat Med J* 2005;46:225-31.
- Di Carli MF, Bianco-Battles D, Landa ME, Kazmers A, Groehn H, Muzik O, *et al.* Effects of autonomic neuropathy on coronary blood flow in patients with diabetes mellitus. *Circulation* 1999;100:813-9.

Address for Correspondence:

Fawad Ahmad Randhawa, 95/7-A/5 Fatima Villa Sarwar Road Lahore Cantt. 54810 Lahore, Pakistan
 Cell: +92-333-4283332, Office: +92-4299204960