Echocardiographic Evaluation of Diastolic Function in Asymptomatic Type 2 Diabetes

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ABSTRACT

Introduction: Diabetes mellitus is an established risk factor for congestive cardiac failure in which the diastolic function is impaired earlier than the systolic function and majority of these patients maybe asymptomatic without signs of overt heart failure.

Methods: A cross sectional hospital based study was done which included 100 asymptomatic patients with type 2 diabetes without evidence of coronary artery disease, congestive heart failure, thyroid or overt renal disease. LVDD was evaluated by Doppler echocardiography, which included the valsalva maneuver to unmask the pseudonormal pattern of left ventricular filling. The prevalence of LVDD and the associated risk factors were assessed.

Results: LVDD was found in 71 subjects (71%), of whom 60 had impaired relaxation and 11 had a pseudonormal pattern of ventricular filling. Systolic function was normal in all subjects, and there was no correlation between LVDD and indexes of metabolic control. It was also found that age ≥45 years was associated with an almost three times higher risk for the development of diastolic dysfunction in type 2 diabetes. Females were at a two times higher risk of developing diastolic dysfunction than when compared to men. Duration of diabetes ≥ two years was associated with a two times higher risk for developing diastolic dysfunction.

Conclusions: LVDD is much more common than previously reported in subjects with well-controlled type 2 diabetes who are free of clinically detectable heart disease. The high prevalence of this phenomenon in this high-risk population suggests that screening for LVDD in type 2 diabetes should include procedures such as the valsalva maneuver to unmask a pseudonormal pattern of ventricular filling.

Keywords: *diabetes mellitus, diastolic dysfunction, echocardiography, impaired relaxation, pseudonormal*

INTRODUCTION

Diabetes mellitus is an established risk factor for congestive heart failure, but the knowledge of the patho-physiology and treatment is limited. Prevalence of diabetes in heart failure ranges from 10 to more than 30%.[1,2] The Framingham Heart study has shown that the incidence of congestive cardiac failure in diabetic patients occurs irrespective of coronary artery disease or hypertension.[1] In overt heart failure, diastolic dysfunction often co-exists with systolic dysfunction as a consequence of ischemic heart disease, but diastolic

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dysfunction is a frequent finding in type 2 diabetes mellitus without signs and symptoms of heart disease and is presumably due to diabetic cardiomyopathy. Left ventricular diastolic function (LVDF) is affected earlier than systolic function in the development of congestive cardiac failure.[3] Therefore left ventricular diastolic dysfunction may represent the first stage of diabetic cardiomyopathy, thus an early examination of left ventricular diastolic function may help detect this condition in patients with diabetes, thereby allowing early intervention for a more favorable outcome.[4]

This study was done to understand the burden of left ventricular diastolic dysfunction (LVDD) in patients with type 2 diabetes and to assess the risk factors for the development of diastolic dysfunction in such patients.

METHODS

A cross sectional study that was conducted in the department of Internal Medicine of B. P. Koirala Institute of Health Sciences, Dharan from June, 2004 to July, 2005. Patients with type 2 diabetes attending the out patients clinic and the diabetes clinic who were asymptomatic were enrolled in the study.

One hundred diabetic patients who were on lifestyle modification and treatment (oral medications or insulin) with an ejection fraction of more than 50% on echocardiogram and no clinical evidence of cardio-respiratory illness were included in the study.

Patients were excluded if they had other co-existing cardiac illnesses like valvular heart disease, prior history of angina or myocardial infarction, regional wall motion abnormalities, hypertrophic cardiomyopathy, constrictive pericarditis, pericardial effusion or thyroid disease. Those with poor cardio echo windows were also excluded.

Informed consent was obtained from the subjects and the hospital ethical board committee ethically approved the study.

All subjects had their fasting blood glucose levels (enzymatic glucose oxidase peroxidase method), creatinine, urinary protein and lipid profiles estimated. They also had an echocardiogram done to assess the presence of diastolic dysfunction and if present it was graded as impaired relaxation, pseudonormal pattern or restrictive physiology. Echocardiograms were done using the commercially available Hewlett Packard Sonos 1800. Echocardiography done to detect diastolic dysfunction was done by assessing the E/A ratio, IVRT isovolumetric relaxation time (IVRT) and the deceleration time (DT) in pulsed wave Doppler. Impaired relaxation (grade I diastolic dysfunction) was detected when the E/A ratio was less than 1, IVRT more than 240 msec, DT more tan 90 msec. Pseudonormal pattern (grade II diastolic dysfunction) was diagnosed when the E/A ratio was less than 1 after valsalva maneuver (E/A more than 1 prior to valsalva) and restrictive physiology (grade III diastolic dysfunction) when E/A ratio of more than 1.5, DT less than 150msec and IVRT less than 70 msec.

The subjects were divided into two groups, those with normal diastolic function and those with diastolic dysfunction. All data were analyzed by using statistical package for social sciences (SPSS) version 10 for windows. Comparisons between proportions were carried out using the χ^2 test, and a P value less than 0.05 was considered as statistically significant. Binary logistic regression analysis was applied to compute odds ratio (95% CI) and variables showing a statistical significance were simultaneously considered in the multivariate logistic regression analysis to determine the significant independent risk factors of diastolic dysfunction.

RESULTS

A total of 122 patients were initially screened for the study. Twenty two were excluded as 11 patients had systolic dysfunction, four had evidence of regional wall motion abnormalities, four had valvular heart disease and three had poor cardio echo window on echocardiography. Of the 100 patients that were included in the study, diastolic dysfunction was detected in 71 patients while 29 of them had normal echocardiographic findings. Among the 71 patients who had diastolic dysfunction, impaired relaxation was detected in 60 (60%) and pseudonormal pattern was detected in 11 (11%) which was unmasked by the valsalva maneuver. Restrictive physiology was not noted in any patients (Figure 1).

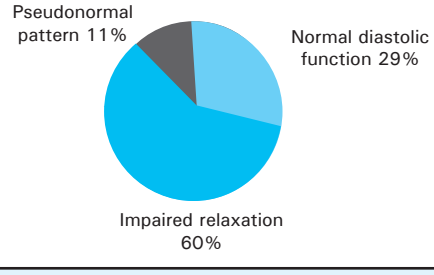

Figure 1. Echocardiographic assessment of left ventricular function

The potential risk factors for the development of diastolic dysfunction in type 2 diabetics that were determined were; (a) age ≥45 years was associated with an almost three times higher risk for the development of diastolic dysfunction, (b) females had almost two times a higher risk for the development of diastolic dysfunction as compared with men, and (c) patients with diabetes of more than two years duration had a two times higher risk of developing diastolic dysfunction (Table 1).

Table 1. Comparison of characteristics between subjects with normal and those with diastolic dysfunction.

Variables	Normal (n = 29)	Diastolic dysfunction (n = 71)	P value	Odds ratio	(95% CI)
Age (years)	46.9 ± 10.2	52.3 ± 9.9	0.015	3.62	1.4 – 8.9
Male: female	20:9	38:33	0.15	1.92	0.7 – 4.8
Duration of diabetes (years)	1.8 ± 0.8	5.3 ± 1.1	0.003	3.2	1.2 – 8.1
Systolic blood pressure (mm Hg)	126.2 ± 14.4	130.1 ± 16.1	0.26	1.3	0.5 – 3.5
Diastolic blood pressure (mm Hg)	81.3 ± 9.3	82.9 ± 8.4	0.41	1.2	0.2 – 6.5
Smokers	12	26	0.65	0.8	0.3 – 1.9
BMI (kg/m^2)	23.6 ± 2.4	23.8 ± 3.1	0.73	1.3	0.6 – 1.7
Waist: Hip ratio	0.96 ± 0.40	0.97 ± 0.63	0.53	1.2	0.5 – 2.8
Fasting plasma glucose (mg/dl)	164.8 ± 49.8	161.7 ± 56.1	0.79	0.8	0.4 – 2.2
Serum creatinine (mg/dl)	0.81 ± 0.21	0.84 ± 0.26	0.58	0.8	0.7 – 2.4
Total cholesterol (mg/dl)	173.1 ± 25.5	176.1 ± 42.9	0.65	2.9	0.8 – 10.9
HDL cholesterol (mg/dl)	42.4 ± 9.1	42.4 ± 8.2	0.96	1.5	0.6 – 3.8
Triglycerides (mg/dl)	164.4 ± 90.8	143.9 ± 63.8	0.21	0.9	0.4 – 2.3
LDL cholesterol (mg/dl)	98.5 ± 26.9	105.7 ± 37.8	0.35	1.3	0.5 – 3.1
24 hour urinary protein excretion (gm/24 hours)	0.71 ± 0.22	0.75 ± .35	0.86	0.9	0.6 – 1.9
LVH on ECG	1	13	0.05		

Table 2. Comparison of echocardiographic parameters between subjects with normal and those with diastolic dysfunction

Echocardiographic parameters	Normal (n = 29)	Impaired relaxation (n = 60)	Pseudonormal pattern (n = 11)
Ejection fraction (%)	61.3±7.6	61.7±8.2	57.7±5.5
E wave (cm/s)	781±131	425±101	816±79 561±86*
A wave (cm/s)	620±105	733±148	673±82 680±89*
E/A ratio	1.26±0.16	0.71±0.05	1.22±0.18 0.76±0.11*
DT (ms)	173±34	246±55	179±24
IVRT (ms)	88.8±14	120.7±13	90.1±12

* after valsalva

DISCUSSION

Epidemiological data indicate a greater risk of cardiovascular morbidity and mortality, particularly congestive cardiac failure, in diabetic subjects as compared with those without diabetes.[5] The prevalence of diabetes mellitus in heart failure population is close to 20% as compared with 4 to 6% in control populations.[6] Diabetic cardiomyopathy was first described in 1972 by Rubler et al on the basis of post mortem findings and the diastolic dysfunction lies independent of ischemic, valvular, congenital, hypertensive or alcohol related heart disease.[7] Left ventricular diastolic dysfunction may represent the first stage of diabetic cardiomyopathy, reinforcing the importance of early examination of diastolic function in individuals with diabetes.

This study showed that the prevalence of diastolic dysfunction in type 2 diabetic patients was 71% and among them impaired relaxation was detected in 60% and pseudonormal pattern of left ventricular filling was noted in 11%. Poirier et al in 2001 in Canada attempted to determine the prevalence of left ventricular diastolic dysfunction in middle-aged asymptomatic subjects with type 2 diabetes in a study, which included 46 men who has no evidence of diabetic complications, hypertension, coronary artery disease, congestive cardiac failure, thyroid or renal disease. Left ventricular

diastolic dysfunction was found in 28 (60%) subjects, of whom 13(28%) had a pseudonormal pattern of ventricular filling and 15(32%) had impaired relaxation.[8] Bajraktari et al in 2004 in Kosovo demonstrated that left ventricular diastolic dysfunction was present in 68.8% of asymptomatic type 2 diabetic patients as compared to 34.9% in the control group without diabetes which was due to the presence of asymptomatic diabetic cardiomyopathy which was present in the diabetic population.[9]

It was also noted that diastolic dysfunction was noted to be more common among diabetic women and they also had a more advanced form of diastolic dysfunction as compared to men, i.e. pseudonormal pattern of left ventricular filling (21.2% vs. 10.5%). The Strong Heart study by Devereuex and colleagues in 2000 also demonstrated that diastolic dysfunction is more prevalent in women then in men.[10] This could be due to hormonal changes that accompany after menopause.

Patients with diastolic dysfunction were older than those without diastolic dysfunction and the duration of diabetes in these group of patients were also longer.

The relationship between diastolic dysfunction and glycemic control is still a matter of debate. Our study did not find any difference between the fasting blood glucose between the two groups. It was noted that among those with diastolic dysfunction the use of oral hypoglycemic agents and/or insulin was higher as compared to those without diastolic dysfunction (80.2% vs. 68.9%), thus this could have resulted in the blood glucose levels being similar despite the presence of asymptomatic diastolic dysfunction. Poirier and colleagues also did not find any difference in the glycemic indices and concluded that fasting blood glucose levels did not correlate with the presence of diastolic dysfunction in type 2 diabetes.[8] However, Holzmann and colleagues demonstrated that the presence of diastolic dysfunction is related to the concentrations of fasting blood glucose.[11]

It was also noted that in both the study groups the body mass index was normal and the difference between the two groups were not significant. This normal body mass index could be due to the racial and dietary factors, which is different between the South East Asian population and the Caucasian and the Black population.

The limitation of our study was that angiography was not performed due to its unavailability at our centre, thus the possibility of coronary artery disease could not be completely excluded however the absence of clinical, electrocardiographic and echocardiographic evidence makes it unlikely.

CONCLUSIONS

Left ventricular diastolic dysfunction is much more common than previously reported in subjects with well controlled asymptomatic type 2 diabetes who are free of clinically detectable heart disease. The high prevalence of diastolic dysfunction in this high-risk population suggests that screening for left ventricular diastolic dysfunction should include procedures such as the valsalva maneuver to umask the pseudonormal pattern of left ventricular filling.

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