Original research article:

Prevalence of diabetic cardiomyopathy -a prospective study

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Abstract:

Aims : Diabetic cardiomyopathy, characterized by left ventricular (LV) dysfunction and LV hypertrophy independent of myocardial ischaemia and hypertension, could contribute to the increased life-time risk of congestive heart failure seen in patients with diabetes However, only limited information is currently available regarding the prevalence and outcome of diabetic cardiomyopathy.in this part of country.

Material and Methods: we randomly selected 1564 diabetic patients attending medicine ,and diabetic out patient departments in Government Coimbatore medical college hospital, coimbatore with no previous history of hypertension or cardiac diseases.The study period was between January 2018 to June 2018

Results: We studied 1564 adults 896 (57%)males and668 (43%)females with diabetes and no previous evidence of structural heart disease,By echocardiography, diabetic cardiomyopathy was present in 42% of patients. Screening with combinations of clinical parameters (gender, systolic blood pressure, and body mass index), resulted in high negative predictive values for diabetic cardiomyopathy

Conclusion: Diabetic cardiomyopathy is common. . Echocardiography, the cornerstone of diagnostic evaluation for LV dysfunction and LVH, Screening with combinations of simple clinical parameters, can be useful to identify those patients needing further evaluation. Patients with diabetic cardiomyopathy are at increased risk for functional deterioration and possibly cardiovascular events during follow-up hense strict control of diabetes and lifestyle modification and regular followup with cardiologist is must.

Introduction:

Cardiovascular complications, mainly as a consequence of premature and accelerated coronary disease, are the leading cause of morbidity and mortality in patients with diabetes worldwide, especially in India. In addition, there is an increased life-time risk of congestive heart failure and these patients are over-represented in large heart failure databases. Clinical and experimental studies support the concept of a diabetic cardiomyopathy with functional, biochemical, and morphological myocardial abnormalities independent of myocardial ischaemia and hypertension, leading to left ventricular (LV) dysfunction and LV hypertrophy (LVH) in a substantial proportion of type I and II diabetics. Besides coronary disease, LV dysfunction and LVH are the most promising therapeutic targets to reduce cardiac morbidity and mortality in diabetic patients. Echocardiography, the

cornerstone of diagnostic evaluation for LV dysfunction and LVH, is not currently performed routinely in diabetic patients because of limited availability and relatively high cost. A simple test to identify those patients with the highest likelihood of LV dysfunction and LVH and therefore requiring further evaluation would be attractive. Brain natriuretic peptide (BNP) and high-sensitivity C-reactive protein, which reflect haemodynamic stress and inflammation, respectively, are potential biochemical screening tests for this purpose.

The objectives of this study in diabetic patients without previously known heart disease were: first, to assess the prevalence of systolic and diastolic LV dysfunction and LVH as diagnosed by comprehensive Doppler echocardiography;.

Methods:

We select patients randomly from our diabetes outpatient and medicine out patients clinic, 1564 adults with type II diabetes treated with insulin and/or oral anti diabetics who were in sinus rhythm. Exclusion criteria were previous diagnosis, symptoms or signs of heart failure, coronary or other structural heart disease, untreated hypertension, acute infections, alcohol or drug abuse, and elevated serum creatinine. After a detailed history and physical examination including the Framingham heart failure criteria non-fasting venous blood samples were obtained, a standard 12-lead electrocardiogram was acquired and Doppler echocardiography was performed on the same day.

Laboratory analysis

high-sensitivity C-reactive protein. In addition, serum creatinine, glucose, haemoglobin A1c, total cholesterol, LDL cholesterol, and triglycerides were measured by standard techniques.

Echocardiography

Doppler echocardiography was performed by one of two cardiologists who were blinded to laboratory results, using a Two-dimensional echocardiography and M-mode measurements were obtained in standard views. Left ventricular ejection fraction was measured using a modified Simpson's rule algorithm or, if volumes could not be quantified due to limited image quality, by visual assessment. Left ventricular mass was determined using Devereux's formula.Each participant underwent pulsed-wave Doppler examination of mitral and pulmonary venous inflow and Doppler tissue imaging of the mitral annulus. Peak values of mitral E- and A-wave velocities and E/A ratios before and during Valsalva manoeuvre, A-wave duration (A_{dur}) and deceleration time of the E-wave (DT) were recorded and ΔE/A was calculated as E/A before − E/A during Valsalva manoeuvre. Pulmonary venous flow measurements included peak systolic (S) and diastolic (D) flow velocities and duration of atrial reversal flow (AR_{dur}). In addition, tissue Doppler imaging of the mitral annulus was obtained in the apical four-chamber view and the early diastolic peak velocity (E′) was recorded

Left ventricular systolic dysfunction was defined as an LV ejection fraction <45% and LV end-diastolic internal dimension index >3.2 cm/m^2 or LV end-diastolic volume index >102 mL/m^2 Diastolic dysfunction was categorized as mild, defined as impaired relaxation without evidence of increased filling pressures ($E/A \leq 0.75$, $\Delta E/A < 0.5$, $E/E' < 10$, $S > D$, $AR_{dur} < A_{dur}$); moderate, defined as impaired relaxation associated with moderate elevation of filling pressures or pseudo normal filling (E/A, >0.75 to <1.50; DT > 140 ms, $\Delta E/A \geq 0.5$, $E/E' \geq 10$, $S < D$ or $AR_{dur} > A_{dur} + 30$ ms); or severe, defined as advanced reduction in compliance or restrictive filling ($E/A > 1.5$, DT < 140 ms, $\Delta E/A \geq 0.5$ (reversible) or <0.5 (fixed), $E/E' \geq 10$, $S < D$or $AR_{dur} > A_{dur} + 30$ ms), as described previously. Participants with $E/A > 0.75$ were required to have two or more additional Doppler criteria consistent with moderate or severe diastolic dysfunction to be so classified and were otherwise classified

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as indeterminate diastolic function. For further comparison, the groups with normal and indeterminate function were combined. Left ventricular hypertrophy was defined as LV mass index ≥131 g/m^2 for men and ≥100 g/m^2 for women.

Electrocardiogram

Electrocardiographic LVH was diagnosed with the Sokolow–Lyons index (SV_1 + $RV_{5–6}$) >38 mm or the Cornell modified index [(RaVL + SV_3) × QRS duration in men; (RaVL + SV_3 + 6 mm) × QRS duration in women)] > 2440 mm ms.

Definition diabetic cardiomyopathy

Diabetic cardiomyopathy was defined as the presence of LV dysfunction and/or LVH by Doppler echocardiography in type II diabetic patients treated with insulin and/or oral antidiabetics in the absence of clinical evidence of coronary/other structural heart disease or untreated hypertension.

Statistical analysis

Values are expressed as mean ± 1 SD, median [inter-quartile range (IQR)], or frequencies as indicated. Between-group differences were compared using the χ^2 test, Fisher's exact test, or Student's t-test, as appropriate. Because BNP and high-sensitivity C-reactive protein values were not normally distributed, the Mann–Whitney test was used for comparison. Receiver operator characteristic (ROC) curves were constructed to calculate the predictive values of BNP and high-sensitivity C-reactive protein for the diagnosis of LV dysfunction, LVH, and diabetic cardiomyopathy and the values with best diagnostic accuracies where obtained. A multiple logistic regression model was used for evaluating the ability of biochemical markers to identify LV dysfunction, LVH, and diabetic cardiomyopathy over and above the information provided by other indicators. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for independent predictors. The effect of diabetic cardiomyopathy on outcome, defined as events (see above), deterioration in NYHA functional class, and both of these outcomes combined, was analysed with the Kaplan–Meier method using the log-rank (Mantel–Cox) test to assess for equality of survival curves. Logistic regression was employed to calculate relative risks (95% confidence interval) for selected outcome variables with sufficient numbers of events and to evaluate the ability of BNP, and clinical and echocardiographic variables to predict prognosis. Statistical analyses were performed using commercially available software A P-value of <0.05 was considered to indicate statistical significance.

Results:

Prevalence of diabetic cardiomyopathy

Baseline characteristics of the total study population (n = 1564) and the groups with and without diastolic dysfunction, LVH, and diabetic cardiomyopathy are shown in Table. Diastolic function was normal in 657 (42%), abnormal in 594(38%), and indeterminate in the remaining 313 (20%) patients. In those with abnormal diastolic function, severity was classified as mild in 421 (71%), moderate in 154 (26%), and severe in 18 (3%) patients. Left ventricular hypertrophy was diagnosed in 142 patients (24%). No patient showed systolic dysfunction, and the mean LV ejection fraction was 62 ± 6%. 249(42%) had diabetic cardiomyopathy.

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Table 1. Baseline characteristics

Parameter	Total population (n = 100)	Diastolic function			LVH			Diabetic cardiom
		Normal (n = 62)	Abnormal (n = 38)	P-value	Absent (n = 76)	Present (n = 24)	P-value	Absent (n = 52)
Age (years)	57.4 ± 10.2	54.3 ± 9.4	62.4 ± 9.3	<0.0001	56.0 ± 9.9	61.6 ± 9.9	<0.02	53.9 ± 9.6
Female gender (%)	44	32	63	<0.004	36	71	<0.005	27
Type II diabetes (%)	78	74	84		76	83		73
Diabetes duration (years)	12.1 ± 10.4	12.4 ± 10.4	11.6 ± 10.5		12.0 ± 10.6	12.3 ± 9.8		11.9 ± 9.9
Haemoglobin A1c (%)	7.4 ± 0.9	7.4 ± 0.9	7.3 ± 0.9		7.3 ± 0.9	7.5 ± 0.9		7.5 ± 1.0
Hypertensiona(%)	58	45	79	0.0009	59	54		48
Systolic BPb(mmHg)	134 ± 19	130 ± 16	141 ± 21	<0.003	132 ± 18	140 ± 21		130 ± 17
Diastolic BP (mmHg)	80 ± 12	79 ± 12	81 ± 12		80 ± 12	81 ± 14		79 ± 12
Hyperlipidaemiac(%)	79	73	89	<0.05	80	75		73
Total cholesterol (mmol/L)	5.0 ± 1.0	4.9 ± 0.9	5.1 ± 1.0		5.0 ± 0.9	4.8 ± 1.1		4.9 ± 0.9
LDL cholesterol (mmol/L)	3.0 ± 0.9	3.0 ± 0.9	3.1 ± 0.9		3.1 ± 0.9	2.9 ± 0.9		3.0 ± 0.9
Triglycerides (mmol/L)	2.5 ± 1.4	2.4 ± 1.5	2.7 ± 1.4		2.5 ± 1.5	2.7 ± 1.3		2.3 ± 1.5
Current smoker (%)	33	36	29		37	21		39
Family historyd(%)	20	21	18		20	21		17
NYHA class I/II (%)	85/15	89/11	79/21		88/12	75/25		88/12
Body mass index	30.1 ± 5.2	29.5 ± 5.0	31.1 ± 5.3		29.5 ± 5.1	32.0 ± 5.2	<0.04	28.7 ± 4.9
Medication history								
Aspirin (%)	28	26	32		24	42		23

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Parameter	Total population (n = 100)	Diastolic function			LVH			Diabetic cardiom	
		Normal (n = 62)	Abnormal (n = 38)	P-value	Absent (n = 76)	Present (n = 24)	P-value	Absent (n = 52)	
ACE-I/ARB e (%)	54	48	63		50	67		48	
Beta-blocker (%)	15	10	24		19	25		6	
Calcium antagonist (%)	12	5	24	<0.009	12	13		4	
Diuretic (%)	30	23	42	<0.05	30	30		27	
Statin (%)	43	44	43		45	38		48	
Insulin (%)	28	32	21		29	25		34	
Oral antidiabetics (%)	32	29	37		33	29		31	
Both (%)	40	39	42		38	46		35	
ECG LVH (%)	3	0	8		3	4		0	

By multivariate logistic regression, BNP, hypertension, and systolic blood pressure were independent predictors of diastolic dysfunction. Female gender, systolic blood pressure, and body mass index (BMI) were predictors of diabetic cardiomyopathy. Female gender remained as the only independent predictor of LVH.. Brain natriuretic peptide alone was only moderately useful to detect diastolic dysfunction alone, whereas combinations of the clinical parameters listed above resulted in high NPVs for diabetic cardiomyopathy.

This study demonstrates that echocardiographic evidence of diabetic cardiomyopathy is common, especially in women, even in diabetic patients without previously known heart disease. Screening with combinations of simple clinical parameters, but not BNP alone, can be useful to identify those patients needing further evaluation. This is of clinical importance as patients with pre-clinical diabetic cardiomyopathy are at increased risk for functional deterioration and possibly cardiovascular events during follow-up. Brain natriuretic peptide was shown to be an independent predictor of future events.

As mentioned earlier, in the strict sense, diabetic cardiomyopathy is defined as LV dysfunction and/or LVH independent of coronary disease and hypertension. However, a number of variations of this definition have been used in clinical studies. In the present analysis, patients did not have a history or symptoms suggestive of coronary disease and therefore no stress testing or coronary angiography was performed in the context of the study. Synergy between diabetes and hypertension is a very frequent coincidence and there is evidence that their

effects on the heart are similar, independent, and synergistic. We decided not to exclude patients with hypertension if they were treated for this condition to better reflect the typical clinical scenario.

Numerous previous studies, using mainly Doppler echocardiography, have attempted to determine diastolic function in subjects with diabetes In our study clinically well-characterized population without evidence of heart disease, diastolic dysfunction was observed in 38%. This prevalence is higher than in the general population. Others, using the same or a comparable definition of diastolic dysfunction, found a prevalence of diastolic dysfunction in large, community-based populations of 27.4 and 29.1%, respectively. However, the mean age was substantially higher in both of these reports when compared with our population, and a history of coronary disease, previous myocardial infarction, reduced ejection fraction, and heart failure were not the exclusion criteria, making a direct comparison with our results difficult.

The prevalence of LVH in the general population is mainly dependent on age and the presence of hypertension, varying from 6 to over 50% in several large series. Increased LV mass and wall thickness have also consistently been documented in diabetics.In the present study, 24% of patients had echocardiographic LVH. A higher prevalence of 43% has been described in unselected older patients with diabetes using the same definition for LVH in the only other publication reporting prevalence

Diastolic dysfunction and/or LVH, as structural and functional evidence for diabetic cardiomyopathy, was present in 42% of our population. Remarkably, the prevalence of this condition was strikingly high in the women in this study. Heart failure with preserved ejection fraction is commonly believed to be more common in women than in men but data regarding gender differences in diabetic cardiomyopathy are rare in the literature. Only in the Framingham study was an independent association reported between diabetes and LV mass only in women.

Brain natriuretic peptide has been shown to reliably predict diastolic dysfunction in diabetic patients with and without clinical indications for echocardiography

Elevated high-sensitivity C-reactive protein levels have been shown to be associated with LVH in patients with type 2 diabetes and were identified as markers of future heart failure in the Framingham population. High-sensitivity C-reactive protein alone or in combination with BNP or clinical parameters did not prove to be useful as a diagnostic or prognostic marker of diabetic cardiomyopathy.

Our finding that patients with Diabetic cardiomyopathy are at increased risk for adverse outcome driven mainly by symptomatic deterioration may be seen as unsurprising in view of the well-established prognostic role of LVH and diastolic dysfunction in cardiovascular morbidity and all-cause mortality. We found an almost four-fold increased risk in patients with evidence of Diabetic cardiomyopathy, underscoring the need for proper diagnostics and appropriate treatment in this population

Conclusion:

The prevalence of diabetic cardiomyopathy is high in diabetics without known structural heart disease and is associated with adverse outcome. Screening of diabetics based on combinations of simple clinical parameters, such as systolic blood pressure, BMI, and gender, can be useful to select those patients needing further evaluation with echocardiography. Brain natriuretic peptide alone was not a powerful screening test for diabetic cardiomyopathy but was shown to be an independent predictor of future events. Whether the structural and functional abnormalities of diabetic cardiomyopathy can be reversed and the outcome proved with treatment remains to be determined.

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