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PRE-CLINICAL DIABETIC CARDIOMYOPATHY: PREVALENCE, SCREENING AND OUTCOME-A PROSPECTIVE STUDY AT TERTIARY LEVEL HOSPITAL IN NORTH INDIA.

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ABSTRACT

Left ventricular function was assessed in preclinical diabetic cardiomyopathy without significant microangiopathy. The results were compared with those in normal controls. Significant microangiopathy was defined as proteinuria over 3 g/24 h or proliferative retinopathy. Left ventricular function was also assessed one and a half years later by echocardiography in four patients with microangiopathy. Patients with angina, previous myocardial infarction, hypertension, and alcoholism were excluded. All had normal electrocardiograms and chest radiographs. Diabetics with microangiopathy had impaired left ventricular function, whereas those with uncomplicated diabetes had normal function. This finding supports the existence of a specific diabetic cardiomyopathy due to microangiopathy rather than the metabolic defect. The association of microangiopathy and impaired left ventricular function may explain the high immediate mortality and the high incidence of cardiogenic shock and congestive heart failure after myocardial infarction in diabeticDiabetic cardiomyopathy, characterized by left ventricular (LV) dysfunction and LV hypertrophy could contribute to the increased life-time risk of congestive heart failure seen in patients with diabetes. We assessed prospectively the prevalence, effectiveness of screening methods [brain natriuretic peptide (BNP) and C-reactive protein in combination with clinical parameters], and outcome of pre-clinical diabetic cardiomyopathyWe studied 99 adults (mean age 57.4 ± 10.2 years, 44% females) with diabetes and no previous evidence of structural heart disease. By echocardiography, diabetic cardiomyopathy was present in 48% of patients. Screening with combinations of clinical parameters (gender, systolic blood pressure, and body mass index), but not BNP, resulted in high negative predictive values for diabetic cardiomyopathy. During a mean follow-up of 48.5 ± 9.0 months, in the groups with and without diabetic cardiomyopathy, 12.5 vs. 3.9% ($P < 0.2$) patients died or experienced cardiovascular events and 37.5 vs. 9.6% ($P < 0.002$) had a deterioration in NYHA functional class. Overall event-free survival was 54 vs. 87% ($P = 0.001$) in the groups with and without diabetic cardiomyopathy, respectively. Brain natriuretic peptide was an independent predictor of events [odds ratio 3.5 (1.1–10.9), $P = 0.02$].Pre-clinical diabetic cardiomyopathy is common. Screening with combinations of simple clinical parameters, but not BNP, can be useful to identify those patients needing further evaluation. Patients with pre-clinical diabetic cardiomyopathy are at increased risk for functional deterioration and possibly cardiovascular events during follow-up.

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.[1] In addition, there is an increased life-time risk of congestive heart failure and these patients are over-represented in large heart failure databases.[2] Clinical and experimental studies support the concept of a diabetic cardiomyopathy with functional, biochemical, and morphological myocardial abnormalities independent of myocardial ischaemia and hypertension,[3] leading to left ventricular (LV) dysfunction and LV hypertrophy (LVH) in a substantial proportion of type I and II diabetics.[4–5] However, only limited information is currently available regarding the prevalence and outcome of pre-clinical diabetic cardiomyopathy. 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.[6–10] The objectives of this pilot 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; second, to evaluate the usefulness of BNP and high-sensitivity C-reactive protein alone or in combination with clinical parameters as screening tools; and third, to study the outcome of pre-clinical diabetic cardiomyopathy.

METHOD

We recruited prospectively from our diabetes outpatient clinic 100 adults with type I or II diabetes treated with insulin and/or oral antidiabetics 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,[11] non-fasting venous blood samples were obtained, a standard 12-lead electrocardiogram was acquired and Doppler echocardiography was performed on the same dataPlasma BNP concentrations were measured with the Biosite® Access BNP immunoassay and high-sensitivity C-reactive protein was determined by immunonephelometry on the Beckman Image Nephelometer. The detection limits were 5 pg/mL for BNP and 0.06 mg/L for high-sensitivity C-reactive protein. In addition, serum creatinine, glucose, haemoglobin A1c, total cholesterol, LDL cholesterol, and triglycerides were measured by standard techniquesDoppler echocardiography was performed by one of two cardiologists (S.K. and P.R.) who was blinded to laboratory results, using a Sonos 5500 system (Philips, Eindhoven, The Netherlands).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.[12] 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 $\Delta E/A$ 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. Mean heart rate during the Doppler study was 75 ± 11 b.p.m.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.[13] 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 pseudonormal 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.[14] 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 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.[12] 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[15] Definition of pre-clinical diabetic cardiomyopathy: Pre-clinical diabetic cardiomyopathy was defined as the presence of LV dysfunction and/or LVH by Doppler echocardiography in type I or 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.Outcome :Patients were evaluated every 6 months for a minimum of 3 years by structured telephone interview using a self-designed flow sheet with the events in question defined according to standard clinical criteria. Medical records were reviewed in the case of hospitalization and referring physicians were contacted for additional information. Besides NYHA functional class (limitations of functional capacity due to shortness of breath when compared with the previous observation period), the following events were recorded: death (cardiac/non-cardiac), acute coronary syndrome, hospitalization for cardiac reasons, and new diagnosis of heart failure. The physicians collecting the follow-up data (S.K., R.H., and P.R.) were blinded to laboratory and echocardiographic results.

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 (Statview version 5.0, SAS Institute Inc., Cary, NC, USA, and SPSS version 12.0, SPSS Inc., Chicago, IL, USA). A *P*-value of <0.05 was considered to indicate statistical significance.

RESULT

Prevalence of diabetic cardiomyopathy

Baseline characteristics of the total study population (*n* = 99) and the groups with and without diastolic dysfunction, LVH, and diabetic cardiomyopathy are shown in *Table* Table 1. Diastolic function was normal in 42 (42%), abnormal in 38 (38%), and indeterminate in the remaining 20 (20%) patients. In those with abnormal diastolic function, severity was classified as mild in 27 (71%), moderate in 10 (26%), and severe in 1 (3%) patients. Left ventricular hypertrophy was diagnosed in 24 patients (24%). No patient showed systolic dysfunction, and the mean LV ejection fraction was 62 ± 6%. Forty-eight patients (48%) had diabetic cardiomyopathy.

Table 1: Baseline characteristics.

Parameter	Total population (*n* = 100)	Diastolic function			LVH			Diabetic cardiomyopathy		
		Normal (*n* = 62)	Abnormal (*n* = 38)	*P*-value	Absent (*n* = 76)	Present (*n* = 24)	*P*-value	Absent (*n* = 52)	Present (*n* = 48)	*P*-value
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	61.2 ± 9.4	0.0002
Female gender (%)	44	32	63	<0.004	36	71	<0.005	27	63	0.0005
Type II diabetes (%)	78	74	84		76	83		73	83	
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	12.3 ± 10.9	
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	7.2 ± 0.9	
Hypertensiona (%)	58	45	79	0.0009	59	54		48	69	<0.05
Systolic BPb (mmHg)	134 ± 19	130 ± 16	141 ± 21	<0.003	132 ± 18	140 ± 21		130 ± 17	139 ± 19	<0.03
Diastolic BP (mmHg)	80 ± 12	79 ± 12	81 ± 12		80 ± 12	81 ± 14		79 ± 12	81 ± 13	
Hyperlipidaemiac (%)	79	73	89	<0.05	80	75		73	85	
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	5.1 ± 1.0	
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	3.0 ± 0.8	
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	2.8 ± 1.4	
Current smoker (%)	33	36	29		37	21		39	27	
Family historyd (%)	20	21	18		20	21		17	23	
NYHA class I/II (%)	85/15	89/11	79/21		88/12	75/25		88/12	81/19	
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	31.6 ± 5.1	<0.005
Medication history										
Aspirin (%)	28	26	32		24	42		23	33	
ACE-I/ARBe (%)	54	48	63		50	67		48	60	
Beta-blocker (%)	15	10	24		19	25		6	25	<0.02
Calcium antagonist (%)	12	5	24	<0.009	12	13		4	21	<0.02
Diuretic (%)	30	23	42	<0.05	30	30		27	33	
Statin (%)	43	44	43		45	38		48	38	
Insulin (%)	28	32	21		29	25		34	21	

Oral antidiabetics (%)	32	29	37		33	29		31	33	
Both (%)	40	39	42		38	46		35	46	
ECG LVH (%)	3	0	8		3	4		0	6	

- a History of or current treatment for arterial hypertension.
- b Blood pressure.
- c Statin treatment or total cholesterol >5 mmol/L or LDL cholesterol >3 mmol/L.
- d Family history of premature coronary artery disease.
- e ACE-inhibitor/angiotensin receptor blocker.

Effectiveness of screening tests

Median (IQR) BNP values in patients with normal, indeterminate, and abnormal diastolic function were 21 (18), 30 (39), and 44 (58) pg/mL, respectively (P = 0.0003 between normal and abnormal diastolic function). Patients with mild, moderate, and severe diastolic dysfunction showed median BNP values of 36 (55), 57 (60), and 167 pg/mL, respectively (P = 0.01 normal diastolic function vs. mild and P = 0.0011 normal vs. moderate dysfunction). There was also a significant difference in median BNP values between patients with and without LVH [37 (54) vs. 29 (30) pg/mL; $P < 0.05$] and in those with vs. without diabetic cardiomyopathy [37 (50) vs. 24 (22) pg/mL, P = 0.0033]. Values of high-sensitivity C-reactive protein were not significantly different in any of the subgroups (data not shown).The areas under the curve for the ROC analyses with BNP used to detect diastolic dysfunction, LVH, and diabetic cardiomyopathy were 0.70 (0.59–0.81, P = 0.001), 0.63 (0.51–0.76, $P < 0.05$), and 0.67 (0.57–0.78, P = 0.003), respectively. A BNP cut-off value of 34 pg/mL had a sensitivity of 66, 58, and 58%, a specificity of 71, 62, and 71%, a PPV of 58, 33, and 65%, and an NPV of 77, 83, and 65% to detect any diastolic dysfunction, LVH, or diabetic cardiomyopathy, respectively.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 (data not shown). Sensitivities, specificities, NPV, and PPV of the independent variables alone or in combination are shown in *Table* **Table 2** and the clinical implications for screening based on these results in *Table* **Table 3**. 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.

Table 2: Sensitivity, specificity, and positive and negative predictive values of selected parameters to identify diastolic dysfunction, left ventricular hypertrophy, and diabetic cardiomyopathy.

Parameter	Sensitivity	Specificity	PPV	NPV
Diastolic dysfunction				
1. Hypertension	79	55	52	81
2. SBP > 134 mmHg	63	72	59	75
3. BNP > 34 pg/ml	66	71	58	77
1. + 2.	87	46	50	85
1. + 3.	100	39	50	100
2. + 3.	84	46	49	82
1. + 2. + 3.	100	26	45	100
LVH				
Female gender	71	64	39	88
Diabetic cardiomyopathy				
1. Female gender	63	73	68	68
2. SBP > 134 mmHg	60	76	71	67
3. BMI > 30.1	65	65	63	67
1. + 2.	88	52	63	82
1. + 3.	88	48	61	81
2. + 3.	94	45	62	89

- [a] SBP, systolic blood pressure; BMI, body mass index.

Table 3: Identification of diastolic dysfunction, left ventricular hypertrophy, and diabetic cardiomyopathy: implications for screening.

Parameter	% screened needing echo	% echos that are negative	% with disease missed
Diastolic dysfunction (prevalence 38%)			
1. Hypertension	58	28	18
2. SBP > 134 mmHg	42	17	14
3. BNP > 34 pg/mL	43	18	13
1. + 2.	66	33	5
1. + 3.	76	38	0
2. + 3.	65	33	6
1. + 2. + 3.	84	46	0
Left ventricular hypertrophy (prevalence 24%)			
Female gender	44	27	7
Diabetic cardiomyopathy (prevalence 48%)			
1. Female gender	44	14	18
2. SBP > 134 mmHg	42	12	19
3. BMI > 30.1	49	18	17
1. + 2.	67	25	6
1. + 3.	69	27	6
2. + 3.	74	28	3
1. + 2. + 3.	85	37	1

- [a] SBP, systolic blood pressure; BMI, body mass index.

Outcome

During a mean follow-up of 48.5 ± 9.0 months (≥36 months in all patients except for one patient who moved to another country after 24 months), the following events were observed in the groups with and without diabetic cardiomyopathy: non-cardiac deaths 2 vs. 1, acute coronary syndrome 2 vs. 1, hospitalization for cardiac reasons 4 vs. 1 and new diagnosis of heart failure 2 vs. 0. The number of patients with events was not significantly different between the groups [6 (12.5%) vs. 2 (3.9%), $P <$ 0.2]. Significantly, more patients with diabetic cardiomyopathy experienced a deterioration in NYHA functional class [18 (37.5%) vs. 5 (9.6%), $P <$ 0.002; odds ratio (OR) 4.5 (1.7–12.3), $P = 0.0009$]. The combined event-free survival was 54 vs. 87% [OR 3.8 (1.6–8.9), $P = 0.001$] in the groups with and without diabetic cardiomyopathy as shown in *Figure* Figure 1. In addition, by univariate analysis, events were more likely to occur in patients with higher BNP ($P = 0.006$) and older age ($P < 0.05$), functional deterioration in patients with higher BMI ($P < 0.003$) and female gender ($P <$ 0.002), and the combined endpoint in patients with higher BNP ($P <$ 0.006), high-sensitivity C-reactive protein ($P < 0.04$), higher BMI ($P < 0.03$), older age ($P <$ 0.03), as well as female gender ($P = 0.007$). Brain natriuretic peptide remained an independent predictor of events [OR 3.5 (1.1–10.9), $P = 0.02$], female gender [OR 3.6 (1.2–10.8), $P <$ 0.02], and diabetic cardiomyopathy [OR 3.7 (1.1–11.0), $P < 0.03$] of functional deterioration and diabetic cardiomyopathy alone [OR 3.5 (1.1–10.9), $P <$ 0.03] of the combined endpoint by multivariate logistic regression.

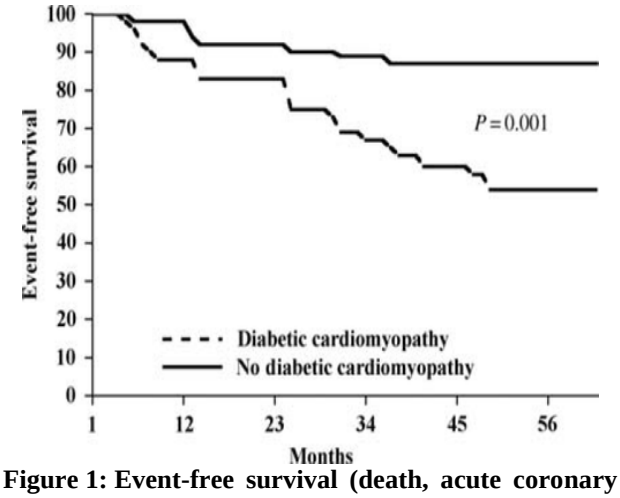

Figure 1: Event-free survival (death, acute coronary syndrome, hospitalization for cardiac reasons, new diagnosis of heart failure, and ≥1 increase in NYHA functional class) in patients with and without diabetic cardiomyopathy.

DISCUSSION

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, andsynergistic.16We 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. Differences in the patient populations studied and in the definition of diastolic dysfunction used most likely account for the high variation in prevalence (30–75%) reported in the literature.[17–24] In our 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[14] or a comparable[25] 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,[14] and heart failure[25] 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.[26–28] Increased LV mass and wall thickness have also consistently been documented in diabetics.[4,5,29] 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.[23] Diastolic dysfunction and/or LVH, as structural and functional evidence for pre-clinical diabetic cardiomyopathy, was present in 48% of our population. Remarkably, the prevalence of this condition was strikingly high in the women in our 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,[5] was an independent association reported between diabetes and LV mass only in women. Clearly, this issue merits further evaluation. Screening for diabetic cardiomyopathy Brain natriuretic peptide has been shown to reliably predict diastolic dysfunction in diabetic patients with and without clinical indications for echocardiography, but unfortunately, very little clinical information was provided in this study.30 In contrast, in a number of large, community-based populations, BNP proved to be a suboptimal screening test to detect pre-clinical LV dysfunction or LVH.[6-8] In addition, BNP was not useful to predict LV dysfunction in asymptomatic patients with diabetes in two small reports.[31,32] In accordance with these results, BNP was moderately predictive for the presence of LV diastolic dysfunction but not for LVH or diabetic cardiomyopathy in the present analysis. The combination of clinical parameters, mainly characteristics of the metabolic syndrome, resulted in high NPVs for diastolic dysfunction and diabetic cardiomyopathy. A substantial proportion of the diabetic population would need an echocardiogram with this approach, around one-third of these would be negative but very few patients with diabetic cardiomyopathy would be missed. Elevated high-sensitivity C-reactive protein levels have been shown to be associated with LVH in patients with type 2 diabetes[9] and were identified as markers of future heart failure in the Framingham population.[10] 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 in our study. Outcome of diabetic cardiomyopathy: Our finding that patients with pre-clinical 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[33] and diastolic dysfunction[34,35] in cardiovascular morbidity and all-cause mortality. However, to our knowledge, this has not been reported previously. We found an almost four-fold increased risk in patients with evidence of pre-clinical diabetic cardiomyopathy, underscoring the need for proper diagnostics and appropriate treatment in this population. In accordance with a recent report,[34] patients with increased BNP levels are at particular risk. The results presented in this study may help to identify these patients.

CONCLUSION

The prevalence of pre-clinical 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 pre-clinical diabetic cardiomyopathy can be reversed and the outcome improved with treatment remains to be determined.

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