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Left ventricular function in patients with uncomplicated well-controlled diabetes mellitus

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Abstract

Background: Recent findings indicate that symptomatic heart disease in patients with diabetes mellitus predicts poor prognosis, but cardiac involvement may occur before clinical manifestation. Diastolic dysfunction may be the first stage of diabetic cardiomyopathy. **Objective:** The aim of this study was to evaluate the cardiovascular function in patients with DM in early stages. **Methods:** we studied a group of 62 patients, males and females, aged between 51 and 65 years old, with well-controlled DM; they were investigated using transthoracic echocardiography (TTE). Two dimensional, pulsed Doppler techniques were used to asses the systolic and diastolic function for left ventricle (LV). **Results:** none of the patients had any clinical signs of cardiac involvement, nor ECG or TTE systolic function impairment. There are significant differences between DM patients and control group for peak A velocity (0.72 ± 0.19 vs 0.56 ± 0.29, P=0.05) and E/A ratio (1.03 ±0.29 vs 1.51 ± 0.26, P = 0.01) which account for filling impairment of LV. **Conclusions:** the analysis of DM heart disease, mainly at a preclinical level, is important in all the cases as an asymptomatic patient may have diastolic dysfunction which can be treated and should be closer observed.

Keywords: diabetes mellitus, ultrasound, cardiovascular function

Rezumat

Premisele studiului: Cercetările recente arată faptul că boala cardiacă simptomatică la pacienţii cu diabet zaharat se asociază cu un prognostic mai prost, dar afectarea cordului poate surveni înaintea oricăror manifestări clinice. Disfuncţia diastolică ar putea fi prima manifestare a cardiomiopatiei diabetice. **Obiective:** Evaluarea funcţiei ventriculului stâng la pacienţii cu diabet zaharat in stadii incipiente de boală. **Metoda:** Am luat în studiu un grup de 62 de pacienţi, bărbaţi şi femei, cu vârste cuprinse între 51 şi 65 de ani, cu DZ bine controlat. Au fost explorați cu ajutorul ecocardiografiei transtoracice. Funcţiile sistolică şi diastolică ale ventriculului stâng au fost analizate cu tehnicile de Doppler pulsat şi ecografie bidimensională. **Rezultate:** Nici unul dintre pacienţi nu a avut semne clinice de afectare cardiacă, iar ECG şi funcţia sistolică evaluată ecografic au fost în limite normale. Au existat diferenţe semnificative statistic între pacienţii cu DZ şi grupul de control în ceea ce priveşte velocitatea maximă a undei A (0.72 ± 0.19 vs 0.56 ± 0.29, P=0.05) şi raportul E/A (1.03 ±0.29 vs 1.51 ± 0.26, P = 0.01), ce reflecta defectul de umplere a ventriculului stâng. **Concluzii:** Analiza afectării cardiace la pacienţii cu diabet zaharat este importantă în toate cazurile, în special în stadiile preclinice, deoarece un pacient asimptomatic poate avea disfuncţie diastolică, tratabilă, şi care va trebui urmarită în timp.

Cuvinte cheie: diabet zaharat, ecografie, funcţie cardiovasculară

Introduction

The cardiovascular prognosis in patients with diabetes mellitus (DM) is worse than in non-diabetic individuals. More than half of the patients with type 2 diabetes mellitus have autonomic neuropathy which involves, among other, the cardiovascular system. Heart rate variability is reduced in DM patients, associated with a poorer cardiovascular prognosis and increased risk of stroke

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[1,2]. Left ventricular (LV) diastolic impairment may be the first stage of diabetic cardiomyopathy; diabetic cardiomyopathy is now recognized as a distinct entity that may lead to heart failure independent of other heart diseases such as hypertension or coronary heart disease. Diastolic dysfunction alone refers to echocardiographic features of an abnormal LV relaxation pattern without clinical heart failure. Diastolic heart failure refers to a clinical syndrome of heart failure with a preserved LV ejection fraction [3,4].

The prevalence of diabetic cardiomyopathy is about 30% in middle-aged type 2 diabetic patients. Left ventricular diastolic dysfunction and cardiac dysautonomy are often associated and may be asymptomatic [1]. The early detection of cardiac involvement in DM is clearly desirable, both for optimal treatment and for implementation of preventive measures in the early stages of the disease [1,5].

Our study was designed to analyze the prevalence of cardiac involvement in patients with diabetes mellitus but no signs of heart disease.

Materials and methods

Patients with diabetes mellitus

Sixty two patients (30 women and 32 men), aged between 51 and 65 years old were studied, according to the following inclusion criteria: uncomplicated and well-controlled DM, assessed by laboratory findings, including HbA1; age < 65 years; normal chest radiographs and normal left ventricular systolic function at echocardiography. In all cases, rest ECG was normal.

Exclusion criteria: chronic renal failure, malignancy, pregnancy, high blood pressure, ischemic or rheumatic heart disease, cardiomyopathy or congenital heart disease, and any other systemic diseases which could affect the heart.

Controls

For comparison, 55 healthy subjects (25 women and 30 men), with a mean age of 54 ± 12.8 years, age-matched and sex-matched, were used as control subjects.

Study protocol

Echocardiographic methods

Transthoracic echocardiography was carried out using an ALOKA alpha 10 Premiere device with a 2.5/3.5 MHz transducer, with patients in the left lateral decubitus position. Left ventricular diameters (EDD: left ventricular end diastolic diameter, ESD: left ventricular end systolic diameter), end diastolic septal thickness and posterior wall thickness were measured in the parasternal long axis view, according to the criteria of the American Society of Echocardiography [6]. Left ventricular ejection fraction (EF) was calculated with a modified Simpson formula from apical two and four chambers views.

Pulsed Doppler transmitral flow velocity profile was obtained from the apical four chamber view, and the sample volume was positioned at the tip of the mitral valve leaflets (fig 1). The following parameters were evaluated for diastolic function: peak E (peak transvalvular flow velocity in early diastole); peak A (peak transvalvular flow velocity in late diastole); E/A ratio; deceleration time (DecT) in ms (time measured between peak E velocity and the point where the deceleration slope of the E velocity crosses the baseline) (fig 2); isovolumic relaxation time (IVRT) (time elapsed between aortic valve

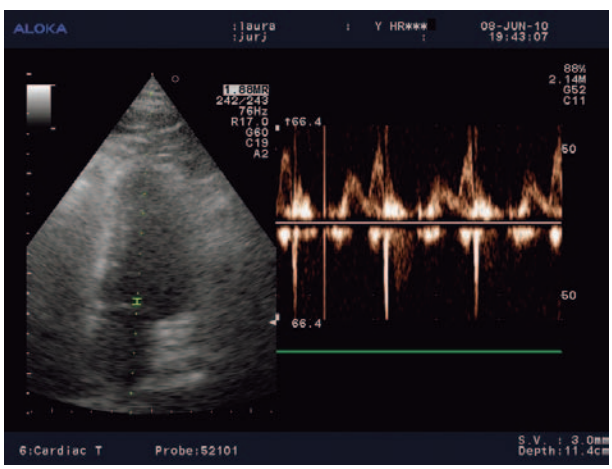


Fig. 1. Pulsed Doppler transmitral flow velocity profile obtained from the apical four chamber view with the sample volume was positioned at the tip of the mitral valve leaflets

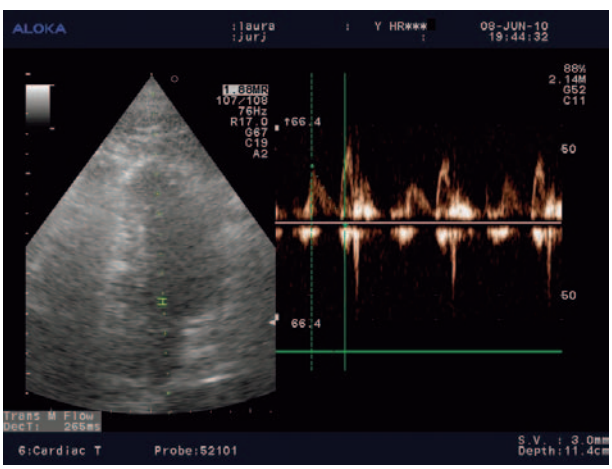


Fig. 2. Calculation of the deceleration time (DecT).

Table 1. Demographic characteristics of DM patients and controls

Parameter	DM patients Value (mean ±SD) or N, %	Controls Value (mean ±SD) or N, %
Number	62	55
Gender	**B:** 32 (51.6%) **F:** 30 (48.3%)	B: 30 (54.5%) **F:** 25 (45.5%)
Age	57.34 (±7.50)	54.11 (± 10.8)
Disease duration (years)	8.22 (±9.67)	NA
Oral drugs	26 (41.9%)	NA
Cholesterol	236.88 (±66.93)	189.77 (±36.73)*
Tryglicerides	183.45 (± 93.07)	121.45 (±85.22)*
Fasting plasma glucose	159.42 (±53.63)	82.33 (±13.52)*
HbA1	7.20 (±1.59)	4.9 (±0.3)*
Blood pressure **SBP** **DBP**	 128 (± 9) 81 (± 5)	 131 ± 10 79 ± 6

NA= not applicable, DM=diabetes mellitus, SBP=systolic blood pressure, DBP=diastolic blood pressure

Table 2. Ultrasonographic parameters in DM patients and controls

Parameter	DM patients (mean ±SD)	Control group (mean ±SD)	P value
LVEDD	49.35 (±6.16)	44.36 (±7.22)	NS
LVESD	36.69 (±6.77)	33.89 (±8.11)	NS
EF	58.13 (±6.82)	61.96 (± 7.19)	NS
Peak A velocity	0.72 (± 0.19)	0.56 (± 0.29)	0.05
Peak E velocity	0.78 (± 0.18)	0.85 (± 0.14)	NS
E/A	1.03 (±0.29)	1.51 (± 0.26)	0.01
IVRT	129 (±48)	82 (± 22)	0.05
DecT	238 (±76)	217 (±84)	NS

LVEDD=left ventricular end diastolic diameter; LVESD=left ventricular end systolic diameter; EF=ejection fraction; IVRT=isovolumic relaxing time; DecT=deceleration time

closure and mitral valve opening). E/A ratio between 1 and 2 was defined as normal [7].

Statistical analysis

Continuous variables were expressed as mean (SD). Differences were tested for significance by unpaired Student's *t* test. Upper and lower 95% confidence limits for each variable were calculated from the two tails of the Student's *t* test distribution. We compared the results with the control group. A p value <0.05 was considered significant. Pearson correlation coefficients were used to explore linear relationships between the study variables.

Ethical issues

All patients and control subjects gave consent to participate in the study, which was approved by the local Ethics Committee.

Results

Table 1 shows the demographic characteristics of both patients and controls.

The main values of echocardiographic parameters were comparable in both DM patients and controls (table 2). In particular, mean values of ejection fraction were comparable in both groups. There were no significant differences also for: left ventricular systolic and diastolic diameters, for left ventricular mass and for wall thickness. We did not find pericardial effusion or any significant valvular involvement.

Of the Doppler parameters, evaluating left ventricular diastolic filling, late peak flow (peak A) velocity was significantly higher in DM patients than controls ($p<0.05$), while early peak flow (peak E) was reduced, but not significantly, if compared with normal controls. The E/A ratio was significantly lower in DM patients ($p<0.01$). DecT and IVRT are prolonged in DM group, but the differences were statistical significant only for IVRT.

We found moderate significant correlations (r=042, p=0.05) between mean duration of disease, expressed in years, and trans-mitral late diastolic velocity flow (A wave) and E/A ratio, but not with IVRT.

The changes in left ventricular filling (peak A wave velocity, E/A ratio and IVRT) significantly correlated with fasting plasma glucose levels, HbA1 levels and the duration of disease (r=0.49, 0.56, 0.70, respectively). E/A ratio significantly correlated with the systolic blood pressure (r=0.66).

Discussion

The diastolic changes observed in DM patients mainly regards the relaxation phase, resulting in an increase of atrial contribution to filling (peak A) and a decrease of early diastolic filling (peak E) [1, 4, 8].

Although the physiopathology of diabetic cardiomyopathy is still under debate, it is widely accepted that it is multifactorial and involves more than metabolic control or autonomic neuropathy alone [3, 4, 9]. Suboptimal glucose control has been associated with abnormal LV relaxations, along with renal microvascular disease, arte-

rial stiffening and endothelial dysfunction, insulin resistance, abnormalities of angiotensin-renin system, and last but not least, left ventricular remodeling and hypertrophy [10, 11]. All of these factors are also connected with the microvascular dysfunction that is strongly correlated with diastolic dysfunction [12, 13].

It is also accepted nowadays that left ventricular diastolic dysfunction is frequent in subjects with diabetes. A comprehensive transthoracic Doppler evaluation of diabetic patients should include assessment of diastolic function with estimation of LV filling pressure by tissue Doppler, and of coronary microvascular function by coronary flow reserve test [4].

Little work has been done to assess the prognosis of asymptomatic isolated diastolic dysfunction, but there is one study [14] which shows that echocardiographic evidence of subclinical contractile dysfunction and diastolic filling abnormalities are both predictive of subsequent chronic heart failure. In our study there were no signs of significant left ventricular hypertrophy (normal wall thickness and normal LV mass), but there were changes in trans-mitral diastolic flow. Our patients had no documented coronary artery disease, nor hypertension; the changes in left ventricular filling significantly correlated with fasting plasma glucose levels, HbA1 levels and duration of disease. There were no significant gender differences in our study group.

Early abnormalities are defined by a preserved LV ejection fraction with reduced early diastolic filling, prolongation of isovolumetric relaxation and increased atrial filling, the presence of which confirms diastolic dysfunction. Such abnormalities have been demonstrated in a group of normotensive diabetic patients without overt microvascular or macrovascular complications [15] and are also present in our study, but only for IVRT E/A ratio and peak A wave velocity.

Conclusions

Diastolic dysfunction without clinical signs of heart failure is the first stage of diabetic cardiomyopathy and should be careful evaluated in all diabetic patients, regardless of the presence or absence of other complications.

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References

1. Poirier P, Bogaty P, Philippon F, Garneau C, Fortin C, Dumesnil JG. Preclinical diabetic cardiomyopathy: relation of left ventricular diastolic dysfunction to cardiac autonomic neuropathy in men with uncomplicated well-controlled type 2 diabetes. Metabolism 2003; 52:1056–1061.
2. Karamitsos TD, Karvounis HI, Didangelos T, Parcharidis GE, Karamitsos DT. Impact of autonomic neuropathy on left ventricular function in normotensive type 1 diabetic patients: a tissue Doppler echocardiographic study. Diabetes Care 2008; 31:325–327.
3. Stein PK, Tereshchenko L, Domitrovich PP, Kleiger RE, Perez A, Deedwania P. Diastolic dysfunction and autonomic abnormalities in patients with systolic heart failure. Eur J Heart Fail 2007; 9:364–369.
4. Galderisi M. Diastolic dysfunction and diabetic cardiomyopathy: evaluation by Doppler echocardiography. J Am Coll Cardiol 2006; 48:1548–1551.
5. Schonauer M, Thomas A, Morbach S, Niebauer J, Schonauer U, Thiele H. Cardiac autonomic diabetic neuropathy. Diab Vasc Dis Res 2008; 5:336–344.
6. Douglas PS, Khandheria B, Stainback RF, et al. ACCF/ASE/ACEP/ASNC/SCAI/SCCT/SCMR 2007 appropriateness criteria for transthoracic and transesophageal echocardiography. J Am Coll Cardiol 2007;50:187–204.
7. Rakowski H, Appleton C, Chan KL, et al. Canadian consensus recommendations for the measurement and reporting of diastolic dysfunction by echocardiography: from the Investigators of Consensus on Diastolic Dysfunction by Echocardiography. J Am Soc Echocardiogr 1996; 9:736–760.
8. Heart rate variability: standards of measurement, physiological interpretation, and clinical use. Task Force of the European Society of Cardiology the North American Society of Pacing Electrophysiology. *Circulation* 1996; 93:1043–1065.
9. Taegtmeyer H, McNulty P, Young ME. Adaptation and maladaptation of the heart in diabetes: Part I: general concepts. Circulation 2002; 105:1727–1733.
10. Boudina S, Abel ED. Diabetic cardiomyopathy revisited. Circulation 2007; 115:3213–3223.
11. Karvounis HI, Papadopoulos CE, Zaglavara TA, et al. Evidence of left ventricular dysfunction in asymptomatic elderly patients with non-insulin-dependent diabetes melitus. *Angiology* 2004; 55:549–555.
12. Yu CM, Sanderson JE, Marwick TH, Oh JK. Tissue Doppler imaging a new prognosticator for cardiovascular diseases. J Am Coll Cardiol 2007; 49:1903–1914.
13. Hayat SA, Patel B, Khattar RS, Malik RA. Diabetic cardiomyopathy: mechanisms, diagnosis and treatment. Clin Sci (Lond) 2004; 107:539–557.
14. Aurigemma GP, Gottdiener JS, Shemanski L, Gardin J, Kitzman D. Predictive value of systolic and diastolic function for incident congestive heart failure in the elderly: the cardiovascular health study. J Am Coll Cardiol 2001; 37:1042–1048.
15. Ahmed SS, Jaferi GA, Narang RM, Regan TJ. Preclinical abnormality of left ventricular function in diabetes mellitus. Am Heart J 1975; 89:153–158.