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Atrial electromechanical delay, and left ventricular strain in pre-diabetic patients

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ABSTRACT

Objectives: The aim of this study was to investigate the subclinical myocardial affection in prediabetics with the evaluation of left ventricular (LV) systolic strain and strain rate by speckle tracking echocardiography (STE), and atrial electromechanical delay.
Study design: Global Longitudinal strain (GLS) and strain rate (GLSR) were assessed by STE, and Intra- and interatrial electromechanical delay (EMD) were measured utilizing tissue Doppler imaging (TDI) in 108 pre-diabetic patients and 72 age and gender matched healthy volunteers.
Results: The GLS (−19.4 ± 2.8 vs. 23.8 ± 2.1%; $p < 0.001$) and GLSR () were significantly lower in prediabetics when compared with the healthy control. Pre-diabetic patients had significantly prolonged PA lateral, PA septum and PA tricuspid. The intra- (PA septum-PA tricuspid) and interatrial (PA lateral-PA tricuspid) electromechanical delays were prolonged compared to controls ($p < 0.0001$, $p < 0.05$, $p < 0.001$, and $p < 0.002$, respectively). The GLS%, GLSR and atrial electromechanical delay were highly significantly correlated with fasting blood glucose, and modestly correlated to systolic blood pressure, total cholesterol, triglycerides, and left ventricular mass index.
Conclusion: GLS%; GLSR assessed by STE was decreased; intra- and interatrial electromechanical delays were prolonged, in pre-diabetic subjects. These non-invasive indices broaden the spectrum of subclinical myocardial dysfunction in pre-diabetic patients.
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1. Introduction

The frequency of cardiovascular disease is increased in diabetic patients, including ischemic heart disease, systolic and/or diastolic heart failure. Moreover, although cardiac involvement is often clinically silent, cardiovascular mortality is higher in diabetic patients [1]. There are several studies showing that left ventricular (LV) diastolic function may be impaired in diabetic patients [2,3]. Additionally, it is well-established that left atrial (LA) mechanical functions play a significant role in maintaining LV stroke volume in patients with impaired LV diastolic function [4]. Atrial fibrillation (AF) is the most common type of tachyarrhythmia encountered in clinical practice and is associated with increased morbidity and mortality [5].

Conventional and tissue Doppler echocardiography measurements have major disadvantages such as angle dependence, limited spatial resolution, and deformation analysis in one dimension [6,7]. The recent development of two-dimensional (2D) speckle tracking echocardiography (STE) overcomes some of these limitations and is used for the quantitative assessment of global and local LV function from 2D images [8]. Previous studies have indicated that 2DSTE is more sensitive than conventional echocardiography for detecting subclinical ventricular dysfunction in various clinical disorders [9,10].

Pre-diabetes defines patients at high risk for diabetes in the future with impaired fasting glucose (IFG; fasting glucose above 100 mg/dL) and/or impaired glucose tolerance (IGT; 2 h oral glucose tolerance test [OGTT] levels of 140––200 mg/dL) and hemoglobin A1c (HbA1c) of a level of 5.7% to 6.4% [11].

The IFG and IGT should not be considered only as clinical symptoms, but should be regarded as risk factors for both diabetes and cardiovascular diseases [12]. Not only diabetes, but also all stages of glucose abnormalities are associated with an increased risk of cardiovascular morbidity and mortality, making it important to identify such conditions as early as possible [13].

We hypothesized that subclinical cardiac dysfunction begins early in all diabetic spectrum even in pre-diabetic state. So the purpose of this study was to evaluate atrial electromechanical coupling, **LA mechanical functions** and ventricular functions in pre-diabetic patients.

2. Patients and methods

The study included 108 consecutive patients (63 males, 45 females; mean age 49.3 ± 11.5 years) the pre-diabetic group who had no overt

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diabetes, whose fasting blood glucose (FBG) was higher than 100 mg/dL and/or whose two hour glucose concentrations on an oral glucose tolerance test was between 140 and 200 mg/d. The control group consisted of 72 healthy volunteers (the non-DM group, 40 male, 32 female; mean age 46.2 ± 9.2 years) with no illnesses, whose examinations were normal and whose laboratory values were within normal ranges.

Exclusion criteria includes subjects with a history of myocardial infarction, angina pectoris or other symptoms of CAD, hypertension, those with right or left bundle branch block, Wolff-Parkinson-White syndrome, intraventricular conduction defect on resting ECG, and those with ischaemic changes on the ECG and stress test, were excluded from the study. Moreover, patients with a history of palpitations, AF, permanent pacemaker implantation, antiarrhythmic drug use and those with thyroid disease, left ventricular (LV) hypertrophy or the use any drug affecting LV function were also excluded from the study.

2.1. Conventional echocardiographic examination

Two-dimensional, M-mode pulsed and color flow Doppler echocardiographic examinations (GE-Vivid 7; General Electric, Milwaukee, WI, USA) with a 2.5–5 MHz phased array transducer were performed. During echocardiography, continuous one-lead electrocardiographic recording was obtained. M-mode measurements and conventional Doppler echocardiographic examinations were performed according to the guidelines of the American Society of Echocardiography [14]. Left ventricular diastolic function was assessed with both conventional and tissue Doppler indices. The myocardial systolic (Sm), early diastolic (Em), and late diastolic (Am) velocities were obtained at the septal mitral annulus by placing a tissue Doppler sample volume. The E/Em and Em/Am ratios were subsequently calculated [15].

2.2. Speckle-tracking imaging

Two-dimensional speckle tracking analyses were performed on grayscale images of the left ventricle obtained in the apical four-chamber, two-chamber and three-chamber views. Three consecutive end-expiratory cardiac cycles using the high frame rate (50 Hz or more) harmonic imaging in each echocardiographic view were acquired. In each view, the myocardium was automatically divided by the software into six segments. The analyzed values within the middle points for all resulting 18 segments were averaged to obtain the global longitudinal strain (GLS) and the global longitudinal peak systolic strain rate (GLSR); in accordance with current conventions GLS and GLSR values were presented as negative (segment shortening) [16].The adequacy of tracking was verified manually, and the region of interest was readjusted to achieve optimal tracking. The segment was excluded if no acceptable border was traced. GLS and GLSR values were not calculated if >1 segment per view was excluded.

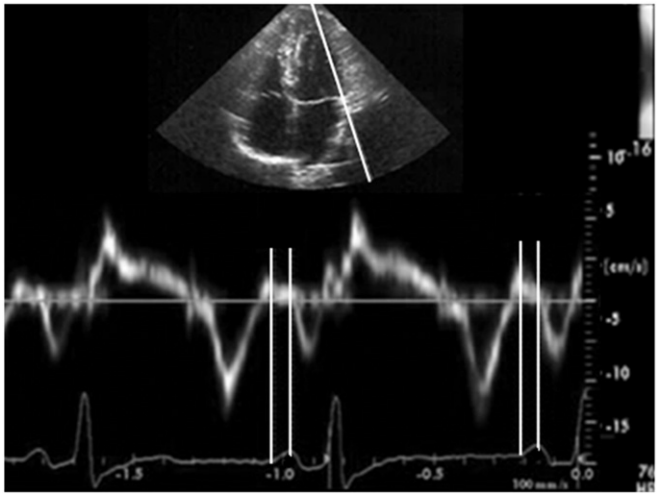

Fig. 1. Measurement of the PA interval with tissue Doppler imaging, (the interval from the onset of P wave on the surface ECG to the beginning of the late diastolic wave: Am).

Table 1
Clinical characteristics of the two groups.

	Pre-diabetics (n = 108)	Control (n = 72)	p Value
Age (years)	52.7 ± 8.2	51.6 ± 7.1	>0.05
Gender (female)	50	30	>0.05
SBP (mm Hg)	132 ± 14	118 ± 11	>0.05
DBP (mm Hg)	82 ± 11	78 ± 8	>0.05
Heart rate (beat/min)	79 ± 22	71 ± 12	>0.05
BMI (kg/m2)	27.5 ± 4.1	26.2 ± 4.2	>0.05
FBG (mg/dL)	123 ± 5.8	89 ± 7.1	<0.001
OGTT level	179 ± 22	123 ± 16	<0.0001
HbA1c (%)	6.1 ± 1.3	4.9 ± 1.02	<0.01
TC (mg/dL)	199 ± 46	165 ± 31	<0.001
TG (mg/dL)	169 ± 55	99 ± 38	<0.05
LDL-C (mg/dL)	125 ± 31	89 ± 34	<0.05
HDL-C (mg/dL)	45 ± 9	49 ± 8	<0.05

BMI — body mass index; DBP — diastolic blood pressure; DM — diabetes mellitus; FBG — fasting plasma glucose; OGTT—Oral glucose tolerance test, HbA1c — glycosylated hemoglobin; HDL-C — high density lipoprotein cholesterol; LDL-C — low density lipoprotein cholesterol; SBP — systolic blood pressure; TC — total cholesterol; TG — triglycerides.

2.3. Atrial electromechanical coupling

Tissue Doppler echocardiography was performed with a transducer frequency of 3.5 to 5.0 MHz, adjusting the spectral pulsed Doppler signal filters to obtain the Nyquist limit of 15 to 20 cm/s, and using the minimal optimal gain setting. The monitor sweep speed was set at 50 to 100 mm/s to optimize the spectral display of myocardial velocities. In apical four-chamber view, the pulsed Doppler sample volume was placed at the level of the LV lateral mitral annulus, and subsequently at the septal mitral annulus and right ventricular tricuspid annulus. The sampling window was positioned as parallel as possible with the myocardial segment of interest to obtain the optimal angle of imaging. Atrial electromechanical coupling was defined as the time interval from the onset of P wave on the surface electrocardiogram to the beginning of the late diastolic wave (A_m wave), i.e. PA interval was measured from the lateral mitral annulus (PA lateral), septal mitral annulus (PA septum), and right ventricular tricuspid annulus (PA tricuspid) [17]. (Fig. 1) All PA intervals were averaged over three consecutive beats. The difference between the lateral and tricuspid PA intervals was defined as interatrial electromechanical delay, and the difference between the septal and tricuspid PA intervals was defined as intra-atrial electromechanical delay [18].

Table 2
Echocardiographic findings of the two groups of the groups.

	Pre-diabetic (n = 108)	Control (n = 72)	p Value
LVEDD (mm)	45.9 ± 2.5	45.2 ± 2.9	>0.05
LVESD (mm)	27.4 ± 2.1	28.4 ± 1.9	>0.05
LA (mm)	36.1 ± 3.2	34.9 ± 2.7	>0.05
AOD (mm)	31.0 ± 3.3	28.1 ± 2.9	>0.05
IVS (mm)	9.2 ± 1.1	8.9 ± 1.2	>00.5
PW (mm)	9.0 ± 1.4	8.5 ± 1.3	>0.05
EF (%)	62.8 ± 2.8	64.1 ± 2.6	>0.05
LV Mass Index (g/m^2)	102.4 ± 19.3	99.3 ± 16.2	>0.05
E/A	0.88 ± 0.29	1.12 ± 0.23	< 0.05
EDT (ms)	225 ± 32	182.5 ± 26	< 0.03
LVs (cm/s)	8.95 ± 1.1	8.64 ± 1.05	>0.5
Em (cm/s)	11.2 ± 1.6	12.5 ± 1.9	>0.5
Am(cm/s)	11.0 ± 1.3	9.1 ± 1.7	>0.5
E/Em	5.3 ± 0.11	4.1 ± 0.11	<0.01

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