Original Article www.enlivenarchive.org Enliven: Clinical Cardiology and Research

ISSN: 2375-7310

Tissue Doppler Imaging in the Early Detection of Diastolic Dysfunction in Asymptomatic Diabetic Patients

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Abstract

Introduction

Tissue Doppler Imaging (TDI) is a new technique, able to record early changes of subclinical ventricular diastolic dysfunction and potentially identifies diabetic patients who may benefit from earlier treatment in order to prevent heart failure.

The Aim

To assess the role of TDI in early detection of diastolic dysfunction in asymptomatic diabetic patients (free of dyspnoe, fatigue, exercise intolerance, increased extracellular volume, angina).

Methods and Materials

Twenty-five asymptomatic diabetic patients and 23 healthy subjects underwent echocardiography (Pulsed-wave Doppler and TDI) to assess diastolic function. We compare the results from both echo-techniques and analyzed the relation of echo cardiographic parameters of diastolic dysfunction (DD) with different risk factors.

Results

We found statistically significant difference between TDI and PW Doppler (E/E´ vs E/A) in diabetic (Z=-3.17, p<0.001) and control group (Z=-2.4, p<0.003). There was no significant difference in E/A between the groups (Z=0.0, p<1.0). But, TDI identified significantly lower E´ (Z= 2.11, p<0.03) and higher E/E´(Z= -2.12, p<0.03) in diabetic vs control group (Z= -2.12, p<0.03). Also, there is statistically significant difference between the two echocardiographic techniques, TDI vs PW Doppler, in terms of detection of DD in both groups (p<0.00 for diabetic and p<0.01 for control group).

Diastolic dysfunction strongly correlate with duration of DM (p<0.00001), age (p<0.00001), female gender (p<0.0001) and obesity indices (BMI, BSA) (p<0.00001, p<0.00001), in both groups.

Conclusion

TDI identifies DD more frequently than transmitral PW Doppler in asymptomatic patients with or without diabetes.

Keywords

Tissue doppler imaging; PW doppler echocardiography; Left ventricular diastolic dysfunction; Diabetic cardiomyopathy; Diabetes mellitus type 2

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Received Date: 01st August 2014
Accepted Date: 11th September 2014
Published Date: 15th September 2014

Citation: Mitrovska S, Jovanova S, Lazeska B (2014) Tissue Doppler Imaging in the Early Detection of Diastolic Dysfunction in Asymptomatic Diabetic Patients. Enliven: Clin Cardiol Res 1(2): 004.

Introduction

Left ventricular diastolic dysfunction (LVDD) is very common in diabetic population even in the absence of coronary artery disease, valve pathology and hypertension. It is an indicator of myocardial damage before heart failure becomes apparent, and serves as a predictor of adverse cardiac events. Hence, the early identification of myocardial dysfunction and correction of potentially modified risk factors, are very important in order to delay the onset of heart failure. Unfortunately, subclinical cardiomyopathy still remains unrecognized in asymptomatic diabetic patients [1].

The conventional Pulsed-wave (PW) Doppler echocardiography is dependent of multiple factors, the influence of volume changes on transmitral flow, heart rate, left atrial pressure, that make the method inadequate for the diagnosis of diastolic dysfunction.

Tissue Doppler Imaging (TDI) is a non-invasive cardiac imaging technique, relatively independent to the loading conditions and provides comprehensive assessment of myocardial tissue velocities [2]. It measures the velocity of the longitudinal motion of the mitral annulus. Systolic wave (S) corresponds to LV ejection and diastolic waves-E´ reflects the LV relaxation (elongation), while A'-wave reflects the left atrial (LA) contraction and late LV filling (shortening). E'-wave progressively decreases with decreasing longitudinal lengthening (relaxation) in various pathological conditions. It is the earliest marker of diastolic dysfunction and is present in all its stages.

Clinical sequelae from early diastolic dysfunction could be averted or delayed if early identification occurs via a reliable noninvasive approach such as TDI [3].

The Aim

To assess the role of TDI in the early detection of diastolic dysfunction in asymptomatic diabetic patients.

Methods and Materials

The cross sectional study consisted of 48 subjects. Twenty-five asymptomatic patients with diabetes mellitus type 2 (free of dyspnoe, fatigue, exercise intolerance, increased extracellular volume, angina) comprised the target (diabetic) group, and the control group included 23 apparently healthy subjects.

Inclusion criteria were type 2 diabetic patients (insulin dependent or non-dependent), duration of diabetes (between 1 to 10 years), free of coronary artery disease (normal resting 12-lead ECG/normal exercise stress test/normal coronary angiogram), hypertension and valve diseases.

Exclusion criteria were systolic dysfunction, defined as ejection fraction (EF) <50% (determined with M mode echocardiography using Teichholz formula), significant arrhythmia and any stage of renal failure.

The study was approved by the ethical committee of Medical Faculty, Skopje, and the patients who met the criteria, signed an informed consent.

All patients under went transthoracic echocardiography using Philips HD7 system echocardiography machine with 3, 5 MHz probe and in accordance with the recommendation of American Society of Echocardiography. Conventional techniques (two-dimensional-2D, M-mode echocardiography, Pulsed-wave Doppler Analysis-PW) and Tissue Doppler Imaging-TDI were used to assess LV morphology and function.

LV systolic function was assessed by Teichholz method - calculation of LV end diastolic and end systolic volumes (LVEDV, LVESV) and ejection fraction, by measuring the LV linear dimensions in systole and diastole (LVEDd, LVESd), interventricular septum thickness (IVS) and the thickness of the posterior wall (PW), in parasternal long axis, at the level of the mitral chords.

Ejection fraction was expressed as a percentage and EF>55% was considered as normal systolic function. EF between 40% and 55% was considered as slightly reduced, EF of 30-40% was considered as moderately reduced and EF less than 30% was considered as severe reduced systolic function.

PW Doppler echocardiography was carried out to assess LV diastolic function. In the apical 4-chamber view, with the sample volume placed at the mitral valve leaflet tips, transmitral flow velocities (early-E and late-A diastolic filling velocities, DT-deceleration time, IVRT- isovolumic relaxation time, E/A ratio) were recorded. Diastolic function was classified into 4 groups: 1-Normal (E/A=0,7-1.3, DT=140-240 ms, IVRT=76±13 ms), 2- Mild LVDD (E/A <1, DT>240 ms, IVRT>90 ms), 3- Moderate LVDD (E/A =1.0-1.5, DT=160-240 ms, IVRT=76 ±13 ms), 4- Severe LVDD (E/A>2, DT < 160 ms, IVRT<60 ms) [4].

During the longitudinal LV movement, the apex remains relatively stationary and measurement of peak velocities of mitral annular motion by Pulsed-wave TDI, give us data of overall longitudinal motion. A 2 mm sample volume was placed on septal corner of mitral annulus. An average of 3 to 5 consecutive cardiac cycles was taken for the calculation of all echo-Doppler parameters and systolic velocity (S'), early diastolic velocity (E') and myocardial velocity associated with atrial contraction (A') - were measured.

E' velocity ≤ 8 cm/s was indicator of diastolic dysfunction. The E/E' ratio was used to estimate LV filling pressures. The value E/E'< 8 indicated normal LV end-diastolic pressure, whereas E/E'>10 was accepted as an elevated LV end-diastolic pressure [5].

Statistical Analysis

The statistical analyses were performed by using the commercial statistical package, Statistica for Windows, Version 7.0. Continuous parameters were expressed as mean+SD. The Mann-Whitney U-test was used for two independent variables and Wilcoxon Matched Pairs Test for two dependent samples. A p value< .05 was considered to indicate significance.

Results

A total of 48 subjects were enrolled in this study. Diabetic group consisted of 25 asymptomatic patients with diabetes mellitus type 2. Fifteen of them (60%) were on insulin, and 10 (40%) patients were on oral hypoglycemic medications. Thirteen patients (52%) were female, mean age 41.8±5.9 and 12 (48%) were male, mean age 41.5±7.8. The control group was composed of 23 apparently healthy subjects. Ten patients (43.5%) were female, mean age 39± 6.33, and 13 (56.5%) were male, mean age 45±6.29.

Demographic and clinical characteristics are summarized in Table 1.

Parameters	Study (diabetic) group (n=25)				Control group (n=23)				p=value
	Mean	**Min**	**Max**	**SD**	**Mean**	**Min**	**Max**	**SD**	
Age (years)	42	30	53	6.56	43	30	54	7.5	NS
Duration of diabetes (years)	6.0	1	10	3.10	/	/	/	/	/
HbA1c (%)	6.8	4.5	9.1	1.31	/	/	/	/	/
Weight (Kg)	68.6	47	92	11.6	71.3	45	95	12.2	NS
Height (cm)	168.6	152	196	10.8	171.1	155	183	7.84	NS
BMI (Kg/m^2)	24	19.2	27.9	2.56	24.1	16.9	28.4	3.02	NS
BSA (m^2)	1.74	1.4	2.1	0.20	1.77	1.4	2.1	0.18	NS
Waist to hip ratio	0.84	0.70	0.98	0.10	0.85	0.70	1.00	0.07	NS

Table 1. Demographic and clinical characteristics of the study patients

Both groups were homogeneous in terms of demographic and clinical parameters. Biochemical analyses showed that 10 (40%) patients in diabetic group and 8 (34.7%) in control group, had dyslipidaemia ($Z=0.32$, $p<0.7$).

Echocardiographic Findings. Pulsed-Wave Doppler Analyses

All patients underwent conventional 2D, PW Doppler echocardiography and Tissue Doppler assessment of myocardial tissue velocities.

In study group, 16 patients (64%) had diastolic dysfunction, assessed by PW Doppler technique and 9 (36%) had normal transmitral flow velocities. Thirteen (81.3%) of patients with DD had abnormal relaxation and 3 (18.7%) patients had pseudonormal type of DD (Figure 1.)

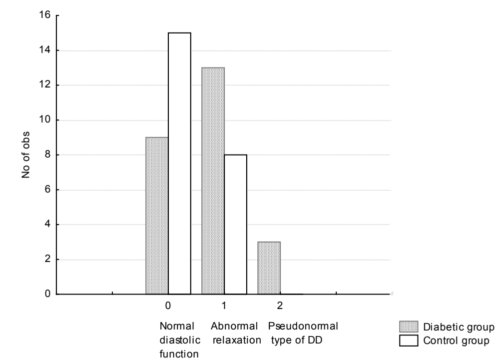

Figure 1. Diastolic function assessed with PW Doppler, in both groups

In control group, PW Doppler noted 15 (65.2%) patients with normal transmitral flow parameters, and 8 (34.7%) patients with abnormal relaxation.

The values of transmitral flow variables derived from PW Doppler techniques are given in table 2.

PW Doppler	Study (diabetic) group (n=25)				Control group (n=23)				p=value
	Mean	**Min**	**Max**	**SD**	**Mean**	**Min**	**Max**	**SD**	
E (cm/s)	0.4	0.3	1.1	0.16	0.7	0.4	1.1	0.16	NS
A (cm/s)	0.6	0.3	1.3	0.20	0.8	0.4	1.3	0.25	NS
E/A	0.7	0.5	1.4	0.31	0.9	0.5	1.3	0.28	NS
DT (ms)	178	132	247	42.6	194	75	276	52.5	NS
IVRT (ms)	80.1	55	120	16.2	74.4	56	120	14.5	NS

Table 2.Transmitral flow velocities derived from Pulsed-wave Doppler techniques

In our study we found no statistically significant differences in mitral inflow velocities (E, A, E/A, DT and IVRT) between two groups ($Z=0.0$, $p<1.0$).

Tissue Doppler Imaging

Tissue Doppler parameters (E´ and E/E´) pointed out diastolic dysfunction in 18 (72%) diabetic patients. Seven (28%) patients had normal diastolic function.

In control group, 13 (56.5%) patients had diastolic dysfunction and 10 (43.4%) had normal diastolic function (Figure 2). E' velocities obtained at the septal side of mitral annulus, were significantly lower in the target group (diabetic patients) vs control group ($Z=2.11$, $p< 0.03$).

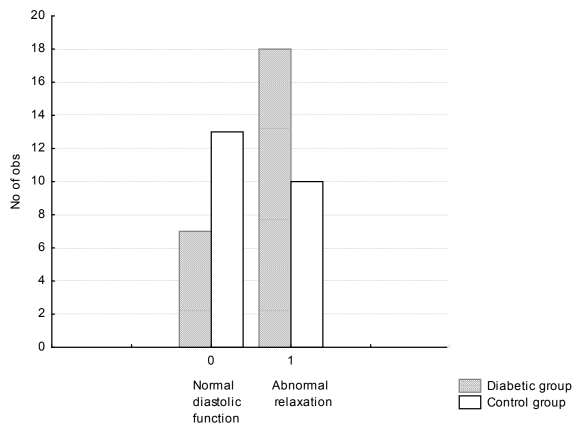

Figure 2. Diastolic function assessed with Tissue Doppler Imaging, in both groups

TDI identified statistically significant higher E/E´ in diabetic group vs control group ($Z= -2.12$, $p<0.03$).

The velocities of the mitral annular motion measured at a septal corner by Tissue Doppler imaging are given in table 3.

We noted statistically significant difference between the two echocardiographic techniques, TDI vs PW Doppler, in terms of detection of diastolic dysfunction (E/E´ vs E/A) within each group.

TDI was more sensitive in identifying DD in diabetic vs control group ($Z=2{,}01$, $p<0.04$).

Mann-Whitney U-test did not show statistical significance comparing presence of DD in diabetic versus control group, with PW Doppler analysis ($Z=1.80$, $p<0.07$).

TDI	Study (diabetic) group (n=25)				Control group (n=23)				p=value
	Mean	Min	Max	SD	Mean	Min	Max	SD	
E´ (cm/s)	4.1	2.0	9.0	2.61	13.1	4.0	28	8.82	p<0.03
E/E´	24.5	7.0	36.0	11.30	8.0	2.0	14.0	4.79	p<0.03

Table 3. Mitral annular velocities measured at a septal corner by Tissue Doppler Imaging

	TDI	PW Doppler	Z	p=value
Study group	18	16	3.38	p<0.00
Control group	10	8	2.48	p<0.01

Table 4. Comparison of Echocardiographic techniques (TDI vs PW Doppler) in detection of DD within each group

	Study group	Control group	Z	p=value
TDI	18	10	2.01	p<0.04
PW Doppler	16	8	1.80	p<0.07

Table 5. Comparison of Echocardiographic techniques (TDI vs PW Doppler) in detection of DD between both groups

Relation of Diastolic Parameters with Risk Factors

Thirteen (52%) patients with diabetes mellitus, had poor glycemic control (HbA1c > 7%) and had higher prevalence of DD than patients with HbA1c < 7% (Z=-4.3,p<0.0004).

Diastolic dysfunction was significantly higher in patients with longer duration of DM, between 5-10 years vs 1-5 years (p<0.00001), in patients older than 40 years (p<0.00001), in female gender (p<0.0001) and obesity indices - BMI and BSA (p<0.00001, p<0.00003).

In control group, we also find statistically significant relation of DD with age, female gender and obesity indices - BMI and WHR (p<0.0002, p<0.0004, p<0.0002 and p<0.0003).

Discussion

Diagnosis of diabetic cardiomyopathy is a challenge for cardiologists. Current technology and methods are still subjects of modification and they do not have routine use in daily practice. Echocardiography is a diagnostic method of choice, from practical and economic point of view, but conventional Pulsed Doppler analysis has limitations and provides inconclusive results. Tissue Doppler Imaging is more sensitive method that measures the velocity of the longitudinal motion (shortening and lengthening) of the mitral annulus and has the capability for early detection of diastolic dysfunction.

In our study we compared the results from the two echocardiographic techniques and demonstrated that TDI is superior to PW Doppler in early detection of subclinical diastolic dysfunction. Kibar and coworkers also demonstrated that TDI of the septal corner of mitral annulus provides better estimation of diastolic dysfunction than PW Doppler parameters [6].

Omen and coworkers in their catheterization study concluded that the ratio of mitral velocity to early diastolic velocity of the mitral annulus (E/E') better correlated with LV filling pressures than other Doppler variables [7].

E'-wave reflects the LV relaxation and progressively decreases with decreasing longitudinal lengthening in patients with diabetes mellitus. In our study we noted statistically significant reduction of E´ wave in diabetic group vs control group (p< 0.03).

Jong-Won in his study, examined the changes of E´ in diabetic patients during the exercise, and find significantly smaller changes in magnitude of E´ in diabetic group, during the exercise compared with control group (p<0.032) [8].

Also, we evaluated the relation of diastolic dysfunction with various risk factors (age, gender, duration of DM, HbA1c, lipid profile and obesity indices - BMI, and WHR). There were statistically significant associations of DD in both groups (p<0.00).

Our findings are comparable to other studies. Thus, Patil et al. [9] noted higher prevalence of DD in patients with longer duration of diabetes (more than 5 years) (p<0.02), bad glycemic control (HbA1c>7%) (p<0.02) and obesity (WHR) (p<0.002).

Shrestha NR and coll. also confirmed strong association between diastolic dysfunction and age, duration of DM and female gender [10].

Although many studies suggest correlation between hyperlipidaemia and diastolic dysfunction, our analysis did not confirm this relationship in both groups (p<0.1 for diabetic and p<1 for control group) [11].

We have no clear explanation why this is so, but if we take into consideration the fact that patients with good glucose regulation (HbA1c<7%) have a lower rate of diastolic dysfunction, we can assume that it may be due to the treatment. Namely, the majority of study subjects with dyslipidaemia were already on statins.

Study Limitations

Our study has few limitations. They relate to the small number of participants in both groups, as well as the type of study which is cross-sectional study.

We believe that prospective study, with a larger number of subjects, will better show the advantage of TDI for early detection of diastolic dysfunction, even in a time frame. That time difference is of great importance for decision of early and intensive treatment of risk factors.

Therefore, we believe that the introduction of TDI as a routine method in everyday practice, will contribute to the early identification of myocardial dysfunction and treatment initiation, in order to delay the onset of heart failure.

Conclusion

TDI unmasks the presence of subclinical LV diastolic dysfunction in asymptomatic diabetic patients with more frequency than PW Doppler.

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