Tissue Doppler Image During Dobutamine Stress for Detection of Sub-Clinical Myocardial Dysfunction in Diabetic Patients

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Abstract

Background: The prevalence of type 2 diabetes mellitus is rapidly increasing. Myocardial dysfunction may be a consequence of diabetic cardiomyopathy and it contributes to the poor prognosis of diabetic patients.

Aim: Evaluation of subclinical myocardial dysfunction in diabetic patients.

Methods: Thirty patients with type 2 diabetes and thirty control subjects without clinical signs of coronary artery disease and with normal left ventricular function by standard 2D echocardiography, were investigated with DTI at rest and at peak stress echocardiography (DSE). Myocardial function was calculated as mean value from four basal left ventricular segments for the peak velocity at systole (Sm), early diastole (Em), atrial contraction (Am) and ratio E/A.

Results: At rest diabetic patients had significantly compromised Em (p<0.01), higher Am (p<0.02), lower E/A (p<0.001) and insignificant Em than in the control group. At stress patients with diabetes showed increased Em by 17.6%, Am by 11.8%, E/A by 6.6% and Sm by 14.6% compared to baseline values. In the control group changes in myocardial function induced by stress were more pronounced: Em increased by 34.3%, Am 15.8%, E/A by 15.4% and Sm by 37.8%. Impaired response of myocardial function during (DSE) in diabetic patients resulted in more significant difference in Em (p<0.001) and significant difference in Sm (p<0.001) between diabetic patients and controls after stress.

Conclusion: Patients with type 2 diabetes have early signs of diastolic and systolic myocardial dysfunction which are more expressed at DSE. Which can be identified by DTI before appearance of signs of cardiovascular disease.

Key Words: Tissue doppler – Dobutamine stress echo – Diabetes – Myocardial dysfunction

Introduction

TYPE 2 diabetes mellitus is a major risk factor for ischemic heart disease and may cause cardiomyopathy. Heart failure has a worse prognosis in diabetic than in non-diabetic patients. Evidence of diastolic dysfunction appears early in the natural history of type 2 diabetes mellitus and evidence of impaired systolic function may subsequently become apparent [1].

Early detection of diabetic heart disease is of paramount importance, because life-style modifications and medical interventions could prevent or delay the subsequent development of heart failure [2].

Early manifestation of diabetic LV systolic dysfunction appeared longitudinally, because subendocardial fibers, which are prone vulnerable to myocardial ischemia, have a longitudinal trajectory. The presence of impaired longitudinal function in diabetic patients has been reported when using tissue Doppler imaging [3].

Even a mild degree of diastolic dysfunction has prognostic impact. Accordingly, there is a need for a sensitive and easily applied technique for the detection and follow-up of myocardial dysfunction in the diabetic patient before clinical evidence of compromised cardiac function is apparent. This has not been achieved by traditional two dimensional echocardiography or Doppler-based studies mitral inflow pattern [4].

Aim of the study:

Early detection and quantification of myocardial dysfunction in diabetic patients.

Patients and Methods

The study included 60 cases (30 patients with type 2 DM and 30 control cases); who were referred to Benha University Hospital, Cardiology Department Echocardiography Unit from Nov. 2012 – Feb. 2013. All patients had normal LVEF with no regional wall motion abnormalities on 2D echocardiography.
Diabetes mellitus (DM) was diagnosed according to World Health Organization (WHO) and the American Diabetes Association (ADA) as fasting blood glucose ≥ 126 mg/dL (≥ 7.0 mmol/L) or 2 hour post-load plasma glucose ≥ 200 mg/dL (≥ 11.1 mmol/L) or random plasma glucose ≥ 200 mg/dL [5] or when patients on regular hypoglycemic drugs or insulin.

Exclusion criteria included a history of coronary artery disease or evidence of ischemia in surface ECG, the presence of moderate-to-severe valvular heart disease, and/or significant rhythm disturbances.

Echocardiography:

Patients were imaged in the left lateral decubitus position using a commercially available system (Vivid 7, General Electric-Vingmed). Images were obtained, with a simultaneous ECG signal.

Conventional echo study:

2D images were acquired during breath hold and saved in cine-loop format from three consecutive beats. The biplane Simpson’s technique was used to calculate LV end-systolic volume (ESV), LV end-diastolic volume (EDV) and LVEF.

M Mode echo: Measurement of the left ventricular dimension in systole (LVIDs), and diastole (LVIDd), Interventricular septum (IVSd, IVSs), posterior wall thickness (PWTd, PWTs), and LVEF %. Pulsed-wave Doppler echo: pulsed-wave Doppler of the mitral valve obtained by placing the Doppler sample volume between the tips of the mitral leaflets. The early (E) and late (A) peak diastolic velocities and E-wave deceleration time were measured.

Tissue doppler study:

By activating tissue Doppler image function in the echocardiography machine, the mitral annular velocities were recorded using the pulsed-wave DTI. From the apical 4- and 2-chamber views, the longitudinal mitral annular velocities were recorded from septal, lateral, inferior and anterior LV sites. A mean value for the above four sites were used. Three major velocities were taken into account: The positive peak systolic velocity when the mitral ring move toward the cardiac apex due to longitudinal contraction of the LV, and two negative diastolic velocities when the mitral annulus move toward the base away from the apex, one during the early phase of diastole and the second wave in the late phase of diastole. A mean of three consecutive cycles was used to calculate all echo-Doppler parameters twice (at rest and during the peak stress test).

Stress echo:

The patients abstain from all oral intakes for at least 3 hours before the procedure. β-blockers were withheld 48 hours before testing. Dobutamine was administrated intravenously by an infusion pump at a starting dosage of 10 µg/kg/min. At 3-minute intervals, the dosage is increased to 20, 30, and 40 µg/kg/min until a predetermined endpoint was reached. If neither target heart rate (85% of age-predicted maximal heart rate) nor any of the other endpoints was reached, the infusion rate was increased up to 50 µg/kg/min for 3 min., or atropine was administrated intravenously. A dose of 0.25 to 0.5 mg of atropine was repeated at 1 minute intervals to a maximal dose of 2 mg or until an endpoint was reached and dobutamine infusion is continued during atropine administration. Throughout the dobutamine infusion the ECG was continuously monitored and recorded at 1 min. intervals and BP is recorded every third minute. End-points for interruption of the test were: 1- Achievement of target heart rate; 2- Maximal dose of both dobutamine and atropine; 3- Extensive new wall motion abnormalities; 4- Severe angina; 5- Symptomatic reduction in systolic blood pressure >40 mmHg from baseline; 6- Hypertension (blood pressure >240/120 mmHg); 7- Significant arrhythmias or 8- Any serious side effect regarded as being due to dobutamine infusion [6].

Statistical analysis:

Data are presented as mean ± standard deviation for normally distributed quantitative data, and as number and percentages for categorical data. Chi square test (X²) “Z” test and student “t” tests were used for between groups comparison in qualitative and quantitative data respectively. Paired sample t-test was used for within group comparison.

Results

The study included 60 patients divided into two groups: Group (I) included 30 diabetic patient and group (II) included 30 control cases of comparable age and gender and insignificant difference diabetes, BMI, smoking and hypertension (Table 1: Shows the demographic data of the study groups).

At rest all conventional echocardiography parameters were within normal in both groups (Table 2) but by activation of the tissue Doppler velocity diabetic group showed statistically significant lower Em (p<0.01), higher Am (p<0.02) and lower E/A (p<0.001) and insignificant lower Sm (Table 3).
At peak stress there were significant increase in all tissue Doppler parameters in both groups but the degree of increase was more pronounced in the control group and the difference in Em, Sm and Am were statistically significant \((p<0.001)\) (Tables 3,4) and Figs. (1,2).

![Graph 1](image1.png)

Fig. (1): Comparison between resting and peak TDI parameters between 2 groups.

![Graph 2](image2.png)

Fig. (2): Comparison between the percent of increase in TDI parameters at peak stress between 2 groups

### Case Presentation

![Image 3](image3.png)

Fig. (3): The above 4 images showing the average Pulsed wave TD (Sm) of the patient at baseline about (12.5cm/s). (A) Pulsed-TD (Sm) at the level of basal inferior about (11cm/s), (B) Pulsed TD (Sm) at the level of basal anterior about (10cm/s), (C) Pulsed-TD (Sm) at the level of basal septum about (12cm/s), (D) Pulsed TD (Sm) at the level of basal lateral about (11 cm/s).

![Image 4](image4.png)

Fig. (4): The above 4 images showing the average Pulsed wave TD (Sm) of the patient during dobutamine stress about (7cm/s). (A) Pulsed-TD (Sm) at the level of basal inferior about (5cm/s), (B) Pulsed TD (Sm) at the level of basal anterior about (6cm/s), (C) Pulsed-TD (Sm) at the level of basal septum about (8cm/s), (D) Pulsed TD (Sm) at the level of basal lateral about (9cm/s) with observed improved values during the stress test.
Table (1): Demographic data of the study groups.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I (n=30)</th>
<th>Group II (n=30)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>45.3±6</td>
<td>43.9±7</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Male/female</td>
<td>16/14</td>
<td>15/15</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>28.5±4</td>
<td>27.3±6</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>14 (46.6%)</td>
<td>17 (56.6%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>10 (33.3%)</td>
<td>8 (26.6%)</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

BMI: Body mass index

Table (2): Conventional echocardiography parameters.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I</th>
<th>Group II</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVSd (mm)</td>
<td>10.41±1.9</td>
<td>11.21±2.3</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>LVIDd (mm)</td>
<td>48.26±4.9</td>
<td>48.21±3.9</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>PWTd (mm)</td>
<td>10.52±2.1</td>
<td>10.68±3.4</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>IVSs (mm)</td>
<td>13.21±1.5</td>
<td>12.67±2.3</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>LVIDs (mm)</td>
<td>3.5±2.3</td>
<td>3.2±3.3</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>PWTs (mm)</td>
<td>13.1±1.5</td>
<td>13.2±2.1</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>EF %</td>
<td>65.9±5.5</td>
<td>67.6±5.8</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>WMSI</td>
<td>1±0.18</td>
<td>1±0.25</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

IVSd: Interventricular septum in diastole.
LVIDd: Left ventricle internal dimension in diastole.
PWTd: Posterior wall thickness in diastole.
IVSs: Interventricular septum in systole.
LVIDs: Left ventricle internal dimension in systole.
PWTs: Posterior wall thickness in systole.
EF: Ejection fraction.
WMSI: Wall motion score index.

Table (3): Tissue Doppler parameters during rest and peak stress test.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Parameter</th>
<th>Group I</th>
<th>Group II</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td>Sm (cm/s)</td>
<td>8.7±3.6</td>
<td>9.4±3.4</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Em (cm/s)</td>
<td>9.3±3.6</td>
<td>9.5±2.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Am (cm/s)</td>
<td>8±3.4</td>
<td>8±3.4</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td></td>
<td>E/A</td>
<td>0.91±0.36</td>
<td>1.1±0.35</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak stress</td>
<td>Sm (cm/s)</td>
<td>10.3±4.2</td>
<td>13.3±3.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Em (cm/s)</td>
<td>10±3.5</td>
<td>12±3.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Am (cm/s)</td>
<td>10.4±3.2</td>
<td>9.5±3.3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>E/A</td>
<td>0.77±0.39</td>
<td>1.3±0.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Sm: Systolic velocity.
Em: Early diastolic velocity.
Am: Late diastolic velocity.

Table (4): Percent of increase in TDI parameters at peak stress.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I</th>
<th>Group II</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sm</td>
<td>14.6%</td>
<td>37.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Em</td>
<td>17.6%</td>
<td>34.3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Am</td>
<td>11.8%</td>
<td>15.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E/A</td>
<td>6.6%</td>
<td>15.4%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Sm: Systolic velocity.
Em: Early diastolic velocity.
Am: Late diastolic velocity.

Discussion

Patients with diabetes are at a greater risk of cardiovascular disease than individuals who are not diabetic and they suffer significantly greater rates of cardiovascular mortality. Cardiovascular disease accounts for up to 80% of mortality in patients with type 2 diabetes and the age-adjusted relative risk of cardiovascular death is three times greater in these patients than in the general population [7].

It has been demonstrated that cardiovascular risk increases before the onset of diabetes is associated, not just with increased cardiovascular disease, but also with a worse outcome. One reason for this appears to be enhanced myocardial dysfunction leading to diabetic cardiomyopathy which predisposes patients to congestive heart failure [8].

Several factors probably underline this condition: Chronic hyperglycemia, severe coronary ath erosclerosis, microvascular disease, prolonged hypertension, glycosylation of myocardial proteins and autonomic neuropathy. According to all, early detection of clinical and subclinical cardiovascular disease in diabetic patients has important therapeutic and prognostic implications. Stress echocardiography and DTI are one the most-effective imaging techniques for assessing myocardial function and ischemia in hyperglycaemic asymptomatic patients.

Our results confirm that PW-DTI is a useful method in the quantification of regional myocardial velocity and that measurement of regional myocardial function can identify the presence of myocardial dysfunction in basal condition as well as during DES. We showed significantly lower baseline values of Em and ratio E/A; higher Am and lower Sm in diabetic patients than in control subjects [8].

Our results for baseline peak myocardial velocity at early diastole and atrial contraction as well as for ratio E/A in diabetic patients reproduced values of the same parameters found by Elnoamany et al., [9].

The present study showed significantly lower basal Em and ratio E/A in diabetic patients indicating the presence of diastolic myocardial dysfunction. Galderisi has shown that diastolic filling abnormalities are common in patients with type 2 diabetes, which may represent early subclinical alterations in cardiac function [10].

Also increase in Em, Am, Sm and ratio E/A during DSE in both examined groups were found, but the rate of these changes was morefavorable
in controls than in diabetic patients. Impaired response of myocardial function during DSE in diabetic patients resulted in more significant difference in Emand significant difference in Sm between the two examined groups, after DSE. Our results are similar to those reported by Bibra et al., [11], who described the use of PW-DTI in diabetic patients during dobutamine/dipyridamole stress echocardiography. The results of this study emphasized the value of Doppler tissue velocity sampling for the assessment of myocardial function in patients with type 2 diabetes mellitus. Early detection of impaired myocardial function using PW-DTI, signals the need for institution of more aggressive preventive measures in diabetic patients with subclinical cardiovascular disease.

**Conclusion:**

In the evaluation of myocardial function, PW-DTI is an important step in the effort to objectively assess early signs of myocardial dysfunction. Quantitative PW-DTI in type 2 diabetic patients identified early signs of predominant diastolic and also systolic myocardial dysfunction.

Application of stress echocardiography with PW-DTI increases the diagnostic capacity of stress echo in detection of myocardial impairment in diabetic patients with subclinical cardiovascular disease.

**Acknowledgment:**

WWW. Bu.edu.eg
WWW.fac.bu.edu.eg

**References**


