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Assessment of Left Ventricular Diastolic Reserve in Diabetic Patients by Stress Echocardiography

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Abstract

Background: Patients with type 2 diabetes mellitus (DM) may develop cardiomyopathy independent of traditional risk factors such as hypertension and epicardial coronary artery disease (CAD). The spectrum of myocardial dysfunction may range from subclinical left ventricular (LV) diastolic and systolic dysfunction through to overt systolic dysfunction.

Aim and objectives: To determine whether diastolic reserve differs in type 2 DM compared with non-DM, and to identify clinical, anthropological, metabolic and resting echocardiographic correlates of impaired diastolic reserve in patients with DM.

Subjects and methods: This study included one hundred consecutive patients (50 patients with DM type I patients without DM), who underwent rest and exercise echocardiography. Clinical data collected included anthropometric, cardiac risk factors, duration of DM, medications and presence of macrovascular and microvascular complications. Mitral septal e and septal E/e were measured at rest, immediately post, and 10 min into recovery.

Results: LDL, cholesterol, triglyceride, creatinine and BMI was significantly higher in in diabetic group than non-diabetic group (P value < 0.05). Regarding rest echocardiography parameters, Septal E/e, Septal e and EF were insignificant between both studied groups. Regarding stress echocardiography parameters, septal E/e was significantly higher and septal e was significantly decreased among diabetic patients among diabetic patients compared to the other group (P < 0.001).

Conclusion: Patients with DM have impaired LV diastolic reserve manifest as septal E/e values were higher among diabetic group in response to exercise leading to an abnormal rise in LV filling.

Keywords: Diabetic patients, Diastolic reserve, Left ventricular, Stress echocardiography

1. Introduction

Patients with type 2 diabetes mellitus (DM) may develop cardiomyopathy independent of traditional risk factors such as hypertension and epicardial coronary artery disease (CAD). The spectrum of myocardial dysfunction may range from subclinical left ventricular (LV) diastolic and systolic dysfunction through to overt systolic dysfunction. Patients may initially be asymptomatic, progressing to exertional dyspnoea, followed by overt symptomatic heart failure in advanced stages of the disease.

Elevation in LV filling pressures is the underlying pathophysiology leading to exertional dyspnoea in patients with LV systolic or diastolic dysfunction. LV filling pressures can be reliably estimated non-invasively with transthoracic echocardiography from the mitral e wave velocity with pulsed wave Doppler to mitral annulus tissue Doppler e velocity ratio.

Diastolic reserve is the ability of the LV to augment diastolic function to maintain normal filling pressures with tachycardia such as that seen during exercise. Analogous to an impaired contractile reserve in latent LV systolic dysfunction, an
impaired diastolic reserve may be seen in early stages of diastolic dysfunction such as that seen in diabetic cardiomyopathy. Previous studies have demonstrated the utility of exercise echocardiography in evaluating patients with exertional dyspnea to unmask diastolic dysfunction.  

Few studies have specifically looked at its utility in estimating LV filling pressures with exercise in patients with DM. The correlates of an impaired LV diastolic reserve in type 2 DM are unclear. Furthermore, no studies have examined the behavior of LV filling pressures into the recovery period after exercise in such patients. Examining diastolic reserve and its behavior post-exercise into recovery may allow even earlier detection of diabetic cardiomyopathy in patients with apparently normal resting LV systolic and diastolic function with normal LV filling pressures at rest.  

The objective of this research was to determine whether diastolic reserve differs in type 2 DM compared with non-DM, and to identify clinical, anthropological, metabolic and resting echocardiographic correlates of impaired diastolic reserve in patients with DM.

2. Patients and methods

One hundred consecutive patients (50 patient with DM type II and 50 patient without DM), who were referred for cardiovascular assessment at the hospital clinic were underwent rest and exercise echocardiography. All patients provided written informed consent. The study approved by the Hospital Human Ethics Committee.

DM type I, known congenital, valvular or CAD, severe hypertension (systolic pressure >200 mmHg and diastolic pressure >120 mmHg at rest), left bundle branch block, rhythm other than sinus and those unable to exercise were excluded.

Mitral septal e and septal E/e were measured at rest, immediately post, and 10 min into recovery.

Analysis of covariance (ANCOVA) and binary regression with continuous outcomes were used to model e and E/e changes with exercise to identify impaired diastolic reserve defined as post-exercise E/e ≥15.

All participants had a normal resting ECG. All cardiac medications were continued throughout the study with no modifications made to the patients’ treatment regimen.

Clinical data collected included anthropometric, cardiac risk factors, duration of DM, medications and presence of macrovascular and microvascular complications.

2.1. Statistical analysis

We used statistical package for social sciences (SPSS) version 24 software for analyzing the data. Numerical data was described in terms of means and standard deviation if parametric. Kolmogrov–Semornov test was used to test the normality of distribution of numerical variables. Chi square test was used to test the association between categorical variables. Fissure exact test was used in case of violation of the assumptions. Independent sample t test was used to test the difference between two groups concerning parametric numerical variables. Paired sample t test was used to test the association between paired numerical data. P value less than 0.05 was considered statistically significant.

3. Results

The sociodemographic characteristics of included patients were illustrated in Table 1.

Mean ages were significantly higher among diabetic patients when compared to the other group (53.86 ± 8.24 vs 48 ± 9.53) years old respectively (P = 0.001). Concerning other risk factors as smoking, positive family history and hypertension, they were statically insignificant different between both studied groups (P > 0.05) Table 2.

Regarding laboratory findings, HDL was significantly lower in diabetic group than non-diabetic group (P value = 0.001). LDL, cholesterol, triglyceride, creatinine and BMI was significantly higher in diabetic group than non-diabetic group (P value < 0.05) Table 3.

Regarding rest echocardiography parameters, Septal E/e, Septal e and EF were insignificant between both studied groups Table 4.

Regarding stress echocardiography parameters, regarding stress echocardiography parameters, septal E/e was significantly higher and septal e was significantly decreased among diabetic patients among diabetic patients compared to the other group (P < 0.001) Table 5.

| Table 1. Sociodemographic characteristics of included patients (n = 100). |
|--------------------------|------------------|
| Variable                 | N (%)            |
| Age (years)              | 50.93 ± 9.34     |
| Smoking                  | 31 (31)          |
| Positive family history  | 11 (11)          |
| Hypertension             | 38 (38)          |
| Diabetes mellitus Nondiabetic | 50 (50) 20 (20) 30 (30) |
| Dm ≤ 5 years Dm > 5 years| 50 (50)          |

DM: diabetes mellitus.
Concerning change between rest and stress echocardiography, among diabetic patients: Septal e was significantly higher in in rest echo than stress (P value < 0.001). LVEDD, Septal E/e significantly lower in in rest echo than stress (P value < 0.001). LVEDS was insignificantly different between rest and study echocardiography. Among non-diabetic patients: LVEDD, Septal E–e, Septal e, Septal S and EF were significantly lower in in rest echo than stress (P value < 0.001). LVEDS was insignificantly different between rest and stress echocardiography Table 6.

4. Discussion

Diabetes is considered one of the most common diseases in the world and the main cause of mortality and morbidity in those patients are cardiovascular complications especially in females as more than 75% of all diabetic patients die from cardiovascular causes.5

Examining diastolic reserve in DM may allow even earlier detection of impairment of LV involvement, at a stage where the resting systolic and diastolic function is still comparable to that of normal healthy subjects. Ha et al. demonstrated a blunted increase in the mitral annular s0 and é velocities in patients with type 2 DM compared with controls despite similar velocities between the two groups at rest.6

Similar impairment in the increase in é velocities was noted by Jellis et al. in patients with DM and normal resting é velocities. However, LV diastolic pressures as a consequence of inducible LV diastolic dysfunction were not examined in these studies. In this study, were able to demonstrate that patients with type 2 DM had worse LV diastolic function and elevated diastolic pressures post-exercise even after controlling for baseline differences.

Studies like Acar et al.,7 Gul et al.,8 and Shaker et al.9 show no significant septal thickening in diabetic patients while other studies show that IVSd is higher in diabetic group like Suys et al.10 Regarding LVEDd, there was no significant difference between diabetic and control group. This is in agreement with Acar et al.,7 Rowland et al.11 and Kimball et al.12 who found that stroke volume significantly increased in diabetic patients while Airaksinen et al.13 found that stroke volume is significantly decreased in diabetic patients with severe complications.

Leung M et al.14 showed that Patients with DM had smaller LV systolic volumes and hence a higher LV ejection fraction, a lower septal é and hence a higher septal E/e.

Septal E/e ratio as an indicator of LV diastolic pressure is not only useful at rest but has also been shown to be reliable post-exercise. Burgess et al.15 studied 37 patients who underwent exercise echocardiography on a supine bike with estimation of E/e and LV filling pressures simultaneously on cardiac catheterization. They found good correlation between exercise E/e and LV diastolic pressures with a cut-off of E/e ≥13 as indicative of LV end-diastolic pressures of ≥15 mmHg. In fact, the correlation between LV diastolic pressures and E/e were of a similar magnitude at rest and during exercise. Similar to the study of Burgess et al. and others, we used septal é instead of lateral é, as assessment of lateral é post-exercise tended to be more unreliable with tachycardia and respiratory motion.6,16

Exercise E/e is of additional diagnostic and prognostic value. An elevated exercise E/e was found to be correlated with exercise capacity.14

Holland et al., 2010 found that an exercise E/e >14.5 independently predicted adverse
Cardiovascular outcome in 538 consecutive patients with normal resting LV systolic function undergoing exercise echocardiography incremental to exercise induced ischemia. Patients with similar degrees of LV diastolic dysfunction at rest may have very different responses in diastolic function to exercise, and impairment in diastolic response to exercise was correlated with exercise capacity. Furthermore, assessment of LV diastolic pressure with exercise allowed earlier identification of patients with heart failure with preserved ejection fraction when filling pressures at rest were normal.12

Regarding rest echocardiography parameters, Septal E complexes, Septal e, and EF were insignificant between both studied groups. Regarding stress echocardiography parameters, septal E/E was significantly higher and septal e was significantly decreased among diabetic patients among diabetic patients compared to the other group (P < 0.001).

LVEDS, LVEDD, and EF were insignificant between both studied groups. Concerning change between rest and stress echocardiography, among diabetic patients: Septal e was significantly higher in stress echo than stress (P value < 0.001), Septal E/E, were significantly lower in in rest echo than stress (P value < 0.001). LVEDS was significantly different between rest and study echocardiography. Among non-diabetic patients: LVEDD, Septal E–e, Septal e, Septal S and EF were significantly lower in in rest echo than stress (P value < 0.001). LVEDS was insignificantly different between rest and study echocardiography.

This may be explained by that in diabetes, there is an increase in apoptosis which lead to fibrosis & connective tissue proliferation, so more collagen is deposited in a diffuse distribution, this causes increased ventricular stiffening and decreased compliance.13,19

These structural changes lead to increased wall stress, increased oxygen demand, ischemia, and left ventricular diastolic dysfunction.20 This result was consistent with Devereux et al.20

In contrast to Nishi et al.21 found that in Resting echocardiograph, patients with DM had higher LVMI, RWT, impaired LVLS, as well as higher E/e ratio. LA volume index did not differ between patients with DM and controls; however, LA reservoir strain was significantly lower in patients with DM.

Of all patients, 44 patients (27%) presented with abnormal morphotype, 49 patients (31%) presented with impaired LVLS, and 72 patients (45%) presented with diastolic dysfunction.

Subclinical HF based on one criterion was present in 65 (40%), by two criteria in 35 (22%) and by three criteria in 10 (6%), while 51 patients (32%) did not present any abnormalities and by Exercise stress test One hundred thirty-six patients with DM (87%) reached peak heart rate (HR)>85% of their age-predicted maximum HR compared with 24 controls (96%) (P = 0.20). Peak METs (P = 0.20) and ppMETs (P = 0.21) were comparable between patients with DM and controls; however, more patients with DM tended to have reduced exercise capacity (P = 0.06).21

Nishi et al.21 showed that during exercise, LVLS and s0 were slightly but significantly impaired in patients with DM while LVEF was comparable. For the detection of subclinical HF, diastolic stress provided the greatest yield; diastolic dysfunction was observed in 72 participants (45%) at rest and in 92 (57%) after exercise. Patients were classified into three groups; no diastolic dysfunction both at rest and after exercise (N = 63, Normal), diastolic dysfunction at rest (N = 72, Resting DD) and no diastolic dysfunction at rest but diastolic dysfunction revealed after exercise (N = 26, Revealed DD).

<table>
<thead>
<tr>
<th>Stress echo</th>
<th>Non-diabetic (n = 50)</th>
<th>Diabetic (n = 50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDS</td>
<td>3.15 ± 0.17</td>
<td>3.17 ± 0.18</td>
<td>0.537</td>
</tr>
<tr>
<td>LVEDD</td>
<td>4.32 ± 0.47</td>
<td>4.51 ± 0.64</td>
<td>0.101</td>
</tr>
<tr>
<td>Septal E/e</td>
<td>10.05 ± 3.78</td>
<td>13.48 ± 3.91</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Septal e</td>
<td>9.94 ± 2.82</td>
<td>7.38 ± 2.64</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Septal S</td>
<td>10.9 ± 1.72</td>
<td>13.82 ± 2.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ejection fraction (EF)</td>
<td>71.96 ± 6.32</td>
<td>70.82 ± 6.15</td>
<td>0.363</td>
</tr>
</tbody>
</table>

Table 6. Difference between rest and stress echocardiography parameters between both study groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diabetic (n = 50)</th>
<th>Non-diabetic (n = 50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rest</td>
<td>Stress</td>
<td></td>
</tr>
<tr>
<td>LVEDS</td>
<td>3.05 ± 0.46</td>
<td>3.17 ± 0.18</td>
<td>0.193</td>
</tr>
<tr>
<td>LVEDD</td>
<td>3.46 ± 0.59</td>
<td>4.51 ± 0.64</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Septal E/e</td>
<td>7.22 ± 1.12</td>
<td>13.48 ± 3.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Septal e</td>
<td>9.46 ± 0.98</td>
<td>7.83 ± 2.64</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Septal S</td>
<td>7.74 ± 0.5</td>
<td>13.8 ± 2.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ejection fraction (EF)</td>
<td>60.04 ± 4.6</td>
<td>70.82 ± 6.15</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Paired sample t test.
In contrast, the yield for detection of subclinical HF was not observed for LVEF, LVLS, or s0. Adding diastolic stress to resting parameters increased the number of patients with subclinical cardiac abnormalities especially patients with more than two abnormal features compared with adding contractile reserve. When compared with the Normal group, patients in either the Resting DD or the Revealed DD group had lower peak METs.

The Resting DD group which also had lower peak METs were the oldest and with a higher proportion of females.

In another study Leung et al. showed that patients with DM immediately post-exercise had a lower septal e, a lower ΔE (1.2 vs. 2.3 cm/s, P = 0.006) and a higher Δ septal E/e (1.7 vs. 0.88, P < 0.001). In patients with normal resting E/e of ≤8 (n = 130), patients with DM immediately post-exercise had a significantly higher septal E/e and a higher Δ septal E/e. patients with DM compared with patients without DM at rest, immediately post-exercise and 10 min into recovery.

5. Conclusion

Patients with DM have impaired LV diastolic reserve manifest as septal E/e values were higher among diabetic group in response to exercise leading to an abnormal rise in LV filling pressures.

Conflicts of interest

There are no conflicts of interest.

References