Original Article

Assessment of left ventricular systolic function by tissue Doppler imaging in controlled versus uncontrolled type 2 diabetic patients

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ABSTRACT

Aim: To detect and quantify early subtle left ventricular (LV) systolic dysfunction using Tissue Doppler Imaging in type 2 diabetic patients with apparently normal LV ejection fraction.

Methods: Ninety age and sex matched subjects were enrolled in the study, sixty of them were suffering from type 2 diabetes mellitus (DM) whom were divided according to HbA1c into 2 groups, 30 uncontrolled diabetic patients with HbA1c > 8% and 30 controlled diabetic patients with HbA1c < 8% and a third group of 30 normal subjects served as controls. We excluded patients with inadequate Doppler signal, all structural heart diseases, systemic disorders with cardiac involvement and patients with false positive HbA1c. Assessment of diastolic function was done by Pulsed Doppler through mitral flow and by propagation flow velocity. Assessment of left ventricular systolic function was done by conventional echocardiography by 2D Simpson method and by Tissue Doppler Imaging (TDI) through detection of mitral annular peak systolic velocities.

Results: Left ventricular diastolic function was compared between the studied groups and showed that the mean peak early mitral inflow velocity E wave and the color M-mode flow propagation velocity of early diastolic flow (Vp) were significantly lower, and the mean peak late mitral inflow velocity A wave was significantly higher in uncontrolled diabetics versus controlled diabetic patients and control group with highly significant statistical difference (p < 0.001). Assessment of global systolic function by conventional Simpson’s modified biplane method didn’t show significant difference between uncontrolled diabetic patients, controlled diabetic patients and normal individuals. However, evaluation of systolic function by Tissue Doppler Imaging showed that the mean peak longitudinal systolic velocity was significantly decreased in uncontrolled diabetic patients when compared to controlled diabetic patients and normal individuals, with highly significant statistical difference (p < 0.001). A cut-off value for systolic dysfunction detected by TDI in uncontrolled diabetic patients was calculated. The peak systolic velocities < 7 cm/s for medial mitral annulus and < 8.2 cm/s for lateral mitral annulus indicated systolic dysfunction in diabetic patients with sensitivity and specificity of 96% and 67% respectively for medial mitral annulus while 98% and 71% respectively for lateral annulus.

Conclusion: TDI is a simple and effective method for detection of subtle LV systolic dysfunction in type 2 uncontrolled diabetic patients.

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1. Introduction

The prevalence of diabetes mellitus in the latest clinical trials of congestive heart failure is as high as 30% and this number will increase, as the number of Type II diabetes mellitus patients is escalating. Various mechanisms may link type 2 diabetes mellitus to heart failure: First; associated comorbidities such as hypertension may play a role; second; type 2 diabetes accelerates the development of coronary atherosclerosis; third; experimental and clinical studies support the existence of a specific diabetic cardiomyopathy.

In these patients the diabetic metabolic derangements, together with early activation of sympathetic nervous system, induce a decrease of myocardial function. The activation of renin-
angiotsin system results in an unfavorable cardiac remodeling. The progression from myocardial damage to overt dysfunction and heart failure is often asymptomatic for a long time and frequently undiagnosed and untreated.

Epidemiological evidence in the community underscores the prevalence of the left ventricular systolic dysfunction in type 2 diabetic patients as 2-fold with respect to non-diabetic ones, with half of them completely asymptomatic. Diastolic dysfunction in type 2 diabetic hearts in comparison with non-diabetic is even more frequent.2

The importance of assessing detailed information of LV myocardial performance in diabetic patients is essential in understanding the development of CHF and gives physicians the opportunity to initiate therapeutic intervention at an early stage.

Echocardiography has evolved as a well-established tool for the non-invasive evaluation of regional and global myocardial function.

Two-dimensional (2D) echocardiography is a simple, non-invasive technique that has been widely used to assess left ventricular function. However, it has some limitations: First; 2-D echocardiography imaging using a gray scale does not always provide effective delineation of the endocardial border for a proper evaluation of regional wall motion in a significant subset of patients3. Second, that technique depend to some extent on subjective judgment even when digital analysis is used, so search for superior techniques to quantify regional and global myocardial function has therefore continued.4

Tissue Doppler imaging (TDI) echocardiography has the potential to analyze quantitatively the myocardial wall performance and can bring a new insights into the understanding of pathophysiology of heart disease. It is a non-invasive imaging modality that directly interrogates myocardial velocities throughout the cardiac cycle. As it does not depend on the amplitude of the reflected wave, it is possible to get information regarding myocardial wall motion from an area that may not have satisfactory gray-scale information on 2-D echocardiography.5

During its initial application, tissue Doppler imaging (TDI) was limited to real-time visualization of only a single myocardial segment. Subsequent investigations in color-coded TDI and other technical improvements allowed a superior temporal and spatial resolution for simultaneous quantification of velocity data from multiple segments of the myocardium.6

2. Objective

The aim of this study is to detect and quantify early subtle left ventricular (LV) systolic dysfunction using Tissue Doppler Imaging in type 2 diabetic patients with apparently normal LV ejection fraction.

3. Methods

This study was approved by our institutional review board and informed consent was obtained from all individuals enrolled in the study.

3.1. Study population

This was a prospective observational study which included patients referred to the echocardiography unit at the cardiology department, Ain Shams University Hospital. This study included 90 subjects divided into three groups:

- **Group A**: Included thirty uncontrolled type II diabetic patients with HbA1c > 8%.
- **Group B**: Included thirty controlled type II diabetic patients with HbA1c < 8%.
- **Group C**: Control group included thirty non diabetic normal individuals with normal HbA1c < 6%.

The exclusion criteria was as follows (i) inadequate Doppler signal, (ii) ischemic heart disease, (iii) cardiomyopathy, (iv) valvular heart disease, (v) other systemic disorders with cardiac involvement (systemic lupus, rheumatoid arthritis), (vi) systemic hypertension, (vii) pulmonary hypertension, (viii) left bundle branch block, (ix) patients with false positive HbA1c (chronic renal failure, chronic excessive alcohol intake), (x) patients with arrhythmias (atrial fibrillation, premature ventricular or atrial extrasystoles).

3.2. Electrocardiography

All subjects had a baseline 12-lead surface ECG performed. The ECG was examined for rate, rhythm, and whether or not Q wave, ST-T wave changes, or LBBB were present within one week of echocardiographic study.

3.3. Laboratory investigations

Including lipid profile, fasting and postprandial blood sugar, HbA1c.

3.4. Standard trans-thoracic echo-cardiographic study

All subjects were examined at rest and lying in the left lateral position. The measurement was made using general electric vivid 5 ultrasound system with tissue Doppler imaging option. A 3.5 MHz phased array transducer was utilized.

All echocardiographic examinations were done by a senior echocardiographer with 10 years’ experience in performing echocardiograms. To avoid personal bias in assessing the left ventricular functions, these parameters were graded by at least two experienced echocardiologists and in case of disparity, by a third one to ensure correct measurements.

2D echo was utilized to assess left ventricular systolic function by eye balling and by 2D Simpson on apical 4 and apical 2 chamber views (Fig. 1) as well as to rule out wall motion abnormality.

Pulsed Doppler was utilized to assess left ventricular diastolic function through mitral flow, measurements were obtained with the transducer in the A4C view, with the Doppler beam aligned perpendicular to the plane of the mitral annulus, the sample volume was placed between the tips of the mitral leaflets. Five

![Fig. 1. Assessment of LV systolic function by 2D Simpson on apical 2 chamber view.](image-url)
consecutive beats during quiet respiration were used for calculation of the Doppler variables (Fig. 2).

- Patients with regurgitant and stenotic valvular diseases were excluded.

Color Doppler mode was used to evaluate left ventricular diastolic function by propagation flow velocity “Vp” by color M-mode that was performed in the apical four-chamber view and with the M-mode cursor aligned parallel with the LV inflow. Adjustments were made to obtain the longest column of flow from the mitral annulus to the apex of the left ventricle. The M-mode cursor was positioned through the centre of the inflow to avoid boundary regions. The velocity flow propagation was measured as the slope of the first aliasing velocity from the mitral annulus in early diastole to 4 cm distally into the ventricular cavity (Fig. 3).

- Patients with regurgitant and stenotic valvular diseases were excluded.

3.5. Tissue Doppler imaging (TDI)

Pulsed wave TDI study was accomplished at the end of expiration or with quiet respiration to minimize the effects of respiration. Assessment of left ventricular systolic function was done in the four-chamber view through detection of mitral annular velocities (Sm) at the junctions of mitral leaflets with LV lateral wall and inferoseptal regions (Fig. 2). When two systolic velocities, Sml and Sm2 were observed, the one with greater amplitude was recorded. Care was taken to align M-mode cursor so that the Doppler angle of incidence was as close to 0° as possible.

3.6. Statistical analysis

All data were gathered, tabulated, and statistically analyzed on a PC using a commercially available statistical software package MedCalc version 11.6.1.0 (MedCalc Software, Mariakerke, Belgium). Qualitative variables were expressed as frequency and percentage. Quantitative variables were expressed as mean ± SD. Qualitative variables were compared using Chi-squared test. Quantitative variables were assessed using paired t-test. Correlations were performed with linear regression and Pearson’s coefficient. Correlation coefficient and intra-class correlation were applied for the substudy to assess inter- and intra-observer variability. ROC Curve was generated to identify the cut off value of systolic dysfunction. P < 0.05 was considered significant, and P < 0.001 was considered highly significant.

4. Results

The study included 90 patients divided into three groups:

- Group A: Included thirty uncontrolled type II diabetic patients with HbAlc > 8%.
- Group B: Included thirty controlled type II diabetic patients with HbAlc < 8%.
- Group C: Control group included thirty non diabetic normal individuals with normal HbAlc < 6%.

The age of the studied groups was ranging from 17 to 68 years. The mean age in years was 46.24 ± 11.99. It included 48 males (53.3 %) and 42 females (46.7 %).

- In group A: the age was ranging from 33 to 68 years. The mean age in years was 48.2 ± 10.097. It included 16 males (53.3%) and 14 females (46.7%).
- In group B: the age was ranging from 32 to 68 years. The mean age in years was 46.5 ± 11.227. It included 17 males (56.7%) and 13 females (43.3%).
- In group C: the age was ranging from 17 to 67 years. The mean age in years was 44.03 ± 14.308. It included 15 males (50%) and 15 females (50%).
  - There was no statistically significant difference between the studied groups as regard age and sex.

4.1. Assessment of LV systolic and diastolic functions by conventional methods

Left ventricular diastolic function was assessed by Pulsed Doppler through mitral flow and also by Color Doppler by propagation flow velocity “Vp” in color M-mode. Left ventricular systolic function was assessed by 2D Simpson method and volumes. The results are shown in (Table 1) and graphically represented in (Fig. 4).

- There was significant statistical difference between the studied groups as regard peak E, E/A ratio and Vp. For peak A, There was no statistically significant difference when was compared between Diabetic controlled group vs. normal control group but there was significant statistical difference when compared between diabetic uncontrolled group vs. diabetic controlled and normal control groups. These data are shown in (Table 2).
- There was no statistically significant difference between the studied groups as regard conventional echocardiography measurements including ejection fraction by 2D Simpson on 4C view and 2C view, LVVs4c, LVVs2c, ejection fraction by M-mode and LVIDs. These data are shown in (Table 2).
4.2. Assessment of LV systolic function by Tissue Doppler imaging

Assessment of left ventricular systolic function for the studied groups was done by Tissue Doppler Imaging through detection of peak systolic velocities (Sm) of medial and lateral mitral annulus from A4C view. The results are shown in (Table 3) and graphically represented in (Fig. 4).

There was no statistically significant difference between diabetic controlled group and normal control group as regard Sm of medial and lateral annulus. But there was significant statistical difference when it was compared between the diabetic uncontrolled group vs. diabetic controlled and normal control groups. These data are shown in (Table 4).

4.3. ROC curve to determine the cut off value of LV systolic dysfunction by TDI

Cut off value for systolic dysfunction detected by tissue Doppler imaging in uncontrolled diabetic patients was calculated. Results are represented as ROC curve (Receiver Operating Characteristic curve) in (Fig. 5) and analyzed in (Tables 5 and 6).

In normal control and diabetic controlled groups, the mean peak systolic velocities of medial and lateral annulus were above the cut off values. However, in diabetic uncontrolled group the mean peak systolic velocities were below the cut off values. Percentages of patients with peak systolic velocity above and below the cut off values are shown in (Table 7).

5. Discussion

Diabetes increases the risk of heart failure independent of coronary heart disease and hypertension and may cause a cardiomyopathy. Diabetic cardiomyopathy has been defined as ventricular dysfunction that occurs in diabetic patients independent of a recognized cause (eg, coronary heart disease, hypertension).

This is thought to result from microangiopathy, deposition of collagen, decreased expression/activation of the K+ channel and Na+ pump and decreased myofilament Ca2+ sensitivity.
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. Even a mild degree of myocardial 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.9

In recent Doppler echocardiographic studies with analysis of combined mitral and pulmonary venous flow and flow during the Valsalva maneuver, abnormal LV diastolic filling was demonstrated to be present in approx. 50% of normotensive patients with Type II diabetes mellitus with normal systolic function.10 However, LV systolic function is often described in terms of LVEF or fractional shortening (FS), reflecting global and radial shortening of the left ventricle, whereas the longitudinal systolic contraction of the outer and inner layer of the myocardium contributes less in these parameters.1

In 1972, Rubier et al. described a specific type of cardiomyopathy related to diabetes mellitus.11

Many epidemiologic studies indicate that patients with DM are at an increased risk of cardiovascular morbidity and mortality.12 A leading cause of death in patients with DM is heart failure, and patients with DM have a worse prognosis after myocardial infarction.13

Clinical studies using conventional echocardiography have shown only global diastolic dysfunction, with a prevalence of about 60% in patients with Type II diabetes who have no clinically detectable heart disease.14

Recent studies have examined left ventricular (LV) function in patients with type 2 DM. Abnormalities in diastolic function have been well confirmed, but abnormalities in systolic function are controversial and inconsistent.15 Part of the inconsistency may be related to concomitant myocardial ischemia and/or scar due to either macrovascular or microvascular coronary artery disease (CAD).16

Radial function of the left ventricle is due mainly to contraction of circumferential myocardial fibres in the mid-wall, whereas long-axis function is governed by longitudinal subendocardial fibres.17

Since the subendocardium is more vulnerable to ischemia and interstitial fibrosis, measurement of the velocity of longitudinal shortening of the ventricle by Tissue Doppler imaging may be a more sensitive marker of subclinical changes in LV performance in diabetes than assessment of global function by conventional echocardiographical methods.9

The present study was undertaken for the purpose of early detection and quantification of left ventricular systolic dysfunction in type 2 diabetic patients using Tissue Doppler Imaging.

**Fig. 4.** Left ventricular systolic and diastolic function of studied groups by conventional echocardiography and by Tissue Doppler Imaging (a. LV diastolic function by Pulsed Doppler – b. LV diastolic function by propagation flow velocity “Vp” – c. LV systolic function by conventional method – d. LV systolic function by TDI).
This study included 90 subjects divided into three groups, 30 uncontrolled type 2 diabetic patients, 30 controlled type 2 diabetic patients and 30 normal subjects served as controls.

In the present study, the studied groups were not statistically different in age and gender by selection of sex and age matched subjects in the three studied groups.

In view of assessment of left ventricular diastolic function, studying the mean peak early mitral inflow velocity E wave, the Strong Heart Study documented lowest E wave in diabetic patients compared to non-diabetic patients (p < 0.05). Hameedullah et al., compared patients with poorly controlled vs. moderately controlled and well controlled diabetic condition. The E wave was higher in well controlled patients than in poor controlled diabetic patients. In the present study the mean peak early mitral inflow velocity E wave was lowest in patients whose diabetic condition was

| Dependent variable | (I) Groups | (J) Groups | Mean Difference (I-J) | Sig. |
|--------------------|------------|------------|-----------------------|------|
| **peak E**         | Normal control | DM controlled | 12.57(*) | 0.001* |
|                    | DM controlled | Normal control | 25.03(*) | 0.001* |
|                    | DM controlled | DM uncontrolled | -12.57(*) | 0.001* |
|                    | DM uncontrolled | Normal control | -12.47(*) | 0.001* |
|                    | DM uncontrolled | DM controlled | -12.47(*) | 0.001* |
| **peak A**         | Normal control | DM controlled | -1.97 | NS |
|                    | DM controlled | Normal control | -13.5(*) | 0.001* |
|                    | DM controlled | DM uncontrolled | -11.93(* | 0.001* |
|                    | DM uncontrolled | Normal control | 13.9(*) | 0.001* |
|                    | DM uncontrolled | DM controlled | 11.93(*) | 0.001* |
| **E/A ratio**      | Normal control | DM controlled | 0.26(*) | 0.001* |
|                    | DM controlled | Normal control | -0.26(*) | 0.001* |
|                    | DM controlled | DM uncontrolled | 0.39(*) | 0.001* |
|                    | DM uncontrolled | Normal control | -0.65(*) | 0.001* |
|                    | DM uncontrolled | DM controlled | -0.39(*) | 0.001* |
| **Vp**             | Normal control | DM controlled | 16.98(*) | 0.001* |
|                    | DM controlled | Normal control | 30.08(*) | 0.001* |
|                    | DM controlled | DM uncontrolled | -16.98(*) | 0.001* |
|                    | DM uncontrolled | Normal control | 13.103(*) | 0.001* |
|                    | DM uncontrolled | DM controlled | -30.08(*) | 0.001* |
|                    | DM uncontrolled | DM controlled | -13.103(*) | 0.001* |
| **EF(Mod Simpson 4C)** | Normal control | DM controlled | 0.4 | NS |
|                    | DM controlled | Normal control | 1.8 | NS |
|                    | DM uncontrolled | Normal control | -0.4 | NS |
|                    | DM uncontrolled | Normal control | 1.4 | NS |
|                    | DM uncontrolled | DM controlled | -1.8 | NS |
|                    | DM uncontrolled | DM controlled | -1.4 | NS |
| **EF (Mod Simpson 2C)** | Normal control | DM controlled | 0.3 | NS |
|                    | DM controlled | Normal control | 2.2 | NS |
|                    | DM uncontrolled | Normal control | -0.3 | NS |
|                    | DM uncontrolled | Normal control | 1.9 | NS |
|                    | DM uncontrolled | DM controlled | -2.2 | NS |
|                    | DM uncontrolled | DM controlled | -1.9 | NS |
| **LWs4c**          | Normal control | DM controlled | -1.92 | NS |
|                    | DM controlled | Normal control | -2.36 | NS |
|                    | DM uncontrolled | Normal control | 1.92 | NS |
|                    | DM uncontrolled | DM controlled | -0.44 | NS |
|                    | DM uncontrolled | Normal control | 2.36 | NS |
|                    | DM uncontrolled | DM controlled | 0.44 | NS |
| **LWs2c**          | Normal control | DM controlled | -1.61 | NS |
|                    | DM controlled | Normal control | 0.63 | NS |
|                    | DM uncontrolled | Normal control | 1.61 | NS |
|                    | DM uncontrolled | DM controlled | -0.63 | NS |
|                    | DM uncontrolled | Normal control | 0.98 | NS |
|                    | DM uncontrolled | DM controlled | 0.082 | NS |
| **EF(M-Mode)**     | Normal control | DM controlled | 1.03 | NS |
|                    | DM controlled | Normal control | -1.03 | NS |
|                    | DM uncontrolled | Normal control | 0.97 | NS |
|                    | DM uncontrolled | DM controlled | -0.97 | NS |
| **LVIDs**          | Normal control | DM controlled | 0.063 | NS |
|                    | DM controlled | Normal control | -0.019 | NS |
|                    | DM uncontrolled | Normal control | -0.063 | NS |
|                    | DM uncontrolled | DM controlled | -0.082 | NS |
|                    | DM uncontrolled | Normal control | 0.019 | NS |
|                    | DM controlled | DM controlled | 0.082 | NS |
Comparison between the different studied groups regarding LV systolic function measured by TDI.

| Test result variables | N | Min. | Max. | Mean | Std. Deviation |
|-----------------------|---|------|------|------|----------------|
| Sm(Med. annulus)\(^a\) | Normal control | 30 | 6.9 | 11.2 | 8.22 | 1.09 |
| DM controlled | 30 | 6.5 | 10.2 | 7.9 | 1.04 |
| DM uncontrolled | 30 | 4.5 | 7.9 | 5.98 | 0.86 |
| Total | 90 | 4.5 | 11.2 | 7.37 | 1.42 |
| Sm (Lat. annulus)\(^a\) | Normal control | 30 | 8.6 | 13.6 | 10.05 | 1.31 |
| DM controlled | 30 | 7.6 | 12.6 | 9.6 | 1.27 |
| DM uncontrolled | 30 | 5.3 | 8.4 | 6.74 | 0.87 |
| Total | 90 | 5.3 | 13.6 | 8.79 | 1.82 |

\(^a\) Results of Sm are shown in cm/s.

Table 4
Left ventricular systolic function characteristics of the studied groups by tissue Doppler imaging.

| Dependent variable | Groups | Groups | Mean Difference (I-J) | Sig. |
|--------------------|--------|--------|-----------------------|------|
| Sm (Med. annulus) | Normal control | DM controlled | 0.32 | NS |
| DM controlled | 2.24\(^*)\ | 0.001* |
| DM uncontrolled | Normal control | -0.32 | NS |
| DM controlled | 1.92\(^*)\ | 0.001* |
| DM uncontrolled | Normal control | -2.24\(^*)\ | 0.001 |
| DM controlled | -1.92\(^*)\ | 0.001 |
| Sm (Lat. annulus) | Normal control | DM controlled | 0.45 | NS |
| DM controlled | 3.31\(^*)\ | 0.001* |
| DM uncontrolled | Normal control | -0.45 | NS |
| DM controlled | 2.86\(^*)\ | 0.001 |
| DM uncontrolled | Normal control | -3.31\(^*)\ | 0.001 |
| DM controlled | -2.86\(^*)\ | 0.001 |

Fig. 5. ROC curve of the cut off values for systolic dysfunction detected by TDI in uncontrolled diabetic patients.

Table 5
Area under the Curve.

| Test result variables | Area | Sig. |
|-----------------------|------|------|
| Sm (Med. annulus) | 0.798 | 0.001 |
| Sm (Lat. annulus) | 0.807 | 0.001 |

\(^*\) Highly significant.

Table 6
Coordinates of the curve.

| Test result variables | Positive if lower than or equal to | Sensitivity % | Specificity % |
|-----------------------|----------------------------------|---------------|---------------|
| Sm (Med. annulus) | 7 cm/s | 90% | 67% |
| Sm (Lat. annulus) | 8.2 cm/s | 98% | 71% |
During assessment of global systolic function by conventional echocardiography, Andersen et al., did not find any statistical significant difference between diabetic patients and normal individuals while comparing LV end systolic dimension, Fractional shortening, LV volumes and ejection fraction by the triplane three-dimensional method in three standard apical views (apical four, two and apical long) were compared between diabetic patients vs. normal individuals, and again showed no statistically significant difference.\(^1\)

Also many others studies confirmed no statistically significant difference between diabetic patients and normal individuals in ejection fraction by Simpson’s modified biplane method.\(^2\)\(^3\)\(^4\)\(^5\)

In Andersson et al., comparing diabetic patients without significant CAD vs. control individuals, the mean peak longitudinal systolic velocity was significantly decreased in diabetic patients \((p = 0.02)\) and the presence of hypertension was not found to modify the impairments of the systolic velocity.\(^6\)

In Gulati et al., color-coded TDI was compared to radionuclide ventriculography, which served as a standard of reference of left ventricular ejection fraction. TDI color M-modes echocardiograms were obtained from six mitral annular sites, including inferoseptal and lateral images from apical 4-chamber views, anterior and inferior images from apical 2-chamber views, and anteroseptal and posterior images from apical long axis views (Fig. 5). The peak mitral annular descent velocity average > 5.4 cm/s had a sensitivity and specificity of 88 and 97 percent for an ejection fraction greater than 50 percent.\(^7\)

Collecting results of our study with these of Gulati et al. study, we may consider patients with peak mitral annular systolic velocity > 5.4 cm/s, but <7 cm/s for medial mitral annulus and <8.2 cm/s for lateral mitral annulus, patients having systolic dysfunction with preserved ejection fraction. Conventional echocardiography may fail to detect these cases.

### 5.1. Study limitations and recommendations

The extensive exclusion criteria applied to the patients before enrolment in the study may suggest that the population is not a real-world population. The main objective of this extensive exclusion criteria was to try to document the presence of subtle changes in LV systolic functions related to DM and not to any other disease process and to test the effect of level of control of diabetes on these changes.

Correlation of decreased LV systolic function by TDI in uncontrolled diabetic patients and future development of LV systolic dysfunction using long term studies should be considered. Such a correlation if proved together with the results of the current study will further support our recommendation to consider tight blood sugar control for patients with subtle LV systolic dysfunction in order to protect these patients from developing progressive LV systolic dysfunction.

### Table 7

Percentages of patients with Sm above and below the cut off values.

| Groups                  | Medial annulus | Lateral annulus | Total |
|-------------------------|----------------|-----------------|-------|
|                         | Sm > 7         | Sm < 7          |       |
| Normal control No.      | 29             | 1               | 30    |
| %                       | 96.6%          | 3.4%            | 100%  |
| DM controlled No.       | 23             | 7               | 30    |
| %                       | 76.6%          | 23.4%           | 100%  |
| DM uncontrolled No.     | 3              | 27              | 30    |
| %                       | 10%            | 90%             | 100%  |

During assessment of global systolic function by conventional echocardiography, Andersen et al., did not find any statistical significant difference between diabetic patients and normal individuals while comparing LV end systolic dimension, Fractional shortening, LV volumes and ejection fraction by the triplane three-dimensional method in three standard apical views (apical four, two and apical long) were compared between diabetic patients vs. normal individuals, and again showed no statistically significant difference.\(^1\)

This result was confirmed by Zhi et al., when the LV end systolic dimension, Fractional shortening, LV volumes and ejection fraction by the triplane three-dimensional method in three standard apical views (apical four, two and apical long) were compared between diabetic patients vs. normal individuals, and again showed no statistically significant difference.\(^1\)

Also many others studies confirmed no statistically significant difference between diabetic patients and normal individuals in ejection fraction by Simpson’s modified biplane method.\(^2\)\(^3\)\(^4\)\(^5\)

In Andersson et al., comparing diabetic patients with poor controlled vs. moderate controlled and well controlled diabetic condition, the LV end diastolic dimension, LV end systolic dimension, ejection fraction by 2D guided M-Mode and Fractional shortening showed no statistically significant difference.\(^6\)

In the present study, there was no statistically significant difference between uncontrolled diabetic patients, controlled diabetic patients and normal control individuals as regards the LV volumes, ejection fraction by Simpson’s modified biplane method, LV end-systolic internal dimension and ejection fraction by 2D guided M-mode. And this was concordant with results of previous studies. We can thus observe a consensus of all studies about absence of any overt systolic dysfunction assessed by conventional echo techniques related to diabetic status including the present study.

In view of assessment of systolic function by Tissue Doppler Imaging, Helene et al., found that the mean peak longitudinal systolic velocity was not significantly different between diabetic patients and control individuals using TDI at rest. While with dobutamine stress TDI, diabetic patients showed significant decrease in systolic velocity \((p < 0.05)\) demonstrating an impaired myocardial response in diabetic patients during stress.\(^7\)

In Andersson et al., comparing diabetic patients without significant CAD vs. control individuals, the mean peak longitudinal systolic velocity was significantly decreased in diabetic patients \((p = 0.02)\) and the presence of hypertension was not found to modify the impairments of the systolic velocity.\(^8\)

In our study, comparing controlled diabetic patients vs. normal individuals, the mean peak longitudinal systolic velocity was not significantly different between the two groups, and this was concordant with results in Helene et al. as diabetic patients in Helene et al. study were mainly controlled diabetic patients with mean HbAlc 6.8 ± 1.4% matching controlled diabetic patients in our study with HbAlc < 8%. There were no uncontrolled diabetic patients in Helene et al. study. While comparing uncontrolled diabetic patients to controlled diabetic patients and normal individuals, revealed a mean peak longitudinal systolic velocity that’s significantly decreased in uncontrolled diabetic patients \((p = 0.001)\).

For clinical application, we calculated the cut off value for systolic dysfunction detected by TDI in uncontrolled diabetic patients in the present study. Peak systolic velocities < 7 cm/s for medial mitral annulus and <8.2 cm/s for lateral mitral annulus were indicators of systolic dysfunction in diabetic patients, with sensitivity and specificity of 96% and 67% for medial mitral annulus and 98% and 71% for lateral one.

Applying these cut off values on our subjects’ data, 90% of uncontrolled diabetic patients (27 patients) had peak systolic velocity of medial mitral annulus < 7 cm/s with mean peak systolic velocity 5.98 cm/s, and 96.6% of these patients (29 patients) had peak systolic velocity of lateral mitral annulus < 8.2 cm/s with mean peak systolic velocity 6.74 cm/s. On the other hand, 76.6% of controlled diabetic patients (23 patients) and 96.6% of normal individuals (29 subjects) had peak systolic velocity of medial mitral annulus > 7 cm/s with mean peak systolic velocity 7.9 and 8.22 cm/s respectively. While for lateral mitral annulus, 83.3% of controlled diabetic patients (25 patients) and 100% of normal individuals (30 subjects) had peak systolic velocity > 8.2 cm/s with mean systolic velocity 9.6 and 10.05 cm/s respectively.

In Gulati et al., color-coded TDI was compared to radionuclide ventriculography, which served as a standard of reference of left ventricular ejection fraction. TDI color M-modes echocardiograms were obtained from six mitral annular sites, including inferoseptal and lateral images from apical 4-chamber views, anterior and inferior images from apical 2-chamber views, and anteroseptal and posterior images from apical long axis views (Fig. 5). The peak mitral annular descent velocity average > 5.4 cm/s had a sensitivity and specificity of 88 and 97 percent for an ejection fraction greater than 50 percent.\(^7\)

Collecting results of our study with these of Gulati et al. study, we may consider patients with peak mitral annular systolic velocity > 5.4 cm/s, but < 7 cm/s for medial mitral annulus and < 8.2 cm/s for lateral mitral annulus, patients having systolic dysfunction with preserved ejection fraction. Conventional echocardiography may fail to detect these cases.
6. Conclusion

TDI is a simple and effective method for detection of subtle LV systolic dysfunction in type 2 uncontrolled diabetic patients.

Conflict of interest

None declared.

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