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Diabetic Cardiomyopathy: Tissue Doppler Imaging a Novel Insight.

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ABSTRACT

Patients with diabetes mellitus (DM) are prone to develop heart failure even in the absence of evident hypertension and coronary artery disease. This entity is difficult to detect in early stages by conventional echocardiographic techniques. 32 asymptomatic TMT (tread mill stress test) negative DM patients compared with control subjects were screened and performed LV (left ventricle) strain, strain rate and tissue Doppler imaging. Tissue Doppler imaging revealed increased E/E' of IVS (Inter ventricular septum) (p value<0.001) among DM suggestive of diastolic dysfunction. The tissue velocities E' of both the LV lateral wall (p value=0.004) and RV (right ventricle) (p value =0.003) were reduced among DM. Similarly, the peak systolic strain (p value<0.001), and strain rate (p value<0.001) were significantly reduced among diabetic subjects. DM is an independent risk factor for myocardial dysfunction even in asymptomatic normotensive subjects. The changes that occur in the myocardium due to diabetic cardiomyopathy can be detected early, as the novel tissue Doppler is a noninvasive technique for early detection of Diabetic cardiomyopathy.

Keywords: Diabetes mellitus, cardiomyopathy, Tissue Doppler, Strain rate

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INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term complications which affects various organs, especially the eyes, kidneys, nerves, heart, and blood vessels [1]. Among the all complications cardiomyopathy is considered to be the life threatening complication. Patients with DM are at an increased risk for cardiovascular disease which can be accelerated by atherosclerosis in large arteries and causing diabetic microangiopathy which may have a role in producing heart failure [2]. Diabetics also have a worse prognosis from heart failure when compared with non-diabetic heart failure patients. A sub-group of diabetics with heart failure have been distinctly identified without any co-existing hypertension or coronary artery disease. For this particular sub-group, the term “diabetic cardiomyopathy” has been proposed [3].

Diabetic cardiomyopathy is abnormal myocardial function, occurring even in the absence of any epicardial coronary artery disease, hypertension and valvular heart disease. The myocardial dysfunction in diabetic cardiomyopathy is probably attributed to the changes that occur in the small coronary vessels as a consequence of the multitude of the metabolic abnormalities in diabetes [4]. Detecting the presence of diabetic cardiomyopathy especially in the absence of coronary artery disease and hypertension is a challenging task. Conventional echocardiographic techniques fail to detect these early changes occurring in the myocardium due to diabetic cardiomyopathy. However, with newer novel echocardiographic modalities like LV strain and strain rate imaging, it is possible to detect even subtle and subclinical changes in myocardial function [5,6].

Therefore the objective of the present study was to detect the presence of early myocardial changes that occur due to diabetic cardiomyopathy among asymptomatic, TMT negative diabetic individuals using advanced echocardiographic indices.

METHODS AND METHODS

Present cross sectional comparative study was carried out at a tertiary care hospital in costal Karnataka, India after obtaining prior approval from the Institutional Ethics Committee (IEC).

A total of 32 subjects aged>40 years, biochemically diagnosed type 2diabetes mellitus as per ADA (American diabetic association) criteria (FBS>126mg/dl, or HBA1>6.5) and on therapy withblood pressure of <140/80mmHg were recruited for the study. The subjects were asymptomatic and negative for exercise induced ischemia after performing a treadmill test as per Bruce protocol were included in the study. Subjects with uncontrolled hypertension, dyslipidemia and co-existing valvular anomalies, congenital heart disease and known IHD (Ischemic heart disease) /LV dysfunction, grossly abnormal resting ECG (Electrocardiogram)changes, LBBB (left bundle branch block), WPW(wolf Parkinson’s-white) syndrome, anemia (<10gm hemoglobin/dl), liver disease, kidney disease, pulmonary hypertension and cardiac pacemakers were excluded from the study.

In control group, 32 subjects who were individuals who approached the hospital for routine health examination and volunteered to take part in the study.

After a complete examination, a TMT was performed as per Bruce protocol to rule out presence of silent myocardial ischemia. Transthoracic echocardiography was performed on all subjects by a trained sonologist using VIVID 7(GE) Echo machine from with 2.5MHz transducer. 2D images, LV M Mode (motion mode), pulsed wave Doppler of mitral valve and colour TDI (Tissue Doppler Imaging) superimposed on 2D gray scale images were recorded according to standard techniques. The images acquired were transferred to work station for offline analysis.

Tissue Doppler imaging derived tissue annular velocities were measured by keeping the sample volume at inter ventricular and lateral wall segments of LV and free wall of RV in apical four chamber view. This consisted of three distinct wave forms including systolic (S), early diastolic (E’) and late diastolic (A’) tissue annular velocities.(Figure 1) Strain is the measure of myocardial deformation derived from TDI, depicts ratio of change in myocardial length to its initial reference length at end diastole (Lagrangian strain). Strain rate is a

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deformation or strain per time unit that explores ratio of myocardial velocity gradient at two points of myocardial wall to the distance between these two sites. The unit of strain rate is s^{-1} [7]. In the present study, longitudinal strain and systolic strain rate were measured by placing the sample volume at the level of six basal and mid ventricular segments of LV at three orthogonal apical views, i.e. apical long axis, two and four chamber view and averaged to detect global LV deformation parameters.(Figure 2 and Figure 3)

Figure 1

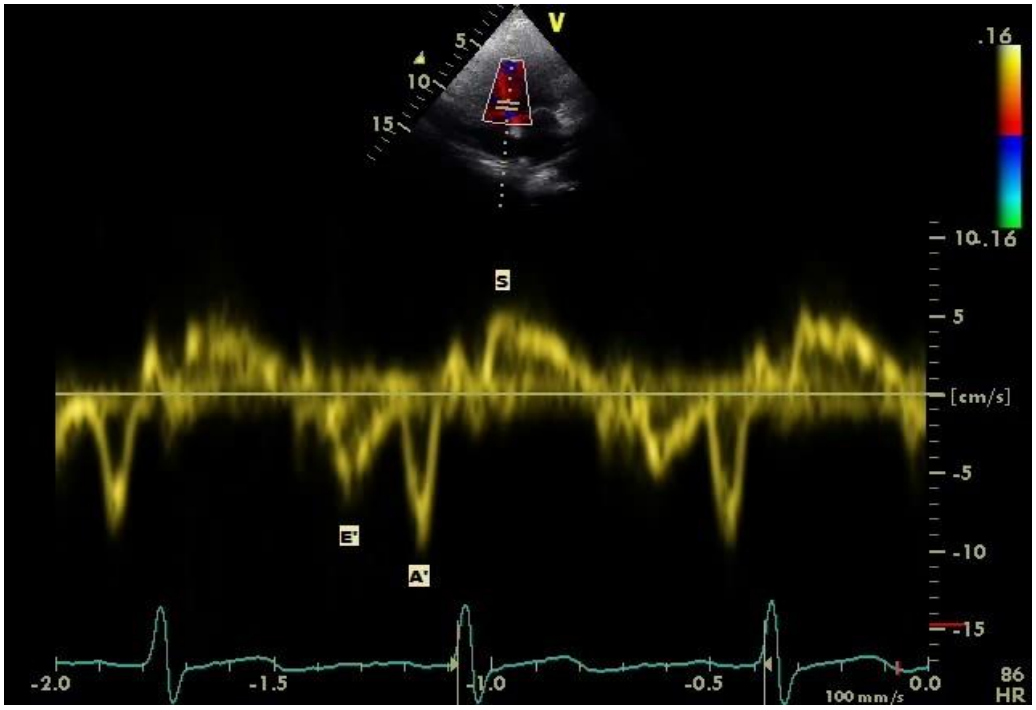

Figure 2

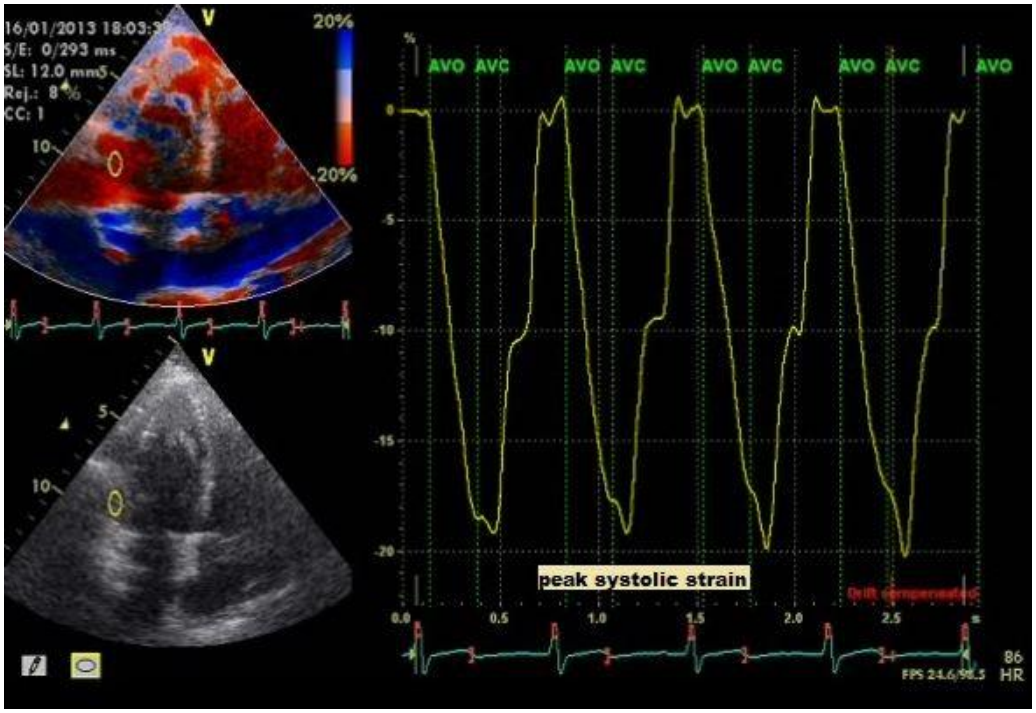

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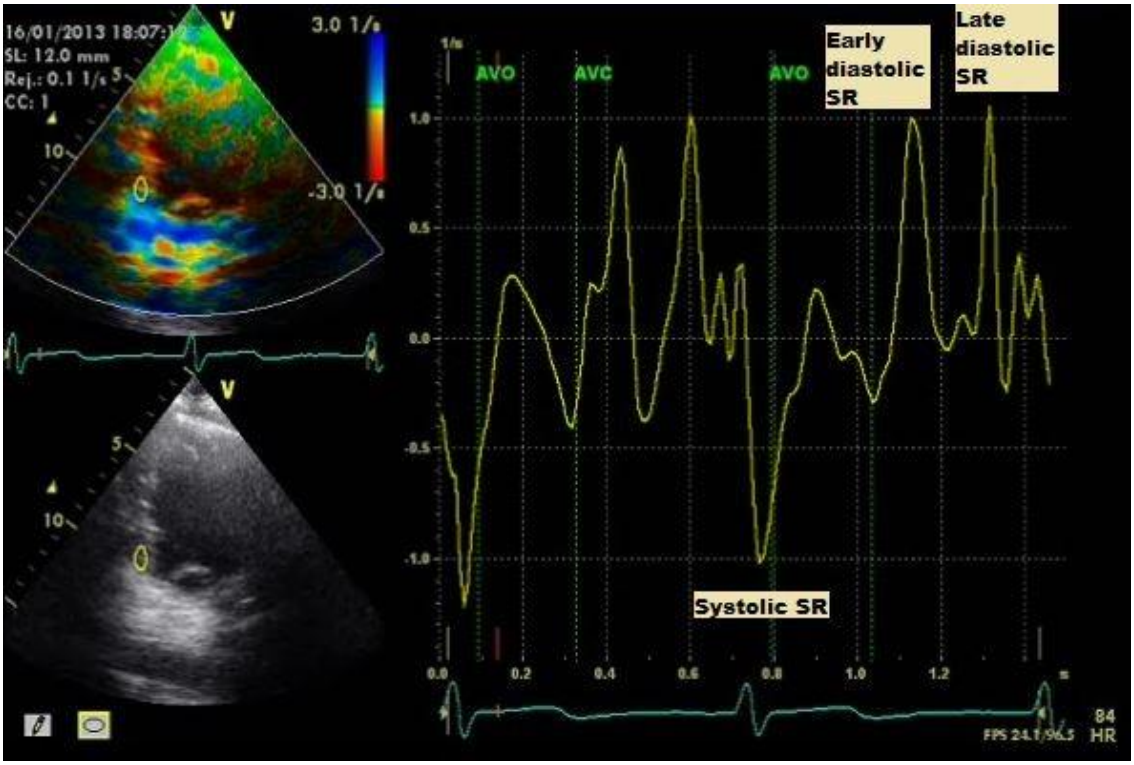
Figure 3



The data was entered and analyzed using SPSS V15.0. Variables with continuous values were expressed as a mean ± standard deviation. Student's independent sample test was used to compare the difference in mean between the two groups. A p-value of <0.05 was considered statistically significant.

2D images, LV M Mode, pulsed wave Doppler and colour TDI (Tissue Doppler Imaging) were performed according to standard techniques. The images obtained were recorded and analyzed with the help of a work station.

RESULTS AND DISCUSSION

The baseline characteristics between the two groups and the conventional echocardiographic measurements are summarized in Table 1. The age and gender distribution were comparable in both the groups and the differences were found to be statistically insignificant. Out of the 32 subjects in each group 21(65.62%) were males and rest females. The mean HbA1c value of the study group was 9.10 ± 1.979. No significant differences were found in LV ejection fraction (p value = 0.64) or left atrial (p value =0.769) and left ventricular dimensions (pValue=0.41).

The trans-mitral E/A (as shown in Table 2) (Figure 1) obtained by pulsed wave Doppler was reduced in diabetics (Mean ± SD, 0.99±0.37 vs. 1.23±0.34, p =0.009). Parameters suggestive of diastolic dysfunction by echocardiographic tissue Doppler imaging,(as shown in table 3) E/E' of IVS (7.11±1.40 v/s 8.65±1.95, p <0.001) was higher among diabetics. Similarly, the tissue velocities E' of both the LV lateral wall (p=0.004) and RV (p =0.003) were reduced among diabetic individuals. The study group also had significantly reduced LV mean longitudinal strain (- 24.07±1.37 vs. -20.29±3.33, p <0.001) (Figure 2), and LV systolic strain rate -1.59±0.14vs -1.16 ±0.17, p <0.001) (table 4) (Figure 3) compared to the control group. In addition, the LV peak longitudinal systolic velocity S which is an indicator of systolic function was also impaired among the cases (p =0.006).

Diabetes mellitus is a major risk factor for coronary artery disease due to accelerated atherosclerosis occurring in the large epicardial coronary vessels. However, the interesting entity of "Diabetic cardiomyopathy" where in there is myocardial dysfunction even in the absence of major coronary vessel involvement is still debatable. The pathogenesis is believed to be contributed due to the microangiopathy

changes that occur due to various metabolic changes in diabetes. Thus, diabetic cardiomyopathy, like retinopathy and nephropathy is said to be a microvascular complication of diabetes.

Table 1: Age and conventional echocardiographic measurements

	Non-diabetics	Diabetics	*p*-value
Age	52.9±8.20	53.9±8.33	0.64
IVS-Diastole	9.47±1.07	9.56±1.26	0.75
IVS-Systole	13.69±1.25	13.78±2.39	0.84
LV Diastole	46.0±3.95	46.91±4.09	0.37
LV Systole	28.50±3.09	29.19±3.53	0.41
Posterior wall Diastole	9.09±1.17	8.160±1.72	0.41
Posterior wall systole	13.38±1.33	13.06±2.22	0.49
EF	68.06±3.36	67.53±5.55	0.64
FS	37.97±2.59	37.44±3.99	0.53
AORTA/LA	0.92±0.06	0.91±0.14	0.76

Table 2: Comparison of Pulse wave Doppler measurements

	Non-diabetics	Diabetics	*p*-value
Mitral E	0.77±0.15	0.68±0.17	0.03*
Mitral A	0.65±0.14	0.75±0.27	0.07
Trans-mitral E/A	1.23±0.34	0.99±0.37	0.009*

Table 3: Comparison of Tissue Doppler measurements

	Non-diabetics	Diabetics	p-value
Lateral E'	0.13±0.02	0.11±0.03	0.004*
Lateral A'	0.10±0.03	0.11±0.02	0.14
Lateral S	0.11±0.02	0.09±0.03	0.006*
Septal E'	0.11±0.02	0.08±0.02	<0.001*
Septal A'	0.10±0.02	0.11±0.02	0.02*
Septal S	0.09±0.01	0.08±0.02	0.02*
RV E'	0.13±0.02	0.11±0.03	<0.001*
RV A'	0.17±0.03	0.17±0.05	0.71
RV S	0.15±0.02	0.14±0.02	0.03*
E/E' Lat	6.02±1.66	6.76±2.49	0.16
E/E' Sep	7.11±1.40	8.65±1.95	<0.001*
E'/A' Lat	1.41±0.57	1.03±0.44	0.005*
E'/A' RV	0.79±0.23	0.67±0.26	0.04*
E'/A' Septal	1.12±0.34	0.73±0.28	<0.001*

Table 4: Comparison of strain and strain rates

	Non-diabetics	Diabetics	p-value
Average peak systolic strain	-24.07±1.37	-20.29±3.33	<0.001*
Average systolic strain rate	-1.59±0.14	-1.16±0.17	<0.001*

The present study showed the presence of subclinical and subtle biventricular systolic and diastolic dysfunction even in completely asymptomatic, TMT negative diabetic patients. The absence of symptoms and negative TMT focused the study among individuals without major coronary vessels being affected. Thus, any difference amongst the study and control group is to be attributed to diabetic cardiomyopathy.

There were no changes detected in any of the conventional echocardiographic measurements like the LV dimensions and LVEF. These similar observations of systolic and diastolic function in diabetic patients even with normal LV dimensions were also obtained by Andersson et al [8].

The tissue annular velocity in early diastole E' derived at basal IVS was reduced ($p< 0.001$), and E/E' ratio at the IVS was significantly increased among diabetics suggestive of early diastolic dysfunction. Systolic tissue annular velocity 'S' obtained at basal IVS and lateral wall was also significantly reduced. Similarly, the

diastolic and systolic annular velocities of RV free wall was also significantly reduced among diabetic subjects($p<0.001$,$p<0.03$ respectively) (Figure 1).

The mean longitudinal strain and strain rate imaging revealed impaired systolic function among cases compared to controls ($p<0.001$,$p<0.001$ respectively) (Figure 2 and Figure 3). Arnold et al, in a similar study found diabetes as an independent risk factor for impaired longitudinal strain and strain rate [9]. These subtle changes could be due to certain pathological changes that occur in the myocardium secondary to diabetes like accumulation of advanced glycated end products(AGEs) secondary to chronic hyperglycaemia, increase in the myocardial tension at rest, and fat deposition in the myocardium [10]. The lipid deposition in the myocardium may cause increase in stiffness and decrease in the LV compliance and lead to diastolic dysfunction [11]. This may eventually lead to the apoptosis of cardiac myocytes, myocardial fibrosis and abnormal contractile proteins causing systolic dysfunction [12,13]. Moreover, Mogelvang etal, found that this subtle and early myocardial dysfunction observed by TDI is an independent predictor of mortality even in general population [14].

CONCLUSION

In present study showed the presence of echocardiographic abnormalities in asymptomatic diabetic individuals that were independent of age, gender and body mass index. As the understanding on the pathogenesis and mechanisms of diabetic cardiomyopathy get better, hopefully there will be novel strategies in the future targeted to reduce the risk of heart failure. Nevertheless, early detection of diabetic cardiomyopathy by novel techniques would also help in identifying diabetic patients at risk and may help to prevent progression of cardiac morbidity.Similarly, the influence of the type, duration, treatment of diabetes and the relative pathogenic impact of each of the multiple risk factors on diabetic cardiomyopathy needs to be elucidated. Hence, future prospective studies are needed to detect the clinical implication of the echocardiographic findings among patients with diabetic cardiomyopathy.

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