Section: Cardiology

Original Research Article

GLOBAL LONGITUDINAL STRAIN IN TYPE 1 DIABETES MELLITUS TO DETECT ASYMPTOMATIC CARDIOVASCULAR DISEASE

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Abstract

Background: Type 1 diabetes mellitus is a significant risk factor for cardiovascular diseases with increased morbidity and mortality due to premature cardiovascular events. Compared to the nondiabetic population, the risk of cardiovascular diseases is 2–3 times higher among women with type 1 diabetes mellitus. The cardiovascular manifestations include premature atherosclerosis, diabetic cardiomyopathy, heart failure, arrhythmias, and increased CVD risk. These are caused by systemic hypertension, metabolic effects, silent ischemia, and decreased left ventricular (LV) function. Early detection of subclinical myocardial dysfunction is important to prevent the disease from progressing. The purpose of this study was to evaluate subclinical myocardial dysfunction in asymptomatic T1DM patients with normal LV systolic function, using tissue Doppler and speckle tracking analysis. **Materials and Methods:** A hospital-based cross-sectional study was conducted at Government Rajaji Hospital, Madurai, among 35 asymptomatic insulin-dependent T1DM patients. Exclusion criteria were pre-existing cardiac diseases. All patients underwent clinical evaluation, including anthropometric measurements, blood investigations, ECG, echocardiography, and speckle tracking imaging to assess LV global longitudinal strain (GLS) and other cardiac parameters. **Result:** The mean age of participants was 36 years with a range of 19–62 years. The median duration of diabetes was 17.3 years. Abnormal LV GLS (<-17%) was observed in 16 patients (45.7%). Significant correlations were found between abnormal GLS and hypertension ($p = 0.032$), frequent hypoglycaemic episodes ($p = 0.044$), and decreased eGFR (<60 ml/min/1.73 m², $p = 0.035$). Diastolic dysfunction was noted in 4 patients (11.4%), with a significant correlation between LV GLS and diastolic dysfunction ($p = 0.016$). However, no significant correlations were found between LV GLS and other factors such as body rounded index, HbA1c, or duration of diabetes. The study reveals that subclinical myocardial dysfunction, indicated by impaired LV GLS, is present in asymptomatic T1DM patients and is associated with comorbidities such as hypertension, frequent hypoglycaemic episodes, and impaired kidney function. This is consistent with previous studies indicating the early onset of myocardial dysfunction in T1DM, with diastolic dysfunction being more prevalent than systolic dysfunction. **Conclusion:** This study indicates that LV GLS is a useful marker for the detection of subclinical myocardial dysfunction in asymptomatic T1DM patients. Monitoring cardiovascular risk factors, such as hypertension, hypoglycemic episodes, and kidney function, is essential for early intervention and prevention of further myocardial damage in T1DM patients.

INTRODUCTION

Type 1 diabetes mellitus is a major cardiovascular risk factor in young adults that is associated with increased morbidity and mortality due to premature cardiovascular events. Risk is 2 to 3 fold higher in Women compared to men in non diabetic population. Despite traditional risk factors involved in Coronary artery disease, T1 Diabetes Mellitus itself acts as an independent risk factor in this subgroup compared to Non diabetic population.[1,2]

Cardiovascular mortality in Type 1 Diabetes manifest with premature atherosclerosis leading to coronary artery disease, diabetic cardiomyopathy (HFpEF), overt heart failure -10 years earlier than background population, Arrhythmias due cardiac autonomic and myocardial dysfunction and increases CVD by 6 to 12 fold . These manifestations are attributed to silent ischemia, reduced LV function occurs even without CAD, Systemic Hypertension due to metabolic effects of Diabetes. Various pathophysiologic mechanisms including oxidative stress, persistent inflammatory state, hypercoagulability, hypoglycemia and Cardiac autonomic neuropathy results in cardiovascular manifestations.[3-5]

Clinical significance of subclinical myocardial dysfunction need to be addressed earlier to halt disease progression and intervene at the earliest. Clinical parameters like age of onset, duration of diabetes, Glycemic control (FBS, HbA1C), dose of insulin, associated comorbid illness, metabolic trait, hypertension, Hemoglobin, Microvascular dysfunction and Dyslipidemia all determines the patients myocardial dysfunction.[6,7]

Subclinical disease like coronary artery anatomical and functional disease can be Identified in Coronary computed Tomography. But identifying subclinical myocardial dysfunction in asymptomatic high-risk individual is challenging. Myocardial diastolic dysfunction occurs earlier than Systolic dysfunction as in the evolution of ischemia cascade. Longitudinal muscle layer in sub endocardium undergoes early contractile dysfunction due to Microvascular disease. Tissue Doppler imaging used in identifying Myocardial contraction is Load and angle dependent and has variable reproducibility. So Techniques assessing longitudinal deformation like speckle tracking- Global peak Longitudinal strain for LV and free wall strain for RV can detect subtle changes in these fibers and they are angle independent. Reservoir, conduit and contractile strain in LA gives add on information in disease progression.[8,9]

The aim of this study is to assess the possible subclinical myocardial dysfunction using Tissue doppler and speckle tracking analysis in asymptomatic T1DM patients with normal LV systolic function.

MATERIALS AND METHODS

This hospital based cross sectional study was conducted in the Department of cardiology, Government Rajaji hospital, Madurai for total period of 4 months after IEC clearance and who volunteered the study-35 patients enrolled in this study.

All patients were insulin dependent and age above 18 years who fulfilled WHO criteria for type 1 Diabetes mellitus. Subjects in this study had no Cardiac disease, normal ECG and normal LVEF > 55% by Simpson's biplane method and linear dimensions with M mode. Patients with known cardiac illness such as coronary artery disease, cardiomyopathy, valvular heart disease, pulmonary hypertension, congenital heart disease, pregnant patients and patients not willing to consent was excluded from study.

A standardized questionnaire with details regarding age of onset, duration of diabetes, duration on treatment, current insulin dose, past history of hypoglycemic episodes, family history of type1 or 2 Diabetes mellitus, comorbid conditions, anthropometric parameters -height (cm), weight (kg), waist circumference (cm), hip circumference (cm), calculated BMI (kg/m2), calculated Body Rounded Index and visceral adipose tissue (VAT)% using webFCE calculator. Blood Pressure and pulse /heart rate recorded and complete physical examination with CVS, RS, ABDOMEN, CNS system focused on microvascular complications and fundus examination.

Blood investigations included complete blood count, FBS, PPBS, HbA1C, Renal Function test, calculated eGFR (CKD-EPI 2021 creatinine), Lipid profile, urine for proteins and deposits. Standard 12 lead ECG and Echocardiographic assessment using General Electric Vivid machine software including,2D, doppler, Tissue doppler and Speckle tracking imaging was done.

LVEF was assessed using the biplane Simpson's method in apical 4 chamber and 2 chamber views. LV end-diastolic dimension and end-systolic dimension, interventricular septal end-diastolic dimension, and LV posterior wall end-diastolic dimension were measured in time motion mode in the parasternal short-axis view.

The left ventricular global longitudinal strain (LV GLS) was measured by 2D speckle-tracking echocardiography, in which deformation of the LV is determined by tracking speckles from frame to frame. Apical images of the two-, three-, and four-chamber views of the LV are divided into 6 segments (basal, mid, and apical segments in opposing walls). For the present analysis, LV GLS was determined as the average of 17 segments, thereby providing a LVGLS measure for the entire LV

Statistical analysis was prepared by SPSS software version 22 (SPSS22 Inc., Chicago, Illinois, USA.) All continuous variables were expressed as mean, median, and SD, categorical variables were reported as frequency and percentage. Group comparison were

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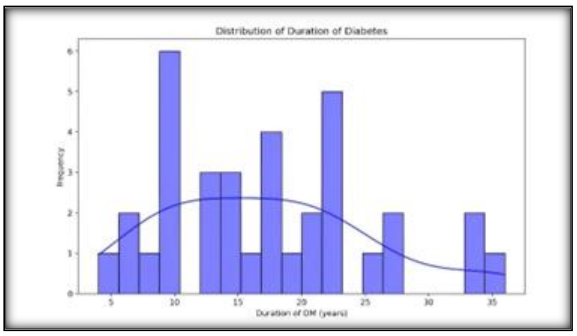
performed with student t test or cross tables. The Chi-square test or Fischer exact test was used for Categorical variables. A p- value of < 0.05 was considered statistically significant. Cramer's value used to define test of significance.

RESULTS

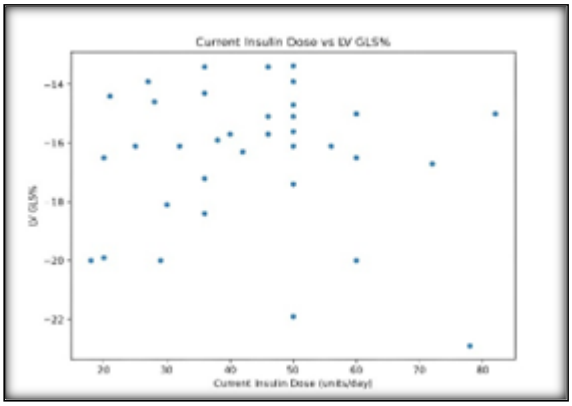
During the study period of 4 months, a total of 35 asymptomatic type 1 diabetes patients fulfilling inclusion criteria who volunteered were enrolled in this study.

The Median age of study participants is 36.54, Mean is 36.00, range 19 to 62 years. most of them belonging to age between 26.5 and 44.5. Patients with duration of Diabetes more than 10 years were 25 numbers and <10 years is 10 numbers. Range is from 4 to 36 years with mean duration of 17.3 years, SD of 8.15. Duration of diabetes had no significant correlation with Abnormal LV GLS (-17%).

Current insulin dose and abnormal LV GLS (-17%) had scattered presentation with mean insulin dose of 43 units/day with range from 18 to 82 units/day and no significant correlation (p value 1.00) exists.



Duration of Diabetes frequency pattern



Comparison of current insulin dose & LV GLS

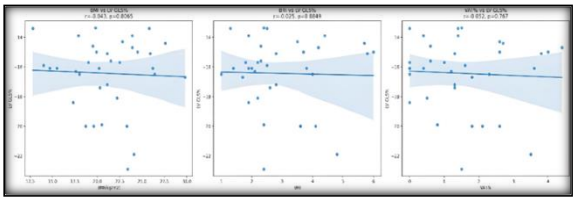
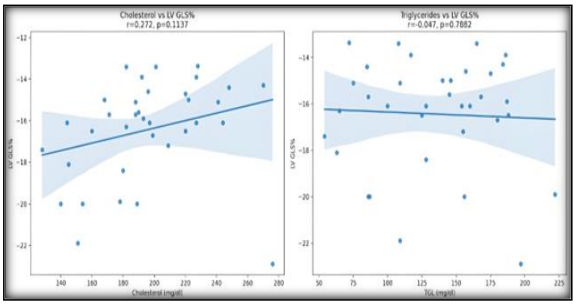
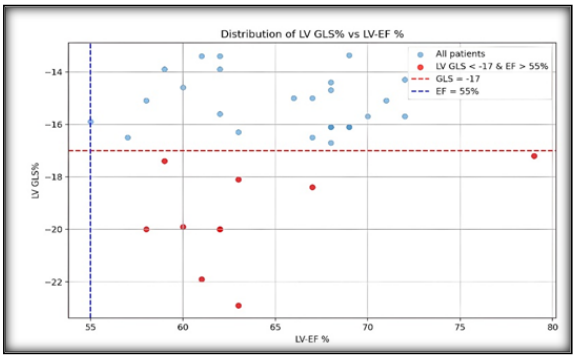


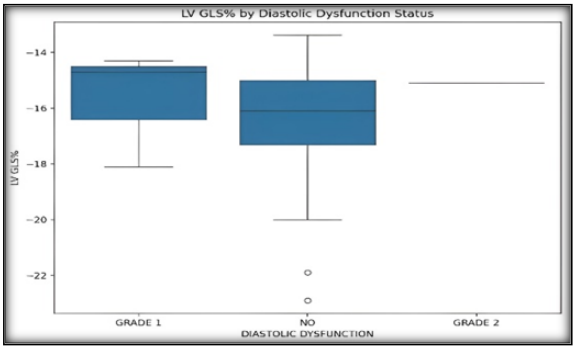
Figure shows comparison of BMI, BRI, VAT with LV GLS - scattered plot



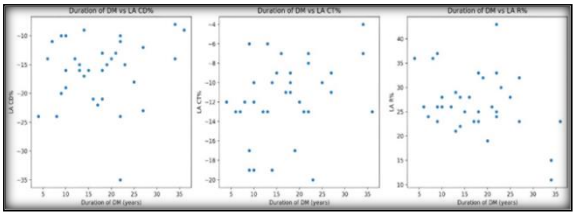
Comparing cholesterol and triglycerides values with LV GLS – showing scattered plot



Distribution of patient with abnormal LV GLS & with normal LVEF



Comparing abnormal LV GLS with diastolic dysfunction



Frequency distribution of LA strain pattern compared with duration of Diabetes

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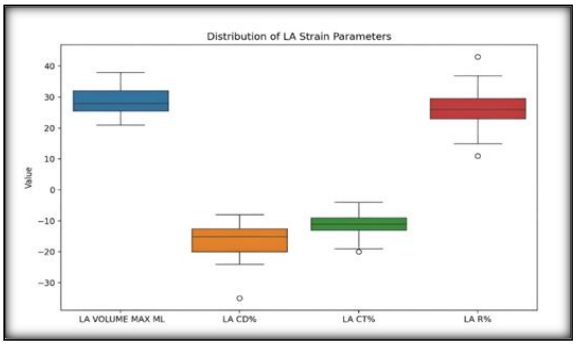

There is no significant correlation between abnormal GLS and Body mass index(p value 0.152),body roundedness index (p value 0.727),FBS (p value 0.424),HbA1C(p value 0.666),total cholesterol (p value 0.179) and non-fasting TGL(p value 0.415),hemoglobin (p value 0.9),VPT(p value 0.19),abnormal fundus examination (p value 0.99).

In our study there was significant correlation of Abnormal LV GLS(<-17%) and number of hypoglycemic episodes with p value <0.044,patients with Hypertension p value < 0.032 and calculated eGFR (by MDRD equation) < 60 ml/min/1.73m2 with p value of <0.035 Cramer's V value 0.391.

Out of 35 patients 3 had grade 1 LV diastolic dysfunction mean duration 25 years and 1 had grade 2 LV diastolic dysfunction with duration of diabetes 34 years had a mean LV GLS of -15.7% and -15% respectively.31 patients with no LV diastolic dysfunction had a mean LV GLS of-16.55% mean duration of Diabetes of !5 years. LV diastolic dysfunction has significant correlation with duration of diabetes with p value of 0.016. There was no significant correlation with duration of diabetes and LA strain parameters (LA reservoir -0.35, LA conduit 0.17 and LA contractile 0.315).

The Median age of study participants is 36.54, Mean is 36.00. study population were divided into group with normal and abnormal values with reference to each parameter and compared to LV GLS.

Table 1: Frequency distribution of variables with percentage showing normal & abnormal values.

		Frequency	Percentage
Gender	Male	23	65.7
	Female	12	34.3
Age at diagnosis (years)	<20 years	20	57.1
	>20 years	15	42.9
Duration of DM (years)	<5 years	1	2.9
	>5 years	34	97.1
Current Insulin dose (Units/day)	<30 U/day	9	25.7
	>30 U/day	26	74.3
Hypoglycemic episodes	Yes	17	48.6
	No	18	51.4
Hypertensive	Yes	7	20.0
	No	28	80.0
BMI (kg/m2)	<23	23	65.7
	>23	12	34.3
BRI (ht in Cm / waist in cm)	<3.4	22	62.9
	>3.4	13	37.1
VAT %	<12	35	100.0
	>12	0	0
Heart rate (beats/min)	<90	29	82.9
	>90	6	17.2
FBS (mg/dl)	<110	8	22.9
	>110	27	77.1
HbA1c %	<7	6	17.1
	>7	29	82.9
Cholesterol (mg/dl)	<200	22	62.9
	>200	13	37.1
TGL(mg/dl)	<175	28	80.0
	>175	7	20.0
e-GFR(ml/min/1.73m2)	<60	4	11.4
	>60	31	88.6

1. GLS and Age at diagnosis

		Age at diagnosis (in years)		Total
		<20	**>20**	
GLS	Normal	12	7	19
	Abnormal	8	8	16
Total		20	15	35

Fischer's exact test, df=1, p value 0.506

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2. GLS and Duration of DM

		Duration of DM (in years)		Total
		<5	>5	
GLS	Normal	1	18	19
	Abnormal	0	16	16
Total		1	34	35

Fischer's exact test, df=1, p value 1.00

3. GLS and Insulin dose

		Current Insulin Dose (U/day)		Total
		<30	>30	
GLS	Normal	5	14	19
	Abnormal	4	12	16
Total		9	26	35

Fischer's exact test, df=1, p value 1.0

4. GLS and Hypoglycaemic Episodes

		Hypoglycaemic Episodes		Total
		Yes	No	
GLS	Normal	6	13	19
	Abnormal	11	5	16
Total		17	18	35

Fisher's Exact test, p value 0.044. Cramer's V value 0.370

5. GLS and Hypertensives

		Hypertensives		Total
		Yes	No	
GLS	Normal	1	18	19
	Abnormal	6	10	16
Total		7	28	35

Fisher's Exact test, p value 0.032, Cramer's V value 0.401

6. GLS and Heart rate

		Heart rate (beats/min)		Total
		<90	>90	
GLS	Normal	17	2	19
	Abnormal	12	4	16
Total		29	6	35

Fischer's exact test, df=1, p value 0.379

7. GLS and BMI

		BMI (kg/m2)		Total
		<23	>23	
GLS	Normal	10	9	19
	Abnormal	13	3	16
Total		23	12	35

Fischer's exact test, df=1, p value 0.152

8. GLS and BRI

		BRI		Total
		<3.4	>3.4	
GLS	Normal	11	8	19
	Abnormal	11	5	16
Total		22	13	35

Fischer's exact test, df=1, p value 0.727

9. GLS and FBS

		FBS (mg/dL)		Total
		<110	>110	
GLS	Normal	3	16	19
	Abnormal	5	11	16
Total		8	27	35

Fischer's exact test, df=1, p value 0.424

10. GLS and HbA1c

		HbA1c (gm/dL)		Total
		<7	>7	
GLS	Normal	4	15	19
	Abnormal	2	14	16
Total		6	29	35

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Fischer's exact test, df=1, p value 0.666

11. GLS and Cholesterol

		Cholesterol (mg/dL)		Total
		<200	>200	
GLS	Normal	14	5	19
	Abnormal	8	8	16
Total		22	13	35

Fischer's exact test, df=1, p value 0.179

12. GLS and Triglycerides

		Triglycerides (mg/dL)		Total
		<175	>175	
GLS	Normal	14	5	19
	Abnormal	14	2	16
Total		28	7	35

Fischer's exact test, df=1, p value 0.415

13. GLS and eGFR

		GLS		Total
		Normal	Abnormal	
eGFR (ml/min/1.73m2)	<=60	0	4	4
	>60	19	12	31
Total		19	16	35

Fisher's Exact test, p value 0.035, Cramer's V value 0.391

DISCUSSION

Our study showed subclinical subendocardial longitudinal fibre contractile dysfunction in patient with significant Hypertension on antihypertensives 20%, frequent hypoglycaemic episodes 48%, eGFR < 60 ml/min/1.73 m2 11% and patients with increasing grades of diastolic dysfunction had significant LV GLS abnormality.[10]

Comparing to previous studies, M. Van Berendoncks MD, PhD et all 2018 where diastolic dysfunction was more prevalent than systolic dysfunction in 66% of subjects and subclinical systolic dysfunction was present in almost 40% of patients with normal LV systolic function. Visceral fat was strong predictor of Increased CACS as well as GLPSS. In our study 45.7% had LV GLPSS< -17%. There was No significant correlation with calculated BMI, BRI, Visceral adipose tissue and abnormal GLPSS.

Diabetes produces asymptomatic myocardial dysfunction via endothelial dysfunction and increased arterial stiffness, both of which are established markers of coronary artery atherosclerosis. Zairi et all in 2109 showed diabetes duration and HbA1c had weak correlation with abnormal GLPSS. In our study there was no significant correlation between diabetes duration and HbA1c with GLPSS.

Magnus Thorsten Jensen et all in 2015 GLS was reduced in T1DM was driven solely in patient with Albuminuria. In our study there was no significant correlation between proteinuria. Patients with eGFR < 60 ml/min/1.73 m2 had Abnormal GLPSS.

Máté Hajdu et all,2022showed impaired myocardial mechanics with HbA1c >7.4% and hypertension. In our study Patients with Blood pressure > 130/80 mm HG had abnormal GLPSS.

CONCLUSION

Our findings suggest that LV GLS is impaired in patients with asymptomatic T1DM and that the decrease in LV GLS is correlated with Co-morbid status such as hypertension, associated diastolic dysfunction and diabetic related risk factors such as frequent hypoglycaemic episodes, early screening of diabetic nephropathy. This endorses further the necessity of stringent control of conventional risk factors and diabetic complications to prevent the subclinical myocardial dysfunction and its progression to established heart disease.

Limitations

There were several limitations to be addressed during study

Study was conducted in targeted population and the sample size was small.

Therefore, extrapolation of these results to general population requires further validation from the larger prospective multi-centre studies.

The study is cross-sectional and therefore any clinical and prognostic

implications of the described findings need to be evaluated in a prospective follow-up study.

Stress testing and coronary computed tomography angiography with coronary calcium scoring will further help to risk stratify these patients.

LV GLS was assessed in our study since it is more reproducible than circumferential or radial strain and GLS values are Vendor specific that cannot be extrapolated to T1DM with other equipment.

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