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Left Ventricle Global Longitudinal Strain Based Heart Failure Assessment in "At Risk" Patients with Type 2 Diabetes Mellitus

[1]Prakhar Aggarwal, Department of General Medicine, GSVM Medical College, Kanpur, U.P
[1]AC Gupta, Department of General Medicine, GSVM Medical College, Kanpur, U.P
[2]Saurabh Agarwal, Department of General Medicine, GSVM Medical College, Kanpur, U.P
[3]Mohit Sachan, LPS Institute of Cardiology, GSVM Medical College, Kanpur, U.P
Corresponding Author: Prakhar Aggarwal, Department of General Medicine, GSVM Medical College, Kanpur, U.P

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Abstract

Type 2 diabetes mellitus (T2DM) is a growing global health burden and is strongly associated with cardiovascular disease, particularly heart failure. The risk of heart failure in diabetic patients is approximately four times higher than in the general population, often due to metabolic, structural, and hemodynamic alterations. Conventional echocardiographic markers such as left ventricular ejection fraction (LVEF) may remain normal in early disease, limiting their ability to detect subclinical dysfunction. Global longitudinal strain (GLS), measured by speckle-tracking echocardiography, is a sensitive parameter for identifying early myocardial dysfunction. Sodium-glucose cotransporter-2 inhibitors (SGLT-2i) have demonstrated cardiovascular benefits in large-scale clinical trials, but most evidence involves patients with established cardiovascular disease. The present study was undertaken to assess the effect of dapagliflozin on GLS in asymptomatic T2DM patients with preserved LVEF.

Objectives:

- To assess baseline left ventricular systolic function using GLS in T2DM patients without symptomatic heart failure.
- To evaluate the impact of dapagliflozin on changes in GLS after 8 weeks of therapy compared to placebo.

Methods: This open-label randomized controlled trial was conducted at LLR & Associated Hospitals, Kanpur, from December 2022 to December 2024. A total of 267 diabetic patients were screened; 171 without symptoms of heart failure were randomized into placebo (n=86) and intervention groups (n=85). After attrition, 156 patients (78 per group) completed the study. The intervention group received dapagliflozin 10 mg daily in addition to standard care, while the placebo group continued standard treatment. Baseline GLS was measured using 2D speckle-tracking echocardiography and reassessed at 8 weeks. Clinical, biochemical, and echocardiographic parameters were compared between groups using appropriate statistical methods.

Results: At baseline, both groups had similar GLS values (mean GLS: -15.54 in intervention vs. -15.37 in placebo; p=0.242). After 8 weeks, the intervention group demonstrated significant improvement in GLS (-16.81 ± 2.09), while the placebo group showed no meaningful change (-15.29 ± 2.04; $p < 0.001$). A higher proportion of patients in the intervention group achieved normalization of GLS (65.38%) compared to the placebo group (17.94%). Conversely, deterioration of GLS (< -14) was more frequent in the placebo group (28.2%) than in the intervention group (12.82%). Other metabolic and renal parameters remained broadly comparable.

Conclusion: Dapagliflozin significantly improved GLS in T2DM patients without symptomatic heart failure, indicating its role in preventing progression to overt cardiac dysfunction. GLS proved to be a sensitive marker for early myocardial changes, supporting its routine use in diabetic populations. SGLT-2 inhibitors may thus offer dual metabolic and cardioprotective benefits even in asymptomatic patients.

Keywords: Type 2 Diabetes Mellitus; Heart Failure; Global Longitudinal Strain; SGLT-2 Inhibitors; Dapagliflozin; Echocardiography

Introduction

Diabetes mellitus (DM) represents a group of metabolic disorders characterized by hyperglycemia, caused by a complex interplay of genetic, environmental, and lifestyle factors. According to the International Diabetes Federation, over 463 million adults were living with diabetes in 2019, with numbers projected to rise to 642 million by 2040. India contributes significantly to this burden, with more than 77 million diabetic individuals, many of whom remain undiagnosed. Among the different types of diabetes, type 2 diabetes mellitus (T2DM) is the most prevalent, accounting for nearly 90% of cases.

The clinical significance of diabetes extends beyond glycemic dysregulation; it is associated with both microvascular complications (retinopathy, nephropathy, neuropathy) and macrovascular complications (atherosclerosis, coronary artery disease, cerebrovascular accident, and peripheral vascular disease). Recently, a direct association between diabetes and heart failure has gained recognition, with studies demonstrating that diabetics have a fourfold higher risk of developing heart failure compared to the general population. Factors such as duration of diabetes, advancing age, hypertension, obesity, renal dysfunction, and coronary artery disease contribute to this elevated risk.

Heart failure is defined as a clinical syndrome resulting from structural or functional cardiac impairment, leading to symptoms such as fatigue, dyspnea, and edema. The condition imposes a significant healthcare and socioeconomic burden. Standard echocardiographic indices, such as left ventricular ejection fraction (LVEF), are traditionally used to evaluate cardiac function; however, they may not detect subclinical myocardial dysfunction. Newer techniques, such as global longitudinal strain (GLS), have emerged as more sensitive markers for identifying early left ventricular dysfunction even when LVEF remains preserved.

Sodium-glucose cotransporter-2 inhibitors (SGLT-2i), a relatively new class of oral antidiabetic drugs, have shown cardiovascular benefits independent of glycemic control. Clinical trials have reported reductions in hospitalization for heart failure and cardiovascular mortality in T2DM patients receiving SGLT-2 inhibitors. Proposed mechanisms include improved myocardial energetics, reduced preload and afterload, and favorable remodeling of cardiac tissue. Despite promising evidence, most large-scale randomized controlled trials (RCTs) have focused on patients with established

cardiovascular disease. The role of SGLT-2 inhibitors in asymptomatic diabetics without overt heart failure remains less explored.

This study was therefore designed to evaluate the effect of SGLT-2 inhibitors, specifically dapagliflozin, on left ventricular global longitudinal strain (LV GLS) in T2DM patients without clinical heart failure and preserved ejection fraction.

Aims and Objectives

Aim: The primary aim of this study was to determine the effect of SGLT-2 inhibitors on left ventricular global longitudinal strain in patients with type 2 diabetes mellitus who do not exhibit symptoms of heart failure and who have preserved left ventricular ejection fraction.

Objectives:

- To assess baseline left ventricular systolic function using GLS on resting echocardiography in T2DM patients.
- To evaluate the effect of SGLT-2 inhibitors on changes in LV GLS at 8 weeks of follow-up compared to placebo.

Null Hypothesis: There is no difference between SGLT-2 inhibitors and placebo in their effect on LV GLS among people with T2DM without symptoms of heart failure and with preserved left ventricular ejection fraction.

Materials and Methods

This study was conducted as an open-label randomized controlled clinical trial at LLR & Associated Hospitals, L.P.S. Institute of Cardiology, and affiliated centers in Kanpur between December 2022 and December 2024. Ethical committee approval was obtained prior to initiation.

Study Design and Population

A total of 267 diabetic patients were screened, of which 96 were excluded due to symptoms suggestive of heart failure. The remaining 171 patients were randomized into two groups: placebo (n=86) and intervention (n=85). After attrition, 156 patients (78 in each group) completed the study.

Inclusion Criteria

Age ≥ 60 years with T2DM of at least 5 years duration.

Either sex, without established CAD or heart failure.

Patients with comorbidities such as hypertension, obesity-related conditions, chronic kidney disease, or atrial arrhythmias but without heart failure or CAD.

Exclusion Criteria

Established CAD or heart failure.

HbA1c > 13%.

Recent episodes of diabetic ketoacidosis or recurrent hypoglycemia.

Orthostatic hypotension.

Intervention

The intervention group received dapagliflozin 10 mg daily in addition to their regular antidiabetic regimen, while the placebo group continued on standard therapy without SGLT-2 inhibitors.

Follow-Up and Measurements

Baseline echocardiography with GLS measurement was performed for all participants, followed by repeat GLS assessment after 8 weeks of treatment. Routine biochemical parameters, HbA1c, lipid profile, renal function tests, and clinical data were collected.

Statistical Analysis

Comparisons between groups were conducted using standard statistical methods, with significance set at $p < 0.05$. Both intra-group and inter-group analyses of GLS changes were performed.

Results

The study enrolled 156 patients, evenly distributed between intervention and placebo groups. The baseline characteristics, including age, sex distribution, BMI,

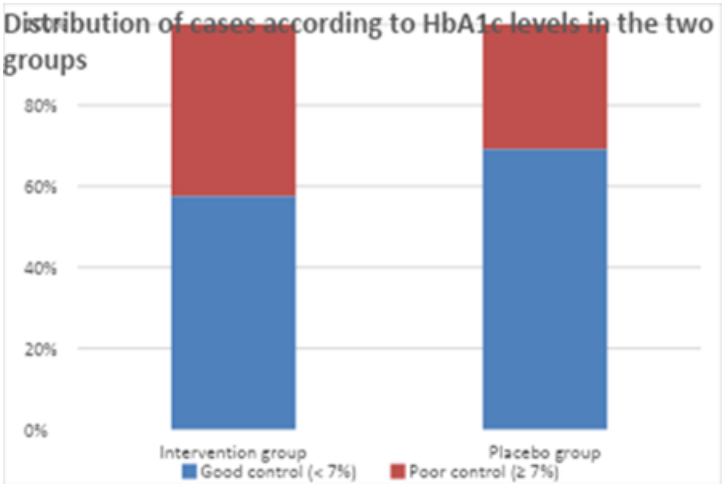
diabetes duration, and hypertension status, were comparable between groups. Mean age was around 67 years in both arms, and approximately two-thirds of participants were male. Average diabetes duration was about 12 years, and more than half had comorbid hypertension.

Glycemic Control and Biochemistry: HbA1c values were generally well controlled (<7%) in most patients across both groups. Biochemical comparisons revealed significantly lower total cholesterol and triglyceride levels in the intervention group, whereas HDL levels were higher in the placebo group. No significant differences were found in hemoglobin, serum creatinine, LDL, or eGFR values between groups.

Table 1: Distribution of cases according to HbA1c levels in the two groups (N = 156)

HbA1c levels	Intervention group	Placebo group	p-value
Good control (< 7%)	45 (57.69%)	54 (69.23%)	0.135
Poor control (≥ 7%)	33 (42.3%)	24 (30.76%)	

Graph 1:



Renal Status

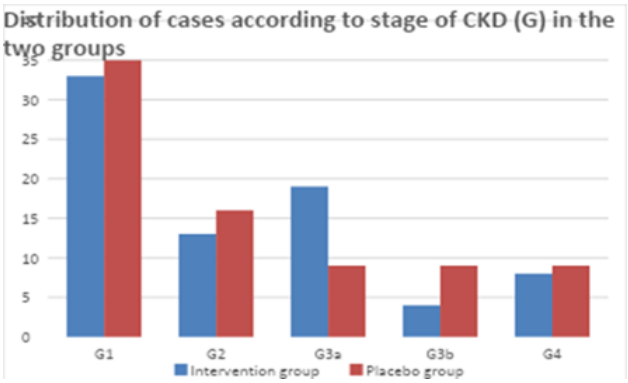
Both groups included patients across CKD stages G1–G4. Albuminuria distribution differed significantly, with more patients in the placebo group showing advanced albuminuria compared to the intervention group.

Table 2: Distribution of cases according to stage of CKD in the two groups (N = 156)

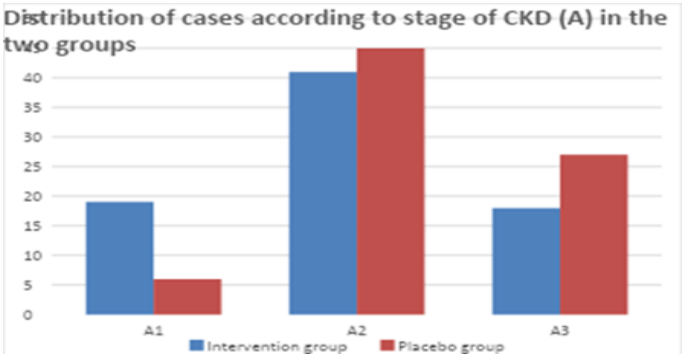
Stage of CKD	Intervention group	Placebo group	p-value
G1	33 (42.3%)	35 (44.87%)	0.226
G2	13 (16.66%)	16 (20.51%)	
G3a	19 (24.35%)	9 (11.53%)	
G3b	4 (5.12%)	9 (11.53%)	

G4	8 (10.25%)	9 (11.53%)	
A1	19 (24.35%)	6 (7.69%)	0.013
A2	41 (52.56%)	45 (57.69%)	
A3	18 (23.07%)	27 (34.61%)	

Graph 2:



Graph 3:



Echocardiographic Findings: At baseline, GLS values were abnormal but comparable across groups (mean GLS: -15.54 in intervention vs. -15.37 in placebo; p=0.242). At follow-up, significant differences emerged:

Intervention group: Mean GLS improved to -16.81.

Placebo group: Mean GLS remained at -15.29, with minimal change.

Between-group difference was statistically significant (p < 0.001).

Table 3: Distribution of cases according to outcome on 2D-ECHO in the two groups (N = 156)

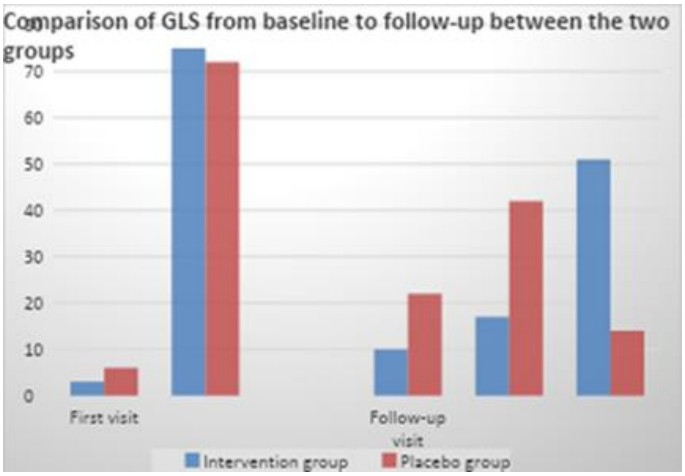
2D-ECHO	Intervention group	Placebo group	p-value
< 50%	0 (0%)	0 (0%)	-
≥ 50%	78 (100%)	78 (100%)	

Table 4: Comparison of GLS from baseline to follow-up between the two groups (N = 156)

GLS		Intervention group	Placebo group	p-value
First visit	< -14	3 (3.84%)	6 (7.69%)	0.303
	Between -14 to -17	75 (96.15%)	72 (92.3%)	
	>= -17	0 (0%)	0 (0%)	

Follow-up visit	< -14	10 (12.82%)	22 (28.2%)	<0.001
	Between -14 to -17	17 (21.79%)	42 (53.84%)	
	>= -17	51 (65.38%)	14 (17.94%)	
GLS		Mean (SD)		p-value (Inter-group)
First visit		-15.54 (0.83)	-15.37 (0.91)	0.242
Follow-up visit		-16.81 (2.09)	-15.29 (2.04)	<0.001
p-value (Intra-group)		<0.001	0.570	

Graph 4:



Categorical analysis further revealed that 65% of patients in the intervention group achieved normal GLS values at follow-up compared to only 18% in the placebo group. Conversely, deterioration of GLS (< -14) was more common in the placebo group (28%) compared to the intervention group (13%).

Discussion

The present study demonstrated that treatment with dapagliflozin significantly improved global longitudinal strain in patients with T2DM without symptoms of heart failure. This improvement was evident after just 8 weeks of therapy, suggesting early cardio protective effects of SGLT-2 inhibitors.

Baseline characteristics were well balanced between groups, minimizing potential confounding. The improvement in GLS was robust, observed in both intra-group and inter-group comparisons, and aligns with prior clinical trials such as the EMPA-HEART study and observational work by Gamaza Chulián et al. These studies similarly showed that SGLT-2 inhibitors improve myocardial strain and reduce left ventricular hypertrophy. The results suggest that GLS is a sensitive marker for detecting subclinical myocardial dysfunction in diabetics. Unlike LVEF, which remained preserved in all patients, GLS was able to capture subtle changes in myocardial mechanics. This highlights its utility for early identification of patients at risk of progression to symptomatic heart failure.

Mechanistically, the benefits of SGLT-2 inhibitors extend beyond glycemic control. Proposed pathways include osmotic diuresis leading to reduced preload, improved myocardial energetics via ketone metabolism, regression of LV hypertrophy, attenuation of inflammation, and reduced oxidative stress. Collectively, these mechanisms improve both structure and function of the diabetic myocardium.

Comparisons with other trials further validate the findings. While Soo Lim et al. demonstrated improvements with ertugliflozin in Korean populations, this study extends evidence to Indian patients using dapagliflozin. Similarly, trials involving empagliflozin

and dapagliflozin in patients with established cardiovascular disease or stable heart failure have shown consistent cardiac benefits. The present study adds novel evidence by focusing on asymptomatic diabetics with preserved EF, a group in whom prevention may yield substantial long-term benefits.

Despite encouraging results, some limitations must be acknowledged. The follow-up period of 8 weeks was relatively short, and long-term outcomes such as hospitalization for heart failure or mortality were not assessed. Additionally, echocardiographic GLS measurement may vary across vendors and operators. The single-center design limits generalizability, and larger multicenter trials with extended follow-up are warranted.

Conclusion

This study provides compelling evidence that SGLT-2 inhibitors, specifically dapagliflozin, significantly improve left ventricular global longitudinal strain in type 2 diabetic patients without overt heart failure. By enhancing subclinical myocardial function, dapagliflozin demonstrates potential in preventing progression to symptomatic heart failure.

The findings highlight the importance of incorporating GLS into routine evaluation of diabetic patients, as it enables early detection of cardiac dysfunction before conventional parameters such as LVEF show abnormalities. Furthermore, SGLT-2 inhibitors should be considered not only as glucose-lowering agents but also as cardio protective drugs in high-risk diabetic populations.

Recommendations

Routine GLS assessment should be performed in diabetic patients to identify early cardiac dysfunction.

SGLT-2 inhibitors may be recommended in diabetics at risk of heart failure, even in the absence of clinical symptoms.

Larger, multicenter trials with long-term follow-up are needed to confirm sustained benefits and impact on major adverse cardiovascular outcomes.

References

1. Tsagalis, G., Akrivos, T., Alevizaki, M., et al. (2009). Incidence, prognostic factors, and outcome of acute renal failure in patients with acute stroke. Nephrology Dialysis Transplantation, 24(1), 194–200.
2. Yahalom, G., Schwartz, R., Schwammenthal, Y., et al. (2009). Chronic kidney disease and clinical outcome in patients with acute stroke. Stroke, 40(4), 1296–1303.
3. Molshatzki, N., Orion, D., Tsabari, R., et al. (2011). Renal dysfunction and clinical outcomes in patients with acute stroke. Stroke, 42(2), 236–241.
4. Hojs Fabjan, T., Hojs, R., & Fabjan, B. (2014). Predictors of long-term renal function decline after acute stroke. Clinical Nephrology, 81(1), 53–60.
5. Tucker, B., Aston, J., & Sear, J. W. (2014). Acute renal dysfunction following stroke. Nephrology, 19(8), 567–572.
6. Synhaeve, N. E., van Alebeek, M. E., Arntz, R. M., et al. (2016). Hypertension and long-term renal dysfunction after stroke. Journal of Hypertension, 34(8), 1565–1572.
7. Watanabe, K., Nagao, T., Matsushita, K., et al. (2016). Albuminuria in acute ischemic stroke: Risk of kidney dysfunction and poor recovery. American Journal of Nephrology, 44(4), 286–294.
8. Hayden, D., Harriott, A., & Rothwell, P. M. (2017). Renal dysfunction in patients with ischemic stroke

and transient ischemic attack: Prevalence and outcomes. Stroke, 48(2), 327–334.

9. Venkat, P., Chopp, M., & Chen, J. (2018). New insights into coupling and uncoupling of neurovascular unit and kidney injury after stroke. Stroke Research and Treatment, 2018, 1–11.
10. Bai, J., Wang, Y., Li, L., et al. (2020). Frequency and outcomes of acute kidney injury after stroke: A systematic review and meta-analysis. Stroke, 51(3), 1090–1099.
11. Liu, M., Liang, Y., Chigurupati, S., et al. (2022). Acute kidney injury after acute ischemic stroke: Risk factors and outcomes. Journal of Neurology & Neurophysiology, 13(1), 88–97.
12. Chen, Y., Zhang, Z., & Zhao, W. (2024). Stroke-induced renal dysfunction: Mechanisms and clinical implications. Frontiers in Neurology, 15, 114–124.