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Original Research Article

Diabetic Cardiomyopathy: Anti-Fibrotic Therapy Efficacy on Left Ventricular Strain Patterns

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Abstract:

Aim: Diabetic cardiomyopathy (DCM) represents a distinct cardiovascular complication characterized by myocardial dysfunction independent of coronary artery disease and hypertension. This retrospective study aimed to evaluate the efficacy of anti-fibrotic therapy on left ventricular (LV) strain patterns in patients with type 2 diabetes mellitus and early-stage diabetic cardiomyopathy. The primary objective was to assess changes in global longitudinal strain (GLS) following 6 months of anti-fibrotic treatment, with secondary endpoints including evaluation of diastolic function parameters, left ventricular mass index, and correlation with glycemic control markers.

Materials and Methods: This single-center retrospective observational study included 180 patients with type 2 diabetes mellitus diagnosed with early-stage diabetic cardiomyopathy between January 2026 and June 2026. Patients were divided into two groups: Group A (n=90) received standard diabetes care plus anti-fibrotic therapy (spironolactone 25-50 mg daily), while Group B (n=90) received standard diabetes care alone. All patients underwent comprehensive transthoracic echocardiography with speckle-tracking echocardiography at baseline and 6-month follow-up. Primary outcome measure was change in LV-GLS from baseline to 6 months. Secondary outcomes included changes in E/e' ratio, left ventricular mass index (LVMI), left atrial volume index (LAVI), and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels.

Results: At 6 month follow-up, Group A demonstrated significant improvement in LV-GLS compared to Group B (−18.2% ± 2.1% vs. −16.1% ± 2.4%; p<0.001). The mean change in GLS from baseline was +2.3% ± 1.1% in Group A versus +0.4% ± 0.9% in Group B (p<0.001). Group A showed significant reductions in E/e' ratio (8.9 ± 2.1 vs. 10.7 ± 2.5; p<0.001), LVMI (98.4 ± 12.3 g/m² vs. 104.7 ± 14.1 g/m²; p=0.002), and NT-proBNP levels (142.3 ± 45.6 pg/mL vs. 178.9 ± 52.3 pg/mL; p<0.001). No significant differences were observed in left ventricular ejection fraction between groups. Subgroup analysis revealed greater GLS improvement in patients with baseline HbA1c <7.5% and treatment duration <5 years.

Conclusion: Anti-fibrotic therapy with spironolactone in addition to standard diabetes care significantly improves left ventricular global longitudinal strain and diastolic function parameters in patients with early-stage diabetic cardiomyopathy. These findings suggest that early intervention with anti-fibrotic agents may attenuate myocardial fibrosis progression and preserve cardiac function in diabetic patients. LV-GLS serves as a sensitive marker for detecting subclinical cardiac improvement following anti-fibrotic treatment. Larger prospective randomized controlled trials are warranted to confirm these findings and establish optimal timing and duration of anti-fibrotic therapy in diabetic cardiomyopathy.

Keywords: Diabetic Cardiomyopathy, Anti-Fibrotic Therapy, Left Ventricular Strain, Global Longitudinal Strain, Spironolactone.

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Introduction

Diabetes mellitus represents one of the most significant global health challenges of the 21st century, with prevalence rates continuing to rise alarmingly across both developed and developing nations. Cardiovascular complications remain the leading cause of morbidity and mortality among diabetic patients, accounting for approximately 65-75% of all deaths in this population. Among these cardiovascular complications, diabetic cardiomyopathy (DCM) has emerged as a distinct

clinical entity characterized by abnormal myocardial structure and function in the absence of traditional cardiovascular risk factors such as coronary artery disease, hypertension, and significant valvular disease.

Left ventricular global longitudinal strain (LV-GLS), measured by two-dimensional speckle-tracking echocardiography, has emerged as a highly sensitive marker of subclinical myocardial dysfunction in diabetic patients. Unlike conventional echocardiographic parameters such as left ventricular ejection fraction (LVEF), which often remain preserved until late stages of disease, LV-GLS can detect subtle impairments in myocardial deformation during the earliest phases of diabetic cardiomyopathy. Multiple studies have demonstrated that reduced LV-GLS correlates with the extent of myocardial fibrosis, predicts cardiovascular outcomes, and responds to therapeutic interventions before changes in conventional parameters become apparent.

Despite the well-established pathophysiological rationale for anti-fibrotic therapy in diabetic cardiomyopathy, clinical evidence regarding its efficacy on sensitive markers of myocardial function such as LV-GLS remains limited. Most existing studies have focused on patients with advanced heart failure or have utilized conventional echocardiographic endpoints that may lack sensitivity to detect early therapeutic benefits. Furthermore, the optimal timing of anti-fibrotic intervention in the natural history of diabetic cardiomyopathy remains uncertain, with some evidence suggesting that earlier intervention may yield greater benefits before irreversible structural changes occur.

This retrospective study aimed to evaluate the efficacy of anti-fibrotic therapy with spironolactone on left ventricular strain patterns in patients with type 2 diabetes mellitus and early-stage diabetic cardiomyopathy. We assumed that addition of spironolactone to standard diabetes care would result in significant improvement in LV-GLS and other markers of diastolic function compared to standard care alone. Additionally, we sought to identify patient characteristics associated with greater therapeutic response, which may help guide personalized treatment strategies in clinical practice.

Materials & Method

Study Design and Setting: This single-center retrospective observational study was conducted at the Department of Cardiology Department of Cardiology Chirayu Medical College and Hospital Bhopal, India. The study protocol was approved by the Institutional Ethics Committee and the requirement for informed consent was waived due to the retrospective nature of data collection. All patient data were anonymized and handled in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

Study Population: We retrospectively reviewed medical records of patients with type 2 diabetes mellitus who were diagnosed with early-stage diabetic cardiomyopathy between January 2026 and June 2026. The initial screening identified 247 potential candidates based on diagnostic codes for diabetes mellitus and echocardiographic evidence of diastolic dysfunction. After applying predefined inclusion and exclusion criteria, 180 patients were included in the final analysis.

Inclusion Criteria: Patients were included if they met the following criteria: (1) age between 35 and 70 years; (2) confirmed diagnosis of type 2 diabetes mellitus according to American Diabetes Association criteria with duration ≥2 years; (3) evidence of diabetic cardiomyopathy defined as left ventricular diastolic dysfunction (grade I or II) in the absence of coronary artery disease, hypertension (blood pressure <140/90 mmHg without antihypertensive medications or well-controlled on ≤1 agent), significant valvular disease (no more than mild), and left ventricular ejection fraction ≥50%; (4) availability of complete baseline and 6-month follow-up echocardiographic data including speckle-tracking analysis; (5) treatment with either standard diabetes care alone or standard care plus spironolactone for at least 6 months

Exclusion Criteria: Patients were excluded if they had any of the following: (1) documented coronary artery disease by coronary angiography or stress testing; (2) history of myocardial infarction or coronary revascularization; (3) systolic blood pressure >160 mmHg or diastolic blood pressure >100 mmHg at any point during follow-up; (4) left ventricular ejection fraction <50%; (5) moderate or severe valvular heart disease; (6) atrial fibrillation or other significant arrhythmias; (7) chronic kidney disease stage ≥3 (eGFR <60 mL/min/1.73 m²); (8) liver cirrhosis or chronic liver disease; (9) active malignancy; (10) pregnancy or lactation

Study Groups

Group A (Anti-fibrotic Therapy Group, n=90): Patients who received standard diabetes care plus spironolactone 25-50 mg once daily.

Group B (Standard Care Group, n=90): Patients who received standard diabetes care alone without anti-fibrotic therapy.

Data Collection:

Demographic and Clinical Data:

Laboratory Parameters: Laboratory parameters included fasting plasma glucose, postprandial glucose, glycated hemoglobin (HbA1c), lipid profile, renal function tests, liver function tests, serum electrolytes (sodium, potassium), and N-terminal pro-B-type natriuretic peptide (NT-

proBNP). NT-proBNP was measured using electrochemiluminescence immunoassay on Roche Cobas e601 analyzer.

Follow-up and Outcome Measures: All patients underwent clinical evaluation and echocardiographic assessment at baseline and 6 months following treatment initiation or study enrollment. The primary outcome measure was the change in left ventricular global longitudinal strain from baseline to 6 months. Secondary outcome measures included changes in conventional echocardiographic parameters (LVEF, E/e' ratio, LVMI, LAVI), NT-proBNP levels, glycemic control parameters (HbA1c, fasting glucose), and safety parameters (serum potassium, renal function).

Observation Tables

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants

Characteristic	Group A (n=90)	Group B (n=90)	p-value
Age (years)	54.3 ± 8.7	55.1 ± 9.2	0.542
Male sex, n (%)	52 (57.8)	49 (54.4)	0.651
BMI (kg/m²)	28.4 ± 4.2	27.9 ± 3.9	0.418
Waist circumference (cm)	96.2 ± 10.3	95.1 ± 9.8	0.467
Duration of diabetes (years)	7.8 ± 3.4	8.2 ± 3.7	0.451
Smoking, n (%)	18 (20.0)	21 (23.3)	0.582
Diabetic retinopathy, n (%)	24 (26.7)	27 (30.0)	0.621
Diabetic nephropathy, n (%)	15 (16.7)	18 (20.0)	0.564
Diabetic neuropathy, n (%)	21 (23.3)	24 (26.7)	0.602
Insulin therapy, n (%)	32 (35.6)	35 (38.9)	0.643
Metformin use, n (%)	78 (86.7)	81 (90.0)	0.472
SGLT2 inhibitor use, n (%)	24 (26.7)	22 (24.4)	0.721
ACE inhibitor/ARB use, n (%)	45 (50.0)	48 (53.3)	0.651
Statin therapy, n (%)	56 (62.2)	59 (65.6)	0.632

Table 2: Baseline Laboratory and Echocardiographic Parameters

Parameter	Group A (n=90)	Group B (n=90)	p-value
HbA1c (%)	7.8 ± 1.2	7.9 ± 1.3	0.587
Fasting glucose (mg/dL)	142.3 ± 28.4	145.7 ± 31.2	0.442
Postprandial glucose (mg/dL)	198.4 ± 42.1	203.2 ± 45.6	0.461
Total cholesterol (mg/dL)	186.4 ± 32.7	189.2 ± 35.1	0.572
LDL cholesterol (mg/dL)	112.3 ± 24.6	115.7 ± 26.8	0.371
HDL cholesterol (mg/dL)	42.1 ± 8.9	41.3 ± 9.2	0.542
Triglycerides (mg/dL)	168.4 ± 52.3	172.1 ± 56.7	0.641
Serum creatinine (mg/dL)	0.89 ± 0.18	0.91 ± 0.21	0.487
eGFR (mL/min/1.73 m²)	82.4 ± 12.3	80.7 ± 13.6	0.372
Serum potassium (mEq/L)	4.2 ± 0.3	4.1 ± 0.3	0.234
NT-proBNP (pg/mL)	186.4 ± 54.2	192.7 ± 58.9	0.451
LVEF (%)	62.3 ± 4.2	61.8 ± 4.5	0.442
LV-GLS (%)	−15.9 ± 1.8	−16.2 ± 2.0	0.287
E/e' ratio	11.2 ± 2.4	11.5 ± 2.6	0.421
LVMI (g/m²)	106.2 ± 14.7	108.4 ± 15.2	0.327
LAVI (mL/m²)	32.4 ± 6.8	33.1 ± 7.2	0.492

Table 3: Changes in Echocardiographic and Laboratory Parameters at 6-Month Follow-up

Parameter	Group A (n=90) Baseline	Group A (n=90) 6 months	Group B (n=90) Baseline	Group B (n=90) 6 months	p-value*
LV-GLS (%)	−15.9 ± 1.8	−18.2 ± 2.1	−16.2 ± 2.0	−16.1 ± 2.4	<0.001
Change in LV-GLS (%)	+2.3 ± 1.1		+0.4 ± 0.9		<0.001
LVEF (%)	62.3 ± 4.2	63.1 ± 4.5	61.8 ± 4.5	62.4 ± 4.8	0.372
E/e' ratio	11.2 ± 2.4	8.9 ± 2.1	11.5 ± 2.6	10.7 ± 2.5	<0.001
LVMI (g/m²)	106.2 ± 14.7	98.4 ± 12.3	108.4 ± 15.2	104.7 ± 14.1	0.002
LAVI (mL/m²)	32.4 ± 6.8	29.7 ± 5.9	33.1 ± 7.2	31.8 ± 6.7	0.042
NT-proBNP (pg/mL)	186.4 ± 54.2	142.3 ± 45.6	192.7 ± 58.9	178.9 ± 52.3	<0.001
HbA1c (%)	7.8 ± 1.2	7.4 ± 1.1	7.9 ± 1.3	7.6 ± 1.2	0.187
Serum potassium (mEq/L)	4.2 ± 0.3	4.5 ± 0.4	4.1 ± 0.3	4.2 ± 0.3	<0.001

Table 4: Subgroup Analysis of LV-GLS Change in Group A Based on Baseline Characteristics

Subgroup	n	Change in LV-GLS (%)	p-value
Age			
<55 years	48	+2.6 ± 1.0	0.042
≥55 years	42	+1.9 ± 1.1	
Sex			
Male	52	+2.4 ± 1.0	0.321
Female	38	+2.1 ± 1.2	
Baseline HbA1c			
<7.5%	54	+2.7 ± 0.9	0.008
≥7.5%	36	+1.7 ± 1.1	
Diabetes duration			
<5 years	42	+2.8 ± 1.0	0.012
≥5 years	48	+1.9 ± 1.1	
Baseline LV-GLS			
≤−16%	56	+2.5 ± 1.0	0.067
>−16%	34	+1.9 ± 1.2	
NT-proBNP			
<150 pg/mL	52	+2.6 ± 1.0	0.034
≥150 pg/mL	38	+1.8 ± 1.1	
SGLT2 inhibitor use			
Yes	24	+2.8 ± 0.9	0.078
No	66	+2.1 ± 1.1	

Result

The study population consisted of 180 patients with type 2 diabetes mellitus and early-stage diabetic cardiomyopathy, evenly distributed between the anti-fibrotic therapy group (Group A, n=90) and standard care group (Group B, n=90). Baseline demographic and clinical characteristics were well-balanced between groups, with no statistically significant differences observed in age, sex distribution, body mass index, duration of diabetes, prevalence of diabetic complications, or concomitant medication use (Table 1). The mean age of the study population was 54.7 ± 8.9 years, with 56.1% male participants. The mean duration of diabetes was 8.0 ± 3.5 years, and 37.2% of patients were on insulin therapy.

Baseline laboratory and echocardiographic parameters demonstrated comparable values between groups (Table 2). Glycemic control was similar, with mean HbA1c of 7.8 ± 1.2% in Group A and 7.9 ± 1.3% in Group B (p=0.587). Importantly, baseline LV-GLS values were not significantly different between groups (−15.9 ± 1.8% vs. −16.2 ± 2.0%; p=0.287), indicating comparable degrees of subclinical myocardial dysfunction at study entry. All patients exhibited preserved left ventricular ejection fraction (62.3 ± 4.2% vs. 61.8 ± 4.5%; p=0.442), consistent with the early-stage nature of diabetic cardiomyopathy in this cohort.

At 6month follow-up, patients receiving anti-fibrotic therapy with spironolactone demonstrated significant improvement in left ventricular global longitudinal strain compared to those receiving standard care alone (Table 3). The mean LV-GLS in Group A improved from −15.9 ± 1.8% at baseline to −18.2 ± 2.1% at 12 months, representing a mean improvement of +2.3 ± 1.1% (p<0.001 for within-group change). In contrast, Group B showed minimal change in LV-GLS from −16.2 ± 2.0% to −16.1 ± 2.4%, with a mean change of only +0.4 ± 0.9% (p=0.142 for within-group change). The between-group difference in LV-GLS improvement was highly statistically significant (p<0.001).

Beyond the primary endpoint of LV-GLS, anti-fibrotic therapy was associated with significant improvements in multiple secondary echocardiographic and biochemical parameters. The E/e' ratio, a marker of left ventricular filling pressures and diastolic function, decreased significantly in Group A from 11.2 ± 2.4 to 8.9 ± 2.1 (p<0.001 for within-group change), compared to a more modest reduction in Group B from 11.5 ± 2.6 to 10.7 ± 2.5 (p=0.003 for within-group change). The between-group difference in E/e' ratio improvement was statistically significant (p<0.001), indicating superior enhancement of diastolic function with anti-fibrotic therapy.

Left ventricular mass index demonstrated favorable remodeling in Group A, with a significant reduction from 106.2 ± 14.7 g/m² at baseline to 98.4 ± 12.3 g/m² at 6 months (p<0.001 for within-group change). Group B also showed a reduction in LVMI from 108.4 ± 15.2 g/m² to 104.7 ± 14.1 g/m² (p=0.008 for within-group change), but the magnitude of reduction was significantly greater in Group A (p=0.002 for between-group comparison). Similarly,

left atrial volume index decreased more substantially in Group A (−2.7 ± 1.8 mL/m²) compared to Group B (−1.3 ± 2.1 mL/m²), with a statistically significant between-group difference (p=0.042).

NT-proBNP levels, a biomarker of cardiac stress and wall tension, showed significant reduction in Group A from 186.4 ± 54.2 pg/mL to 142.3 ± 45.6 pg/mL (p<0.001 for within-group change), whereas Group B demonstrated only a modest decrease from 192.7 ± 58.9 pg/mL to 178.9 ± 52.3 pg/mL (p=0.021 for within-group change). The between-group difference in NT-proBNP reduction was highly significant (p<0.001), corroborating the echocardiographic evidence of improved cardiac function with anti-fibrotic therapy.

Subgroup analysis within Group A revealed several factors associated with greater improvement in LV-GLS (Table 4). Patients with baseline HbA1c <7.5% demonstrated significantly greater GLS improvement compared to those with HbA1c ≥7.5% (+2.7 ± 0.9% vs. +1.7 ± 1.1%; p=0.008), suggesting that better glycemic control enhances the therapeutic response to anti-fibrotic therapy. Similarly, patients with shorter duration of diabetes (<5 years) showed greater GLS improvement than those with longer duration (+2.8 ± 1.0% vs. +1.9 ± 1.1%; p=0.012), indicating that earlier intervention in the disease course yields more substantial benefits.

Younger patients (<55 years) exhibited greater GLS improvement compared to older patients (+2.6 ± 1.0% vs. +1.9 ± 1.1%; p=0.042), potentially reflecting more reversible myocardial changes and greater therapeutic responsiveness in younger individuals. Patients with lower baseline NT-proBNP levels (<150 pg/mL) showed greater GLS improvement than those with elevated NT-proBNP (+2.6 ± 1.0% vs. +1.8 ± 1.1%; p=0.034), suggesting that anti-fibrotic therapy may be more effective in earlier stages of cardiac involvement before significant myocardial stress develops.

No significant differences in GLS improvement were observed based on sex (p=0.321) or baseline LV-GLS severity (p=0.067), although there was a trend toward greater improvement in patients with more impaired baseline GLS (≤−16%). Patients concomitantly treated with SGLT2 inhibitors showed numerically greater GLS improvement (+2.8 ± 0.9% vs. +2.1 ± 1.1%), but this difference did not reach statistical significance (p=0.078), possibly due to limited sample size in this subgroup.

Statistical Analysis: Statistical analysis was performed using SPSS version 26.0 (IBM Corporation, Armonk, NY, USA) and GraphPad Prism version 9.0 (GraphPad Software, San Diego, CA, USA). Continuous variables were tested for normality using the Shapiro-Wilk test and are presented as mean ± standard deviation for normally distributed data or median (interquartile range) for non-normally distributed data. Categorical variables are expressed as frequencies and percentages. A two-tailed p-value <0.05 was considered statistically significant for all analyses. The statistical analysis plan was designed to comprehensively evaluate the efficacy of anti-fibrotic therapy on left ventricular strain patterns while accounting for potential confounding variables and identifying predictors of therapeutic response.

Discussion

Diabetic cardiomyopathy has long been recognized as a distinct myocardial disorder occurring in patients with diabetes mellitus, independent of overt coronary artery disease or significant valvular pathology. The original description by Rubler and colleagues established the concept that diabetic patients may develop a specific cardiomyopathic phenotype, and our study aligns with that foundational observation by demonstrating early myocardial dysfunction in patients with type 2 diabetes despite preserved left ventricular ejection fraction. In our cohort, the mean baseline LVEF remained normal in both groups, while LV global longitudinal strain was already impaired, reinforcing the modern understanding that diabetic cardiomyopathy is often clinically silent at the stage when strain imaging first becomes abnormal. This pattern is consistent with the contemporary literature, which emphasizes that conventional ejection fraction can remain preserved until advanced disease, whereas speckle-tracking echocardiography identifies subclinical impairment much earlier.

The mechanistic framework proposed by Jia, Hill, and Sowers supports the interpretation of our findings, because diabetic cardiomyopathy is driven by a combination of metabolic derangement, oxidative stress, inflammation, altered substrate utilization, and myocardial remodeling. Our study adds clinical support to these mechanistic models by showing that patients receiving spironolactone had significantly greater improvement in LV-GLS, E/e′ ratio, LVMI, and NT-proBNP than those receiving standard care alone. This suggests that attenuation of fibrotic signaling and neurohormonal activation may translate into measurable improvement in myocardial deformation. In contrast to purely mechanistic or experimental studies, our results provide a clinically relevant demonstration that these pathways are not only biologically plausible but also therapeutically modifiable in early-stage diabetic cardiomyopathy.

Tan and colleagues highlighted diabetic cardiomyopathy as a condition in which multiple potential therapeutic strategies may be relevant, including metabolic and anti-fibrotic approaches. Our results are concordant with this framework

because spironolactone, an anti-fibrotic and aldosterone-antagonist agent, produced favorable changes in strain and diastolic indices without any parallel increase in ejection fraction, suggesting that benefits were primarily captured at the level of subclinical myocardial mechanics. This is important because it supports the concept that a therapy may improve myocardial health before conventional systolic measures change. Compared with the broader therapeutic discussion in the review by Tan et al., our study provides direct clinical data suggesting that anti-fibrotic intervention may be particularly useful in the early phase of diabetic cardiomyopathy when myocardial remodeling is still reversible.

Frangogiannis emphasized that fibrosis is a central determinant of diabetic myocardial dysfunction and may represent both a diagnostic target and a therapeutic opportunity. Our study strongly parallels this view, because the spironolactone-treated group demonstrated reductions in LVMI, LAVI, and NT-proBNP, all of which are compatible with decreased myocardial and chamber-level remodeling. The improvement in LV-GLS further supports the likelihood that reduced interstitial fibrosis or fibrosis-related stiffness contributed to better myocardial performance. In the untreated group, changes were modest, which suggests that standard glycemic care alone may be insufficient to alter the fibrotic trajectory once cardiomyopathic changes are established. Thus, our findings are consistent with the fibrosis-centered model of diabetic cardiomyopathy and provide practical evidence that anti-fibrotic therapy may have meaningful functional effects.

Travers and colleagues described diabetic cardiomyopathy as a multifactorial syndrome involving metabolic, structural, and functional disturbances. Our observations fit this broad pathophysiologic concept because the studied patients had preserved LVEF but abnormal strain, elevated filling pressures, and increased NT-proBNP, all of which reflect early but definite myocardial involvement. The magnitude of improvement seen with spironolactone suggests that targeting one component of the syndrome, namely aldosterone-mediated fibrosis and remodeling, may still yield appreciable benefit even though the disease is multifactorial. Compared with the earlier review perspective, our study provides a more focused clinical signal by linking anti-fibrotic therapy to contemporary echocardiographic endpoints. This is clinically relevant because it supports a strategy of phenotype-guided treatment rather than waiting for overt systolic failure.

Marwick and colleagues emphasized that recognizing diabetic cardiomyopathy requires attention to underlying mechanisms and careful use of sensitive imaging tools. Our study is highly consistent with that recommendation because LV-GLS detected myocardial dysfunction when LVEF remained within normal limits. The improvement in GLS in the spironolactone group, compared with minimal change in controls, indicates that speckle-tracking echocardiography is not just diagnostic but also useful for monitoring therapeutic response. In this regard, our results support the role of echocardiography as both a detection and follow-up tool in diabetic cardiomyopathy. They also show that changes in LV-GLS may precede changes in conventional indices, a point that is strongly emphasized in modern management discussions.

Pabello, Singh, and Kumar reviewed anti-fibrotic therapies in diabetic cardiomyopathy and noted that the evidence base remains limited but promising. Our study adds to that evidence by demonstrating significant improvement in strain and diastolic function after 6 months of spironolactone. The direction of benefit is in line with their therapeutic expectations, but our data are particularly valuable because they focus on patients with early-stage disease rather than advanced heart failure. This distinction matters because anti-fibrotic treatment is likely to be more effective before irreversible remodeling becomes dominant. Relative to the review literature, our results offer a clinically measurable signal supporting the early use of anti-fibrotic therapy in selected diabetic patients.

Krumm and Williams focused on hypertension management in patients with diabetes and diabetic kidney disease, highlighting the importance of neurohormonal and blood pressure-related strategies in cardiorenal disease. Although our study was not designed as a hypertension trial, the benefits seen with spironolactone are consistent with the broader principle that aldosterone blockade can improve cardiac remodeling in high-risk metabolic patients. Our findings extend this concept from cardiorenal management to diabetic myocardial disease, where structural improvement occurred despite preserved systolic function. This comparison is important because it suggests that the advantages of mineralocorticoid receptor antagonism may extend beyond blood pressure control and heart failure to early diabetic cardiomyopathy as well. In that sense, our work bridges cardiorenal and cardiomyopathic therapeutic logic.

The landmark trial by Pitt and colleagues established spironolactone as a life-prolonging therapy in severe heart failure, providing major evidence for aldosterone antagonism in advanced cardiac disease. Our study differs in disease stage, endpoint, and population, but it is directionally consistent with that broader therapeutic principle. Whereas Pitt et al. showed benefit in severe heart failure outcomes, our study demonstrates benefit in early diabetic myocardial dysfunction, particularly at the level of strain and diastolic function. This comparison is

important because it suggests that aldosterone blockade may have value across the disease spectrum, not only in late-stage symptomatic failure. Our findings therefore support the extension of spironolactone use into earlier, pre-failure phases of diabetic cardiac remodeling, provided safety monitoring is maintained.

Kosmala and colleagues reported that myocardial fibrosis carries prognostic significance in patients with type 2 diabetes and preserved ejection fraction. Our results are consistent with this prognostic perspective because the patients with higher baseline NT-proBNP and worse strain showed less improvement, whereas those with earlier disease markers appeared more responsive to treatment. The observed reductions in LVMI and NT-proBNP in our spironolactone group suggest that the therapy may have favorably influenced the fibrotic and hemodynamic burden linked to prognosis. Compared with Kosmala's emphasis on the association between fibrosis and outcome, our study adds evidence that fibrosis-targeted treatment may actually modify surrogate markers of that risk. This makes the findings clinically meaningful, especially for patients whose disease has not yet progressed to irreversible remodeling.

Ernande and Derumeaux highlighted echocardiography as central to the evaluation of diabetic cardiomyopathy. Our study directly supports that view by using comprehensive transthoracic echocardiography and speckle-tracking strain analysis to detect and monitor early myocardial impairment. The significant improvement in LV-GLS, E/e′ ratio, and LAVI in the treated group indicates that echocardiographic parameters are sensitive enough to capture treatment-related changes over a relatively short period. Compared with conventional echocardiographic follow-up alone, our approach offers a more nuanced picture of myocardial recovery. This comparison underscores the practical value of advanced echocardiography in both diagnosis and therapeutic assessment.

Muraru and Vinereanu reported in their systematic review that LV-GLS is a sensitive marker of subclinical dysfunction in diabetic patients. Our baseline data are in agreement with that conclusion because strain was already abnormal despite preserved ejection fraction. More importantly, our post-treatment findings extend the review's message by showing that GLS is not only a diagnostic marker but also a responsive therapeutic endpoint. The greater improvement in the spironolactone group suggests that strain imaging can detect early myocardial recovery that would be missed by ejection fraction alone. In this sense, our study moves beyond observational association and demonstrates how GLS can be applied in routine clinical research and longitudinal monitoring.

The randomized trial by Tadic and colleagues examining spironolactone in type 2 diabetes is particularly relevant to our work because it also investigated mineralocorticoid receptor blockade and left ventricular function. Our results are broadly concordant with theirs in that spironolactone was associated with improved myocardial performance, but we extend the evidence by focusing specifically on early diabetic cardiomyopathy and using GLS as a primary endpoint. This endpoint is more sensitive than conventional systolic measures and may capture benefit at an earlier stage. Compared with that trial, our study reinforces the notion that spironolactone has potential cardioprotective effects in diabetes, especially when myocardial dysfunction is still subtle and potentially reversible.

Wong and Gheorghiade discussed aldosterone antagonism as a bridge from pathophysiology to clinical practice in heart failure. Our study mirrors that translational theme by taking the theoretical anti-fibrotic rationale of spironolactone and applying it to a diabetic cardiomyopathy cohort. The favorable changes in LV-GLS and diastolic indices demonstrate that the biological promise of aldosterone antagonism may be realized in a phenotype beyond overt heart failure. This comparison is useful because it shows how principles established in heart failure can inform therapy in metabolic cardiomyopathy. Our data therefore support a more proactive use of mineralocorticoid receptor antagonists in selected diabetic patients with evidence of early myocardial remodeling.

Zile, Baicu, and Ikonomidis emphasized the relationship between endocardial stiffness, myocardial fibrosis, and diastolic dysfunction. Our findings closely match this concept because the spironolactone group experienced significant improvement in E/e′ ratio, LVMI, and LAVI, all of which are linked to reduced stiffness and improved filling dynamics. The absence of a meaningful change in LVEF further supports the idea that the primary effect was on diastolic and structural properties rather than systolic pump function. Compared with their mechanistic framing, our study offers clinical corroboration that modifying the fibrotic environment may improve function even when ejection fraction is preserved. This supports the importance of focusing on diastolic disease biology in diabetic patients.

Shah, Maurer, and Burkhoff discussed the diagnostic and therapeutic implications of myocardial fibrosis in diabetic cardiomyopathy. Our study complements their perspective by showing that an anti-fibrotic agent can improve multiple surrogate markers consistent with reduced fibrotic load. The reduction in NT-proBNP and LVMI in particular suggests beneficial remodeling, while the better GLS response in patients with shorter diabetes

duration indicates that earlier intervention yields greater gains. Compared with the review literature, our data provide a pragmatic clinical example of fibrosis-targeted treatment in a real-world diabetic cohort. This strengthens the argument that fibrosis is not merely a descriptive pathology but a modifiable therapeutic target.

Patel and colleagues reviewed the current status of speckle-tracking echocardiography in diabetic cardiomyopathy and projected an expanding role for this technique in future practice. Our study directly illustrates that future role because strain imaging was the principal endpoint that captured treatment response. The superiority of GLS over LVEF in detecting improvement after spironolactone supports the idea that speckle-tracking should be incorporated into both research and clinical follow-up. In comparison with older studies that relied mainly on conventional echocardiography, our work demonstrates a more refined and clinically informative assessment of myocardial health. Therefore, our findings are aligned with the evolving imaging paradigm described by Patel et al.

The American Diabetes Association standards emphasize comprehensive risk reduction, including glycemic control and management of cardiovascular risk in patients with diabetes. Our results are consistent with this framework, but they also suggest that standard metabolic control alone may not fully address diabetic myocardial disease. The modest change in HbA1c in both groups contrasted with the substantially greater cardiac improvement in the spironolactone arm, indicating that direct anti-fibrotic therapy may be needed in addition to routine diabetes management. This comparison is important because it highlights the gap between glycemic improvement and myocardial remodeling. Our findings therefore support a more integrated model of care that includes cardiac phenotype assessment, imaging surveillance, and targeted adjunctive therapy.

Westermann and colleagues demonstrated in experimental work that deletion of aldosterone synthase ameliorated diabetic cardiomyopathy in mice, providing strong mechanistic support for aldosterone pathway inhibition. Our clinical findings are highly concordant with that preclinical evidence, because spironolactone produced favorable effects on strain, diastolic function, and remodeling markers in human subjects. The consistency between animal and clinical data strengthens the biological credibility of our results and suggests that aldosterone-driven fibrosis is an actionable pathway in diabetic heart disease. When viewed alongside the broader literature, our study indicates that early anti-fibrotic intervention may translate mechanistic promise into patient-level benefit. This supports future randomized trials to determine the best timing, dose, and duration of therapy.

Taken together, the present study adds to the literature by linking established concepts of diabetic cardiomyopathy with modern imaging and targeted anti-fibrotic therapy. In comparison with the cited references, our key contribution is the demonstration that spironolactone improves LV-GLS, diastolic indices, LVMI, and NT-proBNP in early-stage diabetic cardiomyopathy without altering ejection fraction. This pattern is consistent with the mechanistic, imaging, and therapeutic themes reported across the literature, but it also provides direct comparative clinical evidence from our own cohort. The study therefore supports a practical approach in which diabetic cardiomyopathy is detected early with strain imaging and treated before irreversible fibrosis becomes dominant. Larger prospective randomized studies are still needed, but our findings suggest that anti-fibrotic therapy deserves serious consideration in carefully selected patients.

Conclusion

In conclusion, this study demonstrates that anti-fibrotic therapy with spironolactone significantly improves left ventricular strain patterns and diastolic function in patients with early-stage diabetic cardiomyopathy. These findings support the integration of anti-fibrotic strategies into comprehensive management of diabetic cardiovascular complications and provide a foundation for future prospective investigations in this important clinical area.

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