The Egyptian Journal of Hospital Medicine (July 2025) Vol. 100, Page 3300-3307

Effect of Sodium Glucose Cotransporter 2 Inhibitor on Left Ventricular Mechanics in Heart Failure Patients with Preserved Ejection Fraction (Speckle Tracking Imaging Study)

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ABSTRACT

Background: Heart failure with preserved ejection fraction **(**HFPEF) is a common form of heart failure with limited treatment options. Sodium glucose cotransporter 2 **(**SGLT2) inhibitors have shown cardiovascular benefits, but their impact on left ventricular function in HFPEF remains unclear. Speckle tracking imaging may clarify their effects on myocardial mechanics.

Objective*:* This study aimed to evaluate the impact of SGLT 2 inhibitors on left ventricular (LV) mechanics in heart failure (HF) patients with preserved ejection fraction (EF), as assessed via 2D speckle tracking echocardiography.

Methods: 40 patients above the age of 18 years with symptoms and signs of HF with left ventricular EF (LVEF) ≥50% (HFPEF) were involved in prospective cohort observational analytical research at The Department of Cardiology, Menoufia University Hospital's Echocardiography Clinic, through the period from July 2024 to March 2025. There were 2 subgroups divided into 24 patients with sinus rhythm and 16 patients with atrial fibrillation. They were subjected to history taking, clinical examination, and 12-lead ECG, complete 2D conventional echo (including M-mode and Doppler) and 2D speckle tracking. Strain (circumferential, longitudinal, and radial) was activated by using at least three cardiac cycles captured in cine format in the form of apical 4, 3, and 2 chamber views, as well as short-axis views at the mitral valve and papillary muscle levels. Echo examination was done before initiation of sodium-glucose co-transporter-2 inhibitors and after 2 months of drug adherence.

Results: Improvement of symptomatology as detected by improvement of New York Heart Association (NYHA) class, heart rate, control of AF, correction of diastolic dysfunction, improvement of conventional echocardiographic parameters, and speckle tracking-derived indices.

Conclusion: Improved left ventricular mechanics in the form of improvement of diastolic function and speckle tracking parameters such as global longitudinal, radial, and circumferential strain, and it is reflected as improvement of NYHA class.

Keywords: Cardiovascular outcomes, Ejection fraction, Heart failure, Ventricular mechanics, Speckle tracking.

INTRODUCTION

Heart failure with preserved ejection fraction (HF-PEF) is a complex syndrome distinguished by heart failure symptoms and signs such as dyspnea, orthopnea, lower limb edema, bilateral fine basal lung crackles, S3 gallop, and reduced exercise capacity and a normal or near-normal left ventricular ejection fraction equal to or more than 50% **(1).**

Treatment of risk factors, such as hypertension, can effectively prevent HF-PEF; however, there are no particular therapies available after HF-PEF has occurred. **(2)** Regardless of diabetes status, sodium glucose cotransporter 2 inhibitors (SGLT2I) have been illustrated to enhance health status in cases with HF with preserved ejection fraction and lower the possibility of cardiovascular (CV) death or deteriorating HF by targeting cardiometabolic conditions through a variety of mechanisms (3). Because echocardiography is feasible, accessible, low cost, and lacks ionizing radiation, it is the main imaging modality used to assess cardiac disease **(4).**

Speckle tracking echocardiography (STE) has strong inter-observer and intra-observer repeatability and high temporal and spatial resolution, making it a valuable echocardiographic tool for assessing myocardial function. The benefit of being unaffected by the heart's translational movement and independent of insolation angle **(5)**. Alterations in the left ventricle size and shape caused by concurrent longitudinal shortening, circumferential rotation, and radial thickening of the myocardium are determined by myocardial fiber contraction **(6)**.

So, the goal of the research was to assess the impact of sodium-glucose cotransporter 2 inhibitors on left ventricular mechanics in heart failure cases with preserved ejection fraction, as assessed by 2D speckle tracking echocardiography.

PATIENTS AND METHODS

Study design and setting: A group of 40 patients above the age of 18 years with signs and symptoms of HF with left ventricular EF ≥ 50% (HFPEF) and proof of diastolic dysfunction as the reason for symptoms, such as abnormal left ventricle filling, raised filling pressures, left ventricular hypertrophy, and pulmonary hypertension, were enrolled in the study. This was a prospective cohort observational analytical study at The Department of Cardiology, Menoufia University Hospital's Echocardiography Clinic through the period from July 2024 to March 2025. Patient selection was based on the American Society of Cardiology guidelines for HFpEF diagnosis and H2FPEF score **[7].**

Received: 13/03/2025
Accepted: 13/05/2025

There were 2 subgroups divided into 24 patients with sinus rhythm and 16 patients with atrial fibrillation. Complete history taking, clinical examination, and 12-lead ECG were done, and then they underwent complete 2D conventional echo, including M-mode and pulsed wave, continuous wave, and tissue Doppler imaging. Also, 2D speckle tracking Strain (circumferential, longitudinal, and radial) was activated by using at least three cardiac cycles that were captured in cine loop format in the form of apical 4, 3, and 2 chamber views, as well as short-axis views at the mitral valve and papillary muscle levels. Echo examination was done before initiation of sodium glucose co-transporter-2 inhibitors and after 2 months of drug adherence.

Exclusion criteria: Patients who had congenital heart disease, cardiomyopathy, pericardial diseases, patients with poor echogenic window, severe renal impairment (creatinine clearance < 30 ml/min/1.73 m²), severe liver impairment, and patients who weren't adherent to the prescribed medication.

Laboratory investigations: Serum creatinine analysis and eGFR before starting medication.

12-*lead surface electrocardiography* was done for assessment of heart rhythm, presence of arrhythmia, ischemic changes, bundle branch block, & evidence of chamber enlargement.

***2D* transthoracic echocardiography** was performed using Vivid S5 and Vivid 9, General Electric Healthcare (GE Vingmed, Norway), equipped with a harmonic M5S variable-frequency (1.7-4 megahertz) phased-array transducer with the patient supine or in the left lateral position and connected to a single-lead ECG. All necessary conventional echocardiographic data were collected from apical and parasternal views using 2D, M-mode, tissue Doppler imaging and color pulsed, and continuous wave Doppler. Cardiac chamber size and function have been evaluated in line with the American Society of Echocardiography Guidelines [(7)]. At least three cardiac cycles were captured in cine format for apical 4, 3, and 2 chamber views, as well as short-axis views at the mitral valve and papillary muscle levels. The frame rate ranged from 70 to 80% of the patient's heart rate (frames per second), and all images were digitally stored for later offline analysis.

2D echocardiography mode was used for assessment of cardiac chamber size and function, assessment of mitral, tricuspid, pulmonary and aortic valves morphology and assessment of wall motion abnormalities. M-Mode Echocardiography**:** In the parasternal long-axis view to asses left ventricular dimensions (ventricular septal thickness, LV end-diastolic and end systolic internal diameter, posterior wall thickness, ejection fraction, and fractional shortening), as well as aortic root diameter and left atrial diameter.

And in apical 4-chamber view to measure tricuspid annular plane systolic excursion (TAPSE), and mitral annular plane systolic excursion (MAPSE), tissue Doppler imaging, two-dimensional speckle tracking echocardiography (2D STE), LV circumferential strain and LV radial strain.

Ethical consideration: The drug used in the study is confirmed by Faculty of Medicine, Menoufia University. The Ethics Committee of Department of Cardiology permitted the protocol of the research. Before enrollment, written informed permissions were obtained from individuals or their legal representatives in accordance with the individual's conditions. This research aimed to conduct research on humans in compliance with the Declaration of Helsinki, the ethical norm established by the World Medical Association.

Statistical analysis

Using Microsoft Excel 2019 and SPSS v. 25 (SPSS Inc., Chicago, IL, New York, US) on a personal computer, the results were tabulated and statistically evaluated. The descriptive statistics included mean, median, and standard deviation (SD). P values ≤ 0.05 was deemed as statistically significant.

RESULTS

In the current study, statistically significant results in NYHA classes in all patients before and after treatment and improvement of the heart rate after treatment, which was more statistically significant in AF group of patients. 2D conventional and speckle-tracking echocardiographic measurements showed improvement in patients **with sinus rhythm** but no statistically significant differences before and after treatment (p > 0.05). While in **AF group**, EPASP, E/e`, GLS, Radial strain and segmental walls significantly improved after treatment in AF patients, with p value less than 0.05. The other 2D and speckle-tracking echocardiography findings in cases with AF showed non-significant improvement after treatment (p-value above 0.05) (Tables 1 & 2).

Table (1): 2 D conventional and LV strain parameters in patients with sinus rhythm

	Patients with sinus rhythm		**Paired t *test***	***P value***
	Before	**After**		
	Mean± SD	**Mean± SD**		
NYHA class				
NYHA 1	8 (33.33%)	16(66.66%)	2.98	**0.013***
NYHA 2	8 (33.33%)	5 (20.83%)	1.9	**0.047***
NYHA 3	6 (25%)	2 (8.33%)	FE 3.07	**0.001***
NYHA 4	2 (8.33%)	1 (4.16%)	FE 2.88	**0.033***
HR	74.41±4.43	69.22±3.93	1.05	0.0921
2 D conventional and LV strain				
LVEDD (cm)	4.85±0.48	4.56±0.63	0.48	0.73
LVESD (cm)	3.11±0.30	3.00±0.46	1.25	0.22
IVSD (cm)	1.28±0.29	1.24±0.11	1.45	0.14
LVPWD (cm)	1.14±0.20	1.15±0.13	0.18	0.86
FS %	33.96±8.83	34.00±4.26	0.02	0.98
EF %	62.71±14.51	63.13±5.61	0.14	0.89
LA (cm)	3.18±1.80	3.13±0.55	0.63	0.51
AO (cm)	2.87±0.76	2.95±0.28	1.48	0.251
TAPSE (cm)	2.16±0.33	2.11±0.30	0.66	0.52
MAPSE (cm)	1.75±0.11	1.79±0.22	0.66	0.52
EPASP (mm Hg)	33.64±8.18	33.62±5.79	0.01	0.99
E/e`	11.20±2.46	11.16±3.01	0.13	0.90
E/A	0.92±0.37	0.90±0.40	0.19	0.85
Septal wall	19.03±4.72	19.61±4.02	0.47	0.64
Lateral wall	19.77±6.91	20.09±6.03	0.25	0.80
Apical 4 Average	19.40±4.75	19.85±4.17	0.14	0.89
Inferior wall	23.38±5.12	23.46±6.00	0.28	0.79
Anterior wall	24.30±6.87	24.60±6.46	1.44	0.16
Apical 2 chamber average	23.34±5.14	24.03±14.69	1.19	0.25
Posterior wall	26.32±6.74	28.10±7.12	1.44	0.16
Anteroseptal wall	21.55±6.20	23.75±5.43	1.02	0.071
Apical 3 chamber average	24.93±5.87	25.92±5.85	0.17	0.89
GLS	22.55±1.61	23.26±1.71	0.11	0.093
Circumferential strain	20.18±3.96	23.93±5.75	2.8	0.056
Radial strain	35.77±4.09	38.95±5.63	0.38	0.067

AF: Atrial Fibrillation, **LVEDD:** Left ventricular End Diastolic Diameter, **IVSD:** Inter Ventricular Septal Diameter, **LVESD:** Left Ventricular End Systolic Diameter, **FS:** Fractional Shortening, **LVPWD:** Left Ventricular Posterior Wall Diameter, **EF:** Ejection Fraction, **LA:** Left Atrium, **AO:** Aorta, **T:** Student T test, **TAPSE:** Tricuspid Annulus Plane Systolic Excursion, **MAPSE:** Mitral Annulus Plane Systolic Excursion, **EPASP:** Estimated Pulmonary Artery Systolic Pressure, **GLS:** Global Longitudinal Strain, **cm:** Centimeters, **mmHg:** Millimetre mercury, **P value:** Probability value, **SD:** Standard deviation**.**

Table (2): 2 D conventional and LV strain parameters in AF patients

	AF patients		**Paired t *test***	***P value***
	Before	**After**		
	Mean± SD	**Mean± SD**		
NYHA class				
NYHA 1	3 (18.75%)	6 (37.5%)	FE 4.11	**0.002***
NYHA 2	3 (18.75%)	5 (31.25%)	FE 2.89	**0.003***
NYHA 3	8 (50%)	5 (31.25%)	1.16	0.053
NYHA 4	2 (12.5%)	0 (0%)	FE 3.57	**0.001***
HR	90.35±7.54	68.28±5.48	5.20	**0.001***
2 D conventional and LV strain				
LVEDD (cm)	4.69±0.68	4.86±0.65	0.792	0.441
LVESD (cm)	3.08±0.44	3.26±0.53	1.113	0.283
IVSD (cm)	1.23±0.27	1.20±0.52	0.985	0.207
LVPWD (cm)	1.28±0.14	1.18±0.14	1.967	0.76
FS (%)	33.94±5.45	33.94±5.76	0.000	1.000
EF (%)	62.56±7.08	62.19±7.56	0.140	0.891
LA (cm)	4.70±0.82	4.59±0.84	0.808	0.432
AO (cm)	2.89±0.29	2.94±0.35	0.604	0.555
TAPSE (cm)	1.77±0.32	1.87±0.25	0.988	0.339
MAPSE (cm)	1.64±0.20	1.69±0.15	0.271	0.790
EPASP (mm Hg)	40.86±10.73	35.75±5.26	2.038	**0.040***
E/e`	13.87±3.91	11.71±2.73	2.755	**0.046***
Septal wall	18.92±8.19	19.29±4.49	2.362	0.072
Lateral wall	17.60±6.39	18.72±4.92	3.482	0.**037***
Apical 4 chamber average	18.26±7.05	19.18±4.25	2.489	0.**043***
Inferior wall	18.90±6.77	20.06±6.12	2.259	0.**041***
Anterior wall	19.11±6.48	20.41±6.13	2.409	0.**039***
Apical 2 chamber average	19.08±6.07	20.93±5.30	3.320	0.**035***
Posterior wall	17.84±7.51	18.67±6.28	2.655	0.**046***
Anteroseptal wall	15.62±6.05	16.46±5.50	2.030	0.**041***
Apical 3 chamber average	16.33±6.58	17.96±5.71	2.722	**0.040***
GLS	17.47±2.59	19.95±4.09	2.620	**0.040***
Circumferential strain	21.77±5.80	22.67±3.32	0.074	0.150
Radial strain	36.78±4.21	39.33±5.25	2.31	**0.042***

AO: Aorta, **T:** Student T test, **MAPSE:** Mitral Annulus Plane Systolic Excursion, **TAPSE:** Tricuspid Annulus Plane Systolic Excursion, **EPASP:** Estimated Pulmonary Artery Systolic Pressure, **GLS:** Global Longitudinal Strain.

Also before treatment, significant difference of NYHA class has been observed between both groups of the study and H2FPEF score was greater in AF cases compared to sinus cases, which was statistically significant (P-value equal 0.039). There was an insignificant variance regarding demographic data like gender, age, smoking, HTN, DM, BMI (Kg/m^2), among cases with sinus rhythm and AF patients (p-value above 0.05) **(Table 3).**

Table (3): Comparative analysis between NYHA class and H2FPEF score before treatment

	Sinus patients (n=24) (%)		**AF patients** (n=16) (%)		**FE**	
NYHA 1	8 (33.33%)		3 (18.75%)		2.25	**0.017***
NYHA 2	8 (33.33%)		3 (18.75%)		2.25	**0.017***
NYHA 3	6 (25%)		8 (50%)		X^2= 2.99	**0.015***
NYHA 4	2 (8.33%)		2 (12.5%)		FE= 7.75	0.38
H2FPEF score	4.46+-1.12		5.82+-0.97		Z=11.53	**0.039***
Age (years)	63.00±5.85		64.38±6.18		**t**=0.704	0.487
BMI (Kg/m^2)	30.28±5.93		28.18±4.77		**t**=1.184	0.247
Gender						
Male	4	16.7	5	31.3	X^2=	^{FE}P=0.279
Female	20	83.3	11	68.8	1.171	
Smoking	2	8.3	3	18.8	0.952	0.329
HTN	19	79.2	13	81.3	X^2=0.026	0.872
DM	10	41.7	6	37.5	X^2=0.069	0.792

FE: Fisher Exact test, **X^2:** Chi-square test**,** **Z:** Mann Whitney U test, *****Significant.

In addition, before treatment, significant variances have been observed among case with sinus rhythm and AF patients regarding conventional and strain echo parameters in terms of TAPSE, GLS and segmental walls as they were significantly greater in cases with sinus rhythm before treatment, but EPASP was significantly greater in AF cases before treatment (p-value under 0.05). Although, insignificant variances have been observed between patients with sinus rhythm and AF patients in other 2D conventional and speckle tracking echocardiographic indices. (P-value abovec 0.05) **(Table 4).**

Table (4): Comparison between AF patients and cases with sinus rhythm regarding conventional echocardiographic data and LV strain parameters before treatment

Before treatment	**Groups**		**U**	***P value***
	AF patients (n=16)	**Patients with sinus rhythm(n=24)**		
	Mean ± SD.	**Mean ± SD.**		
LVEDD (cm)	4.69±0.68	4.85±0.48	149.000	0.234
LVESD (cm)	3.08±0.44	3.11±0.30	182.000	0.781
IVSD (cm)	1.23±0.27	1.28±0.29	188.500	0.922
LVPWD (cm)	1.28±0.14	1.14±0.20	140.000	0.140
FS (%)	33.94±5.45	33.96±8.83	154.500	0.299
EF (%)	62.56±7.08	62.71±14.51	152.500	0.275
LA (cm)	4.70±0.82	3.18±1.80	123.500	0.058
AO (cm)	2.89±0.29	2.87±0.76	139.500	0.145
TAPSE (cm)	1.77±0.32	2.16±0.33	176.000	**0.001***
MAPSE (cm)	1.64±0.20	1.75±0.11	163.000	0.409
EPASP (mm Hg)	40.86±10.73	33.64±8.18	95.000	**0.007***
E/e	13.87±3.91	11.20±2.46	180.000	0.740
Septal wall	18.92±8.19	19.03±4.72	155.000	0.307
Lateral wall	17.60±6.39	19.77±6.91	177.500	0.689
Apical 4 Average	18.26±7.05	19.40±4.75	157.000	0.879
Inferior wall	18.90±6.77	23.38±5.12	190.530	**0.037***
Anterior wall	19.11±6.48	24.30±6.87	180.500	**0.039***
Apical 2 chamber average	19.08±6.07	23.34±5.14	122.500	**0.040***
Posterior wall	17.84±7.51	26.32±6.74	227.000	**0.002***
Anteroseptal wall	15.62±6.05	23.55±6.20	263.000	**0.023***
Apical 3 chamber average	16.33±6.58	24.93±5.87	236.000	**0.012***
GLS	17.47±2.59	22.55±1.61	251.000	**0.008***
Circumferential strain	21.77±5.80	23.18±3.96	169.000	0.525
Radial strain	36.78±4.21	37.77±4.09	147.000	0.214

Also, after treatment, significant variances have been observed among cases with sinus rhythm and AF cases in 2D conventional echocardiographic parameters as TAPSE, segmental walls and GLS were significantly greater in patients with sinus rhythm, but LA was significantly higher in AF cases after treatment ($P < 0.05$). Insignificant variances have been found among cases with sinus rhythm and AF cases in other conventional or speckle tracking echocardiographic data after treatment ($P > 0.05$) **(Table 5).**

Table (5): Comparative analysis between AF patients & patients with sinus rhythm regarding conventional echocardiographic data and LV strain parameters after treatment

After treatment	Groups		U	*P value*
	AF patients (n=16)	Patients with Sinus rhythm (n=24)		
	Mean ± SD	Mean ± SD		
LVEDD (cm)	4.86±0.65	4.56±0.63	144.500	0.189
LVESD (cm)	3.26±0.53	3.00±0.46	135.500	0.118
IVSD (cm)	1.20±0.52	1.24±0.11	184.000	0.818
LVPWD (cm)	1.18±0.14	1.15±0.13	174.000	0.607
FS (%)	33.94±5.76	34.00±4.26	177.500	0.688
EF (%)	62.19±7.56	63.13±5.61	167.000	0.489
LA (cm)	4.59±0.84	3.13±0.55	57.000	**<0.001***
AO (cm)	2.94±0.35	2.95±0.28	184.000	0.824
TAPSE (cm)	1.87±0.25	2.11±0.30	109.500	**0.022***
MAPSE (cm)	1.69±0.15	1.79±0.22	149.000	0.227
EPASP (mm Hg)	35.75±5.26	33.62±5.79	158.000	0.347
E/e`	11.71±2.73	11.16±3.01	189.000	0.671
Septal wall	19.29±4.49	19.61±4.02	172.03	0.802
Lateral wall	18.72±4.92	20.09±6.03	78.54	0.930
Apical 4 Average	19.18±4.25	19.85±4.17	110.02	0.544
Inferior wall	20.06±6.12	23.46±6.00	127.000	0.073
Anterior wall	20.41±6.13	24.60±6.46	163.000	0.423
Apical 2 chamber average	20.93±5.30	24.03±14.69	136.000	0.122
Posterior wall	18.67±6.28	28.10±7.12	250.06	**0.004***
Anteroseptal wall	16.46±5.50	23.75±5.43	173.500	**0.020***
Apical 3 chamber average	17.96±5.71	25.92±5.85	186.500	**0.012***
GLS	19.95±4.09	23.26±1.71	168.000	**0.036***
Circumferential strain	22.67±3.32	23.93±5.75	175.000	0.639
Radial strain	39.33±5.25	38.95±5.63	126.500	0.071

DISCUSSION

The main findings of this paper were improvement of symptomatology as detected by improvement of NYHA class, heart rate, control of AF, and correction of diastolic dysfunction. In addition, improvement of conventional echocardiographic parameters and speckle tracking-derived indices. In this context, recent research by **El-Saied *et al.*** [8] in 2024 found that the addition of SGLT2 inhibitors to standard anti-diabetic therapy in HFpEF was associated with less progression of presenting symptoms, no hospitalizations, and better control of HbA1c, in spite of greater baseline levels.

Also, **Solomon *et al.*** [9] in the DELIVER trial that focused on patients with HFpEF. Participants were categorized based on NYHA class at baseline: approximately 80.5% were class II, 19.4% class III, and 0.1% class IV. Dapagliflozin treatment led to significant improvements in NYHA class over time. By week 32, 18.7% of patients on dapagliflozin experienced enhancement in NYHA class compared to 14.5% on placebo. Additionally, cases treated with dapagliflozin were more probable to achieve NYHA class I status at thirty-two weeks. Additionally, **Cannon *et al.*** [10], in the Evaluation of Ertugliflozin Efficacy and Safety Cardiovascular Outcomes (VERTIS-CV) trial, demonstrated that ertugliflozin improved heart failure outcomes, particularly with respect to hospitalization for heart failure.

The study stated a 30% reduction in both first and total hospitalizations for heart failure. This benefit was consistent across the entire spectrum of ejection fraction, including both reduced and preserved ejection fractions. Improved symptomatology and functional class of our patients may be due to the added benefit of controlled heart rate using SGLT-2I beside other heart rate controlling agents and better control of blood pressure. This improvement maybe attributed to the following: Improvement of conventional echocardiographic indices, reduction of heart rate, more control of blood pressure and reduction of oxidative stress through enhanced mitochondrial function,

metabolic efficiency, anti-inflammatory effects and improved endothelial and ionic homeostasis.

Our study revealed a reduction in heart rate among all patients who received SGLT2 inhibitors in addition to their standard heart rate-controlling therapy. Notably, this heart rate–lowering effect was more evident in cases with atrial fibrillation. In this regard, **Sano** [(11)] demonstrated that SGLT2 inhibitors significantly reduced heart rate in cases with elevated baseline heart rates (≥70 bpm) following 12 weeks of luseogliflozin therapy. Similarly, **Storgaard *et al.*** [(12)] reported a significant decrease in heart rate with the addition of SGLT2 inhibitors and suggested that the underlying mechanism may involve suppression of cardiac sympathetic activity and/or enhancement of parasympathetic tone. In this regard, **Lau *et al.*** [(13)] reported in their 2022 study that SGLT2 inhibitors were associated with a 37% decrease in the possibility of atrial fibrillation in comparison with placebo. The antiarrhythmic effects of SGLT2 inhibitors seem to extend beyond their glucose-lowering properties. **Matsubayashi *et al.*** [(14)] further observed that treatment with the SGLT2 inhibitor tofogliflozin significantly normalized the circadian rhythm of blood pressure. Notably, tofogliflozin reduced nocturnal blood pressure and restored the physiological nighttime dip, which is often blunted in patients with diabetes and hypertension. Regarding heart rate, SGLT2 inhibitors (SGLT2i) were found to lower blood pressure without eliciting a compensatory increase in heart rate, an effect that may contribute to their favorable cardiovascular outcomes in high-risk T2DM populations. However, the study did not specify whether the participants were in atrial fibrillation or sinus rhythm. A study published in the European Heart Journal suggests that patients with AF may experience greater benefits from SGLT2i compared to those with sinus rhythm. This is due to the ability of SGLT2i to reduce the possibility of cardiovascular events, including hospitalization for heart failure and cardiovascular death. The potential reasons for this greater benefit in patients with AF include increased oxidative stress and inflammation. SGLT2i possesses anti-inflammatory and antioxidant properties that may help alleviate these effects. Additionally, patients with AF may experience more pronounced glycosuria-induced natriuresis, which could lead to greater reductions in blood pressure and fluid overload [(15)].

Our study showed that patients with sinus rhythm showed improvement in conventional indices, left ventricular (LV) dimensions, and LV diastolic function as proven by E/e’ and E/A ratios before and after treatment, but this was not statistically significant. In contrast, in cases with atrial fibrillation (AF), several conventional echocardiographic indices, such as EPASP and E/e', showed notable and significant improvements. In line with our results, **Tanaka *et al.*** [(16)] investigated the effect of adding dapagliflozin to standard anti-diabetic treatment in diabetic cases with various types of chronic stable HF. The study specifically excluded cases with atrial fibrillation (AF) and focused on those in sinus rhythm. It found a significant enhancement in the E/e′ ratio, from 9.3 (7.7–11.8) to 8.5 (6.6–10.7). The study included patients across all heart failure categories, though the majority were classified as HFpEF (69%). Additionally, **Thiele *et al.*** [(17)] conducted a recent study in 2023, enrolling 44 diabetic patients with sinus rhythm who received 10 mg of empagliflozin for 3 months. The study demonstrated a significant enhancement in the E/e′ ratio, which has been observed from the 1st day of therapy and sustained throughout the research period. Though they measured diastolic filling pressures, participants were a general diabetic cohort rather than a diagnosed HFpEF group. In contrast, **Roy *et al.*** [(18)] investigated the effect of SGLT-2 inhibitors in HFpEF cases with T2DM but did not observe improvements in conventional indices of diastolic function.

Our study demonstrated a significant improvement in 2D speckle tracking-derived indices, including global longitudinal and radial strains, in cases with atrial fibrillation. However, there was improvement in patients with sinus rhythm, but this was not statistically significant. Our results were in line with research by **El-Saied *et al.*** [(8)], which found a significant enhancement in speckle tracking echocardiographic parameters, involving LV-GLS, from baseline to six-month follow-up in SGLT-2 inhibitor users when compared to non-users. Additionally, **Tanaka *et al.*** [(16)] reported an improvement in LV-GLS from 15.4 ± 3.4% to 16.8 ± 4.0% following dapagliflozin administration in heart failure cases. Nevertheless, this enhancement was more pronounced in HFpEF cases compared to non-HFpEF cases. Notably, the study had a limited representation of HFmrEF (17%), with the majority of participants having HFpEF (69%).

Also, **Santos-Gallego *et al.*** [(19)] whose study was performed on 90 HFPEF patients using empagliflozin 10 mg daily for 3 months, found that GLS improved modestly from –15.8 ± 3.4% to –17.1 ± 3.1% ($p = 0.004$). As well as **Tanaka *et al.*** [(16)], which was conducted on 58 T2DM patients with stable HF, stratified into HFrEF and HFpEF and resulted in improved GLS overall from 15.5 ± 3.5% to 16.9 ± 4.1% but in the HFpEF subgroup, GLS rose from 17.0 ± 1.9% to 18.7 ± 2.0%, whereas HFrEF patients showed no significant change. And **Soga *et al.*** [(20)] who included 60 T2DM patients with chronic HF (including HFpEF) receiving dapagliflozin 10 mg daily for 6 months demonstrated that GLS improved by ~1.4% points ($p = 0.02$).

LIMITATIONS

A small study scale with limited number of candidates. So, it is recommended that further research be done with bigger study groups in order to confirm and expand on the results of the current study, as well as to get more sufficient power to test the hypothesis and possibly reveal any insignificant associations. Due to the limited

number of RCTs available currently, there is a need for more multi-center, randomized, double-blind, placebo-controlled studies.

RECOMMENDATIONS

Further researches with larger study groups are recommended to replicate, extend the present research results and to attain more adequate power to test the hypothesis and so that some insignificant correlations may prove to be significant. Maybe, there will be more beneficial outcomes on left ventricular mechanics if patients are stick to SGLT2 inhibitors for a longer period more than 2 months.

CONCLUSION

Improved left ventricular mechanics in the form of improvement of diastolic function and speckle tracking parameters such as global longitudinal, radial and circumferential strain and it is reflected as improvement of NYHA class.

- **Consent for publication:** I certify that each author has granted permission for the work to be submitted.
- **Funding:** No fund.
- **Availability of data and material:** Available.
- **Conflicts of interest:** None.
- **Competing interests:** None.

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