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EFFECTS OF GLIFLOZIN THERAPY ON CARDIAC STRUCTURAL CHANGES

Yusupova N.A.

Andijan State Medical Institute

Abstract

Background: Sodium–glucose cotransporter-2 (SGLT2) inhibitors reduce the risk of hospitalization and mortality in patients with heart failure (HF) across the spectrum of left ventricular ejection fraction (LVEF). The mechanisms underlying these benefits remain incompletely understood, particularly with regard to cardiac remodeling.
Objective: To evaluate the effects of SGLT2 inhibitors on parameters of ventricular and atrial remodeling in patients with chronic HF, irrespective of LVEF.
Methods: This multicenter, prospective, open-label interventional study included clinically stable patients with chronic HF receiving optimized guideline-directed therapy. Cardiac structure and function were assessed at baseline and after 6 months using echocardiography, complemented by biomarker analysis.
Results: A total of 162 patients (mean age 70.5 ± 10.6 years, 64.2% male) were enrolled. Treatment with SGLT2 inhibitors was associated with significant reductions in left ventricular mass index and ventricular volumes, accompanied by improvements in LVEF and global longitudinal strain. Left atrial volumes decreased significantly, indicating favorable atrial reverse remodeling. NT-proBNP concentrations showed a progressive decline, while high-sensitivity troponin T levels remained stable.
Conclusion: In patients with chronic HF, SGLT2 inhibitor therapy promotes global reverse cardiac remodeling, including both ventricular and atrial compartments, independent of baseline LVEF.

Keywords: SGLT2 inhibitors, heart failure, cardiac remodeling, left atrium, left ventricular function

Heart failure is a progressive clinical syndrome characterized by structural and functional alterations of the myocardium that ultimately lead to impaired cardiac performance and adverse clinical outcomes[2,6]. Cardiac remodeling represents a central pathophysiological mechanism in HF progression and is traditionally evaluated through changes in left ventricular geometry and systolic function. However, increasing evidence highlights the importance of atrial remodeling, particularly of the left atrium, as an independent determinant of prognosis.SGL [1,3]T2 inhibitors were initially introduced for the management of type 2 diabetes mellitus, but large randomized trials have demonstrated their substantial benefits in reducing HF-related events regardless of diabetic status. These findings suggest that SGLT2 inhibitors exert pleiotropic cardiovascular effects that extend beyond glycemic control. Understanding their influence on cardiac remodeling may provide valuable insight into their disease-modifying potential.

Methods

This study was designed as a multicenter, single-arm, prospective interventional investigation conducted over a 6-month period. Eligible participants were adults (>18 years) with a documented diagnosis of chronic HF who were clinically stable and receiving optimized

guideline-directed medical therapy for at least 4 weeks prior to enrollment. Patients were excluded if they had received SGLT2 inhibitors within the preceding 6 months, had type 1 diabetes mellitus, recent HF decompensation, estimated glomerular filtration rate <30 mL/min/1.73 m^2, or symptomatic hypotension.Baseline clinical data encompassed a comprehensive assessment of patient characteristics, including demographic information such as age, sex, body mass index (BMI), and ethnicity. In addition, detailed documentation of comorbid conditions was performed, covering cardiovascular diseases, diabetes mellitus, hypertension, chronic kidney disease, and other relevant systemic disorders. Functional status was evaluated using the New York Heart Association (NYHA) classification, providing insight into the severity of heart failure symptoms, while a thorough review of prior heart failure–related hospitalizations offered context on disease burden and healthcare utilization[2,5].

Biomarker analysis was conducted to monitor cardiac stress and injury, including serial measurements of N-terminal pro–B-type natriuretic peptide (NT-proBNP) and high-sensitivity cardiac troponin T (hs-TnT). These biomarkers were assessed at baseline, 30 days, and 180 days, allowing for evaluation of both short-term and longer-term trends in cardiac function. NT-proBNP levels provided information on ventricular wall stress and fluid overload, while hs-TnT served as a sensitive marker of myocardial injury, even in the absence of overt ischemic events. The combination of clinical and biomarker data aimed to offer a robust framework for risk stratification, prognostic assessment, and monitoring of therapeutic response in patients with heart failure.Cardiac structure and function were assessed using transthoracic echocardiography performed according to standardized protocols. Measurements included left ventricular end-diastolic and end-systolic volumes, LVEF, left ventricular mass index, global longitudinal strain, and left atrial volume index.Continuous variables are presented as mean ± standard deviation or median with interquartile range, as appropriate. Changes over time were analyzed using paired statistical tests, with a two-sided p value <0.05 considered statistically significant.

Results

A total of 162 patients were included in the final analysis, with a mean age of 70.5 ± 10.6 years; 64.2% of the cohort were male. At baseline, the majority of patients were classified as New York Heart Association (NYHA) functional class II, and all participants were receiving optimized guideline-directed medical therapy. A substantial proportion of patients had relevant comorbidities, including atrial fibrillation and ischemic heart disease, reflecting a representative chronic heart failure population.Following initiation of SGLT2 inhibitor therapy, significant structural and functional changes in cardiac remodeling parameters were observed over the 6-month follow-up period. Left ventricular mass index demonstrated a marked reduction, consistent with regression of myocardial hypertrophy. In parallel, both left ventricular end-diastolic and end-systolic volumes decreased significantly, indicating favorable reverse ventricular remodeling. These structural improvements were accompanied by a significant increase in left ventricular ejection fraction and a notable enhancement in global longitudinal strain, suggesting improved systolic performance and myocardial mechanics.In addition to ventricular changes, significant remodeling of the left atrium was documented. Left atrial volume index decreased progressively during follow-up, reflecting reverse atrial remodeling independent of baseline LVEF phenotype. These findings underscore the potential impact of SGLT2 inhibitor therapy on atrial structure, an important determinant of diastolic function and clinical outcomes in heart failure.Biomarker analysis revealed a gradual and statistically significant decline in N-terminal pro–B-type natriuretic peptide (NT-proBNP) concentrations,

with early trends observed at 30 days and more pronounced reductions at 180 days. In contrast, levels of high-sensitivity cardiac troponin T remained stable throughout the study period, suggesting an absence of ongoing myocardial injury during treatment [3,8].Collectively, these results demonstrate that SGLT2 inhibitor therapy is associated with comprehensive reverse cardiac remodeling, involving both ventricular and atrial compartments, alongside favorable biomarker dynamics in patients with chronic heart failure.

Discussion

The present study demonstrates that SGLT2 inhibitor therapy is associated with favorable reverse remodeling of both ventricular and atrial structures in patients with chronic HF. Importantly, these effects were observed irrespective of baseline LVEF, supporting the concept that SGLT2 inhibitors target fundamental mechanisms of HF pathophysiology rather than phenotype-specific pathways.The observed reduction in left atrial volume is of particular clinical relevance, given the strong association between atrial remodeling, atrial fibrillation, and adverse outcomes. These findings suggest that improvement in atrial structure may represent an additional mechanism contributing to the prognostic benefits of SGLT2 inhibitors.

Conclusion

In stable patients with chronic HF receiving optimized therapy, SGLT2 inhibitors induce global reverse cardiac remodeling, including significant improvements in left ventricular geometry and left atrial structure. These effects appear independent of LVEF and support the role of SGLT2 inhibitors as disease-modifying agents in HF management.

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