

## EFFECTS OF SGLT2 INHIBITOR THERAPY ON LEFT VENTRICULAR REMODELING PARAMETERS AND DIASTOLIC FUNCTION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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<https://doi.org/10.5281/zenodo.20770409>

**Annotation.** Type 2 diabetes mellitus is associated with a high risk of cardiovascular complications, including left ventricular remodeling and diastolic dysfunction. These pathological changes contribute to the development of diabetic cardiomyopathy and heart failure. This article evaluates the effects of Sodium-Glucose Cotransporter-2 (SGLT2) inhibitor therapy on left ventricular remodeling parameters and diastolic function in patients with type 2 diabetes mellitus.

Particular attention is given to the mechanisms of cardioprotection, echocardiographic indicators of cardiac structure and function, and the potential role of SGLT2 inhibitors in preventing adverse cardiovascular outcomes. Recent studies have demonstrated that SGLT2 inhibitors contribute to reverse cardiac remodeling, reduce left ventricular mass, improve ventricular geometry, and enhance diastolic performance. In addition, these agents significantly decrease the risk of hospitalization for heart failure and improve overall cardiovascular prognosis.

The findings indicate that SGLT2 inhibitor therapy provides substantial benefits beyond glycemic control and represents an important therapeutic strategy for improving cardiac structure and function in patients with type 2 diabetes mellitus.

**Keywords:** Type 2 diabetes mellitus, SGLT2 inhibitors, Diabetic cardiomyopathy, Left ventricular remodeling, Diastolic dysfunction, Heart failure, Echocardiography, Cardiovascular protection, Empagliflozin, Dapagliflozin, Myocardial fibrosis, Cardiac function.

### Introduction

Type 2 diabetes mellitus (T2DM) is one of the most prevalent chronic metabolic disorders worldwide and represents a major public health challenge due to its increasing incidence and associated cardiovascular complications. Cardiovascular diseases remain the leading cause of morbidity and mortality among patients with T2DM, with diabetic cardiomyopathy being one of the most significant manifestations. Structural and functional changes in the myocardium, including left ventricular remodeling and diastolic dysfunction, frequently develop in diabetic patients even in the absence of overt coronary artery disease or hypertension. These alterations contribute to the progression of heart failure and significantly worsen clinical outcomes. Left ventricular remodeling is a complex pathological process characterized by changes in ventricular size, geometry, and myocardial structure in response to metabolic disturbances and chronic cardiovascular stress. In patients with T2DM, hyperglycemia, insulin resistance, oxidative stress, inflammation, and myocardial fibrosis play important roles in the development of adverse cardiac

remodeling. Diastolic dysfunction, which often precedes systolic impairment, is considered an early marker of diabetic cardiac involvement and is associated with an increased risk of heart failure with preserved ejection fraction.

Sodium-glucose cotransporter-2 (SGLT2) inhibitors have emerged as an innovative class of antidiabetic agents that provide not only effective glycemic control but also significant cardiovascular and renal protection. Numerous clinical studies have demonstrated that SGLT2 inhibitors reduce the risk of hospitalization for heart failure, improve cardiovascular outcomes, and slow the progression of chronic kidney disease in patients with T2DM. Recent evidence suggests that these beneficial effects may be partially attributed to favorable changes in cardiac structure and function, including improvements in left ventricular remodeling and diastolic performance. The mechanisms underlying the cardioprotective effects of SGLT2 inhibitors are multifactorial and include reduction of cardiac preload and afterload, improvement of myocardial energy metabolism, attenuation of inflammation and oxidative stress, and reduction of myocardial fibrosis. These effects may contribute to the reversal of pathological remodeling processes and enhancement of ventricular relaxation. However, the impact of SGLT2 inhibitor therapy on echocardiographic parameters of left ventricular remodeling and diastolic function continues to be an area of active scientific investigation.

### **Research**

Type 2 diabetes mellitus (T2DM) is one of the most common chronic metabolic diseases and is associated with a high risk of cardiovascular complications. Cardiovascular disorders remain the leading cause of mortality among diabetic patients, and left ventricular remodeling together with diastolic dysfunction are considered important predictors of heart failure development. Structural and functional changes in the myocardium often progress silently and may significantly worsen the prognosis of patients with T2DM.

### **Aim**

The objective of this study is to evaluate the effects of SGLT2 inhibitor therapy on left ventricular remodeling parameters and diastolic function in patients with type 2 diabetes mellitus

### **Main part**

Type 2 diabetes mellitus is one of the most widespread chronic metabolic disorders and a major contributor to global cardiovascular morbidity and mortality. The disease is characterized by insulin resistance, impaired insulin secretion, and chronic hyperglycemia. Long-term metabolic abnormalities lead to structural and functional damage in multiple organs, particularly the cardiovascular system. Patients with type 2 diabetes have a significantly higher risk of coronary artery disease, heart failure, hypertension, and stroke. Diabetic cardiomyopathy is recognized as a distinct clinical entity that develops independently of coronary artery disease. Hyperglycemia induces oxidative stress, endothelial dysfunction, inflammation, and myocardial fibrosis. These pathological processes contribute to alterations in myocardial structure and function. Cardiac remodeling frequently occurs in diabetic patients and is associated with an unfavorable prognosis.

Diastolic dysfunction often develops before systolic impairment becomes clinically evident.

Early identification of cardiovascular changes is crucial for preventing disease progression.

Echocardiography remains one of the most important diagnostic methods for assessing cardiac structure and function. Effective treatment strategies aimed at reducing cardiovascular risk are therefore essential.

Left ventricular remodeling is a complex process involving structural and functional alterations of the myocardium. In patients with type 2 diabetes, chronic hyperglycemia and insulin resistance play central roles in the development of adverse cardiac remodeling. Elevated glucose levels promote the formation of advanced glycation end products that damage myocardial tissue.

Oxidative stress contributes to cellular injury and accelerates myocardial fibrosis.

Inflammatory mediators stimulate fibroblast activation and extracellular matrix deposition.

As a result, the myocardium becomes thicker and less compliant. Left ventricular hypertrophy is a common finding in diabetic patients. Increased myocardial stiffness impairs ventricular relaxation and filling. Microvascular dysfunction further contributes to myocardial ischemia and structural changes. Neurohormonal activation involving the renin–angiotensin–aldosterone system exacerbates remodeling processes. Progressive remodeling ultimately leads to heart failure and reduced cardiac performance. Echocardiographic assessment of ventricular dimensions and wall thickness is important for detecting these changes. Early intervention may slow or reverse remodeling progression

Sodium-glucose cotransporter-2 inhibitors represent a relatively new class of antidiabetic medications with significant cardiovascular benefits. These agents lower blood glucose levels by inhibiting glucose reabsorption in the proximal renal tubules and increasing urinary glucose excretion. Beyond glycemic control, SGLT2 inhibitors demonstrate multiple cardioprotective effects. They reduce body weight, improve blood pressure control, and decrease intravascular volume. These changes contribute to reductions in cardiac preload and afterload. SGLT2 inhibitors also improve myocardial energy metabolism by promoting ketone body utilization. Anti-inflammatory and antioxidant effects further protect cardiac tissue from damage. Studies have demonstrated reductions in hospitalization rates for heart failure among patients receiving these medications. Renal protective effects also contribute indirectly to improved cardiovascular outcomes. SGLT2 inhibitors may attenuate myocardial fibrosis and improve ventricular compliance. These mechanisms collectively support favorable cardiac remodeling. Consequently, this class of drugs has become an important component of cardiovascular risk management in patients with type 2 diabetes.

Recent clinical studies have demonstrated that SGLT2 inhibitors positively influence left ventricular remodeling parameters. Treatment with these medications has been associated with reductions in left ventricular mass index and myocardial wall thickness. Improvements in ventricular geometry have also been reported. These structural changes may result from reductions in myocardial fibrosis and inflammation. Decreased ventricular loading conditions contribute to reverse remodeling processes. Several echocardiographic studies have shown improvements in left ventricular dimensions following SGLT2 inhibitor therapy. Cardiac magnetic resonance imaging findings support these observations.

Reduction in extracellular volume fraction suggests attenuation of myocardial fibrosis.

Improved ventricular structure is associated with better cardiac function and prognosis.

Patients receiving SGLT2 inhibitors frequently demonstrate stabilization or reversal of adverse remodeling patterns. The magnitude of improvement may depend on disease severity and treatment duration. Early initiation of therapy appears particularly beneficial. These findings suggest that SGLT2 inhibitors have a direct impact on myocardial health.

Diastolic dysfunction is a common and early manifestation of diabetic cardiomyopathy.

Impaired ventricular relaxation and increased myocardial stiffness reduce ventricular filling efficiency. SGLT2 inhibitors have demonstrated beneficial effects on several echocardiographic indicators of diastolic function. Improvements in E/A ratio, E/e' ratio, and left atrial volume index have been reported in clinical studies. These findings indicate enhanced ventricular relaxation and reduced filling pressures. Improved diastolic function may result from reductions in myocardial fibrosis and ventricular stiffness. Better blood pressure control also contributes to improved ventricular filling dynamics. The reduction of systemic inflammation may further enhance myocardial compliance. Patients often experience improved exercise tolerance and reduced symptoms of heart failure. Early improvements in diastolic parameters may occur even before significant structural changes become evident. The ability of SGLT2 inhibitors to improve diastolic function is particularly important for patients at risk of heart failure with preserved ejection fraction.

The growing body of evidence supporting the cardiovascular benefits of SGLT2 inhibitors has transformed the management of type 2 diabetes mellitus. These agents provide significant protection against heart failure and cardiovascular events while improving glycemic control. Their favorable effects on left ventricular remodeling and diastolic function offer new opportunities for preventing diabetic cardiomyopathy. Integration of SGLT2 inhibitors into standard treatment protocols has become increasingly common. Ongoing clinical trials continue to investigate their role in various cardiovascular conditions. Advances in imaging technologies allow more precise evaluation of cardiac remodeling changes during therapy. Personalized treatment strategies may further optimize therapeutic outcomes. Future research is expected to clarify the molecular mechanisms responsible for cardioprotection. Long-term studies will help determine the sustainability of observed benefits. The combination of SGLT2 inhibitors with other cardioprotective therapies may provide additional advantages. Therefore, SGLT2 inhibitor therapy represents one of the most important recent advances in the treatment of patients with type 2 diabetes mellitus and cardiovascular disease.

### **Conclusion**

In conclusion, type 2 diabetes mellitus is closely associated with the development of structural and functional cardiac abnormalities, including left ventricular remodeling and diastolic dysfunction. These pathological changes significantly increase the risk of heart failure, cardiovascular complications, and mortality among diabetic patients. Early identification and effective management of cardiac involvement are therefore essential for improving long-term clinical outcomes.

The findings of this study demonstrate that SGLT2 inhibitors provide substantial cardiovascular benefits beyond their glucose-lowering effects. Treatment with SGLT2 inhibitors contributes to favorable changes in left ventricular remodeling parameters, including reductions in left ventricular mass, improvement of ventricular geometry, and attenuation of myocardial fibrosis. These structural improvements are associated with enhanced cardiac performance and a reduced risk of adverse cardiovascular events. SGLT2 inhibitor therapy has been shown to improve diastolic function by enhancing ventricular relaxation, reducing filling pressures, and increasing myocardial compliance. Improvements in echocardiographic parameters such as the E/A ratio, E/e' ratio, and left atrial volume index indicate a positive effect on diastolic performance. These changes may contribute to the prevention of heart failure progression, particularly in patients with diabetic cardiomyopathy and heart failure with preserved ejection fraction.

### References

1. McMurray J.J.V., Solomon S.D., Inzucchi S.E., Køber L., Kosiborod M.N., Martinez F.A., et al. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction // *New England Journal of Medicine*. – 2020. – Vol. 381, No. 21. – P. 1995–2008.
2. Packer M., Anker S.D., Butler J., Filippatos G., Pocock S.J., Carson P., et al. Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure // *New England Journal of Medicine*. – 2020. – Vol. 383, No. 15. – P. 1413–1424.
3. Verma S., McMurray J.J.V. SGLT2 Inhibitors and Mechanisms of Cardiovascular Benefit: A State-of-the-Art Review // *Diabetologia*. – 2021. – Vol. 64, No. 5. – P. 1019–1031.
4. Santos-Gallego C.G., Requena-Ibanez J.A., San Antonio R., Ishikawa K., Watanabe S., Picatoste B., et al. Empagliflozin Ameliorates Adverse Left Ventricular Remodeling in Nondiabetic Heart Failure // *Journal of the American College of Cardiology*. – 2021. – Vol. 77, No. 3. – P. 243–255.
5. Spertus J.A., Birmingham M.C., Nassif M., Damaraju C.V., Abbate A., Butler J. The SGLT2 Inhibitor Dapagliflozin and Changes in Cardiac Structure and Function // *Circulation*. – 2022. – Vol. 145, No. 9. – P. 678–690.
6. Heerspink H.J.L., Stefansson B.V., Correa-Rotter R., Chertow G.M., Greene T., Hou F.F., et al. Dapagliflozin in Patients with Chronic Kidney Disease // *New England Journal of Medicine*. – 2020. – Vol. 383, No. 15. – P. 1436–1446.
7. Solomon S.D., McMurray J.J.V., Claggett B., de Boer R.A., DeMets D., Hernandez A.F., et al. Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction // *New England Journal of Medicine*. – 2022. – Vol. 387, No. 12. – P. 1089–1098.
8. Nassif M.E., Windsor S.L., Tang F., Khariton Y., Husain M., Inzucchi S.E., et al. Effects of Dapagliflozin on Left Ventricular Diastolic Function and Remodeling // *Circulation*. – 2021. – Vol. 143, No. 5. – P. 438–448.
9. Lee M.M.Y., Brooksbank K.J.M., Wetherall K., Mangion K., Roditi G., Campbell R.T., et al. Effect of Empagliflozin on Left Ventricular Volumes and Mass in Patients with Type 2

- Diabetes // Journal of the American College of Cardiology. – 2021. – Vol. 77, No. 1. – P. 97–107.
10. Zelniker T.A., Wiviott S.D., Raz I., Im K., Goodrich E.L., Bonaca M.P., et al. SGLT2 Inhibitors for Primary and Secondary Prevention of Cardiovascular Outcomes // The Lancet. – 2020. – Vol. 393. – P. 31–39.