

SGLT2 Inhibitor Cardioprotection: Redefining Cardiovascular Care in Diabetes and Beyond

Introduction

Sodium–glucose cotransporter 2 (SGLT2) inhibitors were initially developed as glucose-lowering agents for the treatment of type 2 diabetes. By promoting urinary glucose excretion, they improve glycemic control in an insulin-independent manner. However, large cardiovascular outcome trials have revealed that the benefits of SGLT2 inhibitors extend far beyond glucose regulation [1,2]. These agents have demonstrated significant cardioprotective effects, reshaping the management of patients with diabetes, heart failure, and chronic kidney disease.

Discussion

The cardioprotective effects of SGLT2 inhibitors were first observed in major clinical trials showing reductions in hospitalization for heart failure and cardiovascular mortality among patients with type 2 diabetes. Importantly, these benefits were seen early after treatment initiation and were largely independent of glycemic control, suggesting mechanisms beyond blood glucose lowering.

Several pathways contribute to the cardiovascular benefits of SGLT2 inhibitors. Hemodynamically, these agents promote osmotic diuresis and natriuresis, leading to reduced preload and afterload on the heart [3,4]. This effect improves cardiac efficiency and reduces congestion, particularly beneficial in patients with heart failure. Additionally, SGLT2 inhibitors modestly lower blood pressure and body weight, further reducing cardiovascular stress [5].

Metabolic and cellular mechanisms also play a role. SGLT2 inhibitors improve myocardial energy utilization by shifting substrate metabolism toward ketone bodies, which may enhance cardiac efficiency. They also reduce inflammation, oxidative stress, and myocardial fibrosis, contributing to improved cardiac structure and function. Improvements in endothelial function and vascular stiffness further support cardiovascular protection.

Notably, cardioprotective benefits have been demonstrated in patients both with and without diabetes. Clinical trials in heart failure with reduced and preserved ejection fraction have shown consistent reductions in heart failure hospitalization, establishing SGLT2 inhibitors as foundational therapy in heart failure management. Their favorable safety profile and oral administration make them well suited for long-term cardiovascular care.

Conclusion

SGLT2 inhibitors have emerged as powerful cardioprotective agents, transforming the therapeutic landscape of diabetes and cardiovascular disease. By delivering robust heart failure and mortality benefits through multiple complementary mechanisms, they offer protection that extends beyond glucose control. As evidence continues to grow, SGLT2 inhibitors are increasingly integrated into cardiovascular and renal care guidelines. Their broad applicability and proven outcomes position them as key agents in improving long-

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term cardiovascular health across diverse patient populations.

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