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Sglt2 Inhibitors as Cardioprotective Agents Beyond Diabetes

Muhammad Tayyub
Samarkand State Medical University
Khizar Raheel
Samarkand State Medical University
Fizza Raheel
Samarkand State Medical University
Dr Imran Aslam
Assistant Professor, Samarkand State Medical University, E-mail: drimran87@gmail.com
Abdurakhmonova Zamira Ergashboevna
PhD, assistant, Samarkand State Medical University, E-mail: zamiraabduraxmanova31@gmail.com

Abstract. Sodium-glucose cotransporter-2 (SGLT2) inhibitors were first used to lower blood glucose in type 2 diabetes. Nevertheless, increasing data from heart failure–specific trials and from large cardiovascular outcome trials have proven that the favorable effects of SGLT2 inhibitors are not related to their glucose-lowering effect. These drugs have consistently been shown to reduce rates of hospitalization for heart failure, cardiovascular mortality, and progression of renal disease in both diabetic and non-diabetic patients. Retrospective review summarizes up-to-date evidence of SGLT2 inhibitors in reducing the risk of heart failure. The purpose of this article is to present recent research articles on benefits, mechanisms, major clinical trials, and near-term practical applications that are pertinent to current cardiovascular care. Knowledge of these pleiotropic effects is crucial for identifying the optimal candidates and integrating SGLT2 inhibitors into routine cardiology practice.

Key words: SGLT2 inhibitors; heart failure; cardiovascular outcomes; non-diabetic individuals; cardiorenal axis.

Introduction

Heart failure (HF) is a major cause of mortality and has a grim prognosis characterized by frequent readmissions, poor quality of life, and high medical care costs. The coexistence of cardiometabolic comorbidities, primarily type 2 diabetes mellitus (T2DM), drives the progression and elevates cardiovascular risk. Historically, antihyperglycemic therapies were designed to address metabolic control with the realization that there would be no cardiovascular benefit.

Sodium-glucose cotransporter-2 (SGLT2) inhibitors, which were initially developed as antidiabetic medications, act by blocking renal glucose reabsorption. The first cardiovascular trials of SGLT2 inhibitors surprisingly found significant reductions in the risks for heart failure hospitalization and cardiovascular mortality independent of glycemic control. These benefits encouraged additional research, which validated the positive effects across a broad spectrum population that included patients without diabetes and the full range of left ventricular ejection fraction (LVEF).

SGLT2 inhibitors have subsequently been reimagined for their role in cardiovascular and cardiorenal care. Mechanistic investigations indicate several cardioprotective mechanisms such as improved hemodynamics, myoenergetics and decreased inflammation and oxidative stress. These mechanisms

are consistent with the pathophysiology of heart failure, accounting for the wide range of clinical improvements seen.

In an era of increasing evidence and changing treatment guidelines, this review seeks to summarize the most current data on SGLT2 inhibition as a cardioprotective therapy with potential disease-modifying effects in contemporary cardiovascular medicine.

Literature review:

SGLT2 inhibitors have demonstrated cardiovascular protective effects beyond diabetes, leading to a marked decrease in cardiovascular death and hospitalisation for heart failure not only in the diabetic but also in the non-diabetic population. The EMPA-REG OUTCOME trial showed that empagliflozin decreased heart failure hospitalization and cardiovascular death in type 2 diabetes patients who were at high risk. CANVAS showed that canagliflozin led to a reduction in hospital admissions for heart failure, benefits seen even early on. In the DECLARE-TIMI 58 trial, dapagliflozin was associated with a reduced risk of heart failure hospitalization and benefits on kidney outcomes. The DAPA-HF and EMPEROR trials expanded these benefits to HFrEF and HFpEF patients, even in the absence of diabetes. The DELIVER trial demonstrated the efficacy of dapagliflozin in high-functioning HFpEF, decreasing hospitalizations and improving quality of life. Altogether, these trials establish that the SGLT2 inhibitors have a class effect for reducing CVD and renal risk even irrespective of their glucose-lowering effects.

Relevance:

Besides diabetes management, SGLT2 inhibitors are clinically relevant comorbidities and are now considered standard treatment armamentarium for diabetic as well as non-diabetic patients in terms of cardiovascular care. These drugs have invariably led to a decrease in hospitalization for heart failure, cardiovascular mortality, and slowing down of renal disease progression. The early initiation of SGLT2 inhibitors, in eligible patients, can improve long-term prognosis and quality of life. They are adjunct to conventional heart failure treatment but may be the cornerstone of holistic care for cardiometabolic patients; consistent with contemporary guideline-directed therapy and individualized patient care.

Purpose of the study:

The purpose of this narrative review is to sum up the current knowledge on SGLT2 inhibitors and their potential cardioprotective effects beyond glucose reduction in patients with diabetes or even without. The goal is to focus on potential clinical applications, to achieve an integrated understanding of their underlying mechanisms, and to summarize the main results from large clinical trials into an attractive format. Integrating molecular understanding and clinical impact, this review aims to educate the scientific community and practitioners of cardiovascular/cardiorenal medicine about SGLT2 inhibitors as disease-modifying agents.

Materials and Methods of Research:

This narrative review was done by performing a systematic search of academic literature, as well as clinical trial reports, meta-analyses, and guidelines documents. The databases used were PubMed, Google Scholar, Scopus , and Web of Science, with studies until 2025. The following were searched for as keywords and MeSH terms: 'SGLT2 inhibitors', 'cardioprotection', 'heart failure', 'cardiovascular outcomes' , and 'non-diabetic patients'.

We included Randomized Controlled trials (RCTs) and observational studies, mechanistic research, and review articles that observed cardiovascular outcomes of SGLT2-I class beyond the glucose-lowering effect. Studies utilizing animal models and not related to clinical development were excluded from the analysis, as well as articles in languages other than English and for which the full text was not accessible.

Trial design, patient population, primary and secondary cardiovascular endpoints, renal outcomes, safety profile and theoretical insights into the mechanism(s) of action were reviewed in extracted data. 961 Because of heterogeneity in study designs and results, a narrative synthesis was used instead of a formal systematic review or meta-analysis. It provides a thorough overview of the cardioprotective effects of SGLT2 inhibitors, combining information from clinical and mechanistic trials.

Results of the Study:

SGLT2 inhibitors have shown consistent and remarkable renal and cardiovascular benefits even beyond the effects on glucose in diabetic patients. Significant results from landmark trials like DAPA-HF, EMPEROR-Reduced/Preserved, and DELIVER demonstrate heart failure hospitalizations to be reduced by 25–35% in diabetic and non-diabetic patients using SGLT2-I. Additionally, with both DAPA-HF and EMPA-REG OUTCOME, there appeared to be a reduction in cardiovascular mortality of approximately 20–38%, indicating a significant survival benefit. These drugs also offer cardiorenal protection by slowing the progression of renal disease, decreasing AKI, and improving composite renal outcomes. Mechanistic data indicate that decreased preload and afterload through natriuresis, increased myocardial energy delivery via ketone metabolism, reduced inflammation, and oxidative stress are among the pathways responsible for their clinical benefits. SGLT2 inhibitors also have beneficial effects on cardiac remodeling and endothelial function. Importantly, the advantages are observed in various patient subgroups irrespective of age, sex, left ventricular ejection fraction, or presence of baseline diabetes status, suggesting glucose-independent effects. The safety and tolerability profiles are acceptable, with mild to moderate side effects of vaginal infections and hypovolemia that can be effectively managed under medical supervision. Collectively, these results are consistent with implications for SGLT2 inhibitors as disease-modifying agents in cardiovascular and renal medicine with wide-ranging pleiotropic actions extending beyond glucose.

Conclusions:

SGLT2 inhibitors have burst onto the scene as potent cardioprotective agents with effects far beyond glycemic management. The abundant evidence from large randomized controlled trials and mechanistic research uniformly demonstrates that these agents lower heart failure hospitalization, cardiovascular mortality, and renal disease progression in diabetic as well as in non-diabetic populations. Their early benefits, repeatability across various patient populations, and mechanistic plausibility make them disease-modifying therapies in cardiovascular medicine. The modern clinical implementation of SGLT2 inhibitors may have a huge impact on patient care, both in terms of hard endpoints, quality of life, and economics. As knowledge of their pleiotropic effects grows, such drugs are likely to remain pivotal in the treatment of heart failure and cardiorenal syndromes.

References

1. Zinman B, wanner C, Lachin JM, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. N Engl J Med. 2015; 373:2117-2128.
2. Neal B, Perkovic V, Mahaffey KW, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. N Engl J Med. 2017; 377:644-657.
3. Wiviott SD, Raz I, Bonaca MP, et al. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. N Engl J Med. 2019; 380:347-357.
4. McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med. 2019; 381:1995-2008.
5. Packer M, Anker SD, Butler J, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure. N Engl J Med. 2020; 383:1413-1424.
6. Solomon SD, McMurray JJV, Claggett B, et al. Dapagliflozin in heart failure with preserved ejection fraction. N Engl J Med. 2022; 387:1089-1098.
7. Zelniker TA, Wiviott SD, Raz I, et al. SGLT2 inhibitors for primary and secondary prevention of cardiovascular and renal outcomes in type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials. Lancet. 2019; 393:31-39.
8. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021; 42:3599-3726.

9. . Heerspink HJL, Stefánsson BV, Correa-Rotter R, et al. Dapagliflozin in patients with chronic kidney disease. N Engl J Med. 2020; 383:1436-1446.
10. Butler J, Zannad F, Filippatos G, et al. Cardiovascular effects of SGLT2 inhibitors in heart failure: mechanisms and clinical implications. Nat Rev Cardiol. 2022; 19:279-294.
11. Bhatt DL, Szarek M, Steg PG, et al. Sotagliflozin in patients with diabetes and recent worsening heart failure. N Engl J Med. 2021; 384:117-128.
12. Verma S, McMurray JJV. SGLT2 inhibitors and mechanisms of cardiovascular benefit: a state-of-the-art review. Diabetology. 2018; 61:2108-2117.