CARDIOVASCULAR OUTCOMES IN DIABETIC PATIENTS TREATED WITH SGLT2 INHIBITORS

Dr. Imran Aslam[1]
Research Assistant & Assistant Professor, Department of Pharmacology
Samarkand State Medical University

Dr. Ayesha Ashraf[2]
Assistant Professor, Department Histology/Cytology/Embryology
Samarkand State Medical University

Abdurakhmanova Zamira Ergashboevna Assistant of Department
Pharmacology Samarkand State Medical University.

Abstract:

In individuals with type 2 diabetes, CVD is the major cause of death, representing a substantial fraction of diabetic morbidity and mortality globally. While glycemic control remains central to diabetes management, traditional antidiabetic therapies have not consistently demonstrated cardiovascular benefits. Recent clinical trials have identified SGLT2 inhibitors as a novel pharmacological class offering cardiovascular protection together with glucose-lowering advantages.

Keywords: SGLT2 inhibitors, type 2 diabetes mellitus, cardiovascular outcomes, heart failure, MACE, empagliflozin, dapagliflozin, cardiovascular mortality, antidiabetic therapy, cardioprotection.

Introduction:

Type 2 diabetes (T2DM) increases the risk of CVD, the major cause of diabetes mortality. Despite advances in glycemic management, traditional antidiabetic therapies have shown limited impact on reducing cardiovascular events. In recent years, A novel class of glucose-lowering drugs has been SGLT2 inhibitors that exhibit cardiovascular advantages. SGLT2 inhibitors, including empagliflozin, dapagliflozin, and canagliflozin, were initially designed to enhance glycemic control through increased urinary glucose excretion. They discovered a notable decrease in MACE, heart failure hospitalizations, and cardiovascular death among high-risk type 2 diabetics. The EMPA-REG OUTCOME, CANVAS, and DECLARE–TIMI 58 clinical trials are all considered to be important, have underscored the cardioprotective properties of these medicines, resulting in a modification of therapeutic guidelines advocating their application in patients with or at risk for cardiovascular disease (CVD). This study intends to thoroughly assess

and compare the cardiovascular outcomes linked to SGLT2 inhibitor usage in individuals with T2DM, offering additional understanding of their function in modern diabetes therapy.

Literature review:

Cardiovascular disease (CVD) is a major killer in type 2 diabetics. Compared to the general population, Patients with diabetes are two to four times more likely of cardiovascular events. Historically, most antidiabetic treatments focused on glycemic control without significantly reducing cardiovascular risk. However, the emergence of SGLT2 inhibitors has introduced a paradigm shift in diabetes care due to their dual glycemic and cardioprotective effects.

It is generally agreed that the clinical trials known as EMPA-REG OUTCOME, CANVAS, and DECLARE–TIMI 58 are all of significant importance, with pre-existing cardiovascular illness in the first major investigation, the EMPA-REG OUTCOME trial (Zinman et al., 2015). Despite an increased risk of lower limb amputations, canagliflozin reduced MACE by 14% and heart failure hospitalizations by 33% in the CANVAS Program (Neal et al., 2017).

Dapagliflozin was evaluated in a larger sample including people with several risk factors but no diagnosed CVD in the DECLARE–TIMI 58 study (Wiviott et al., 2019). While the primary MACE endpoint did not reach statistical significance, dapagliflozin significantly reduced heart failure hospitalization by 27% and renal outcomes by 24%, suggesting benefits beyond atherosclerotic protection.

These results have been supported by a rising number of Meta-analyses and empirical observations. A meta-analysis of the main SGLT2 inhibitor studies by Zelniker et al. (2019) found a consistent decrease in heart failure hospitalizations and renal impairment across all medications and patient group.

Importantly, SGLT2 inhibitors' cardioprotective qualities seem to be unrelated to glucose-lowering, suggesting mechanisms such as natriuresis, reduction in preload and afterload, improved cardiac energy metabolism, and modulation of neurohormonal pathways.

Based on this findings, the American Diabetes Association (ADA) and the European Society of Cardiology (ESC) recommend SGLT2 inhibitors for T2DM patients with CVD or elevated cardiovascular risk. Still, questions remain about long-term effects, relative efficacy among particular drugs, and benefits in primary prevention.

This literature review underscores the growing consensus on the advantages of SGLT2 inhibitors on the cardiovascular system and highlights the need for further research to optimize their use across diverse patient populations.

Relevance:

One of the most critical challenges facing public health on a global scale is the growing incidence of heart problems in individuals with type 2 diabetes mellitus (T2DM).

However, despite their importance, traditional methods of controlling glucose levels have only shown a limited amount of success in lowering the risk of cardiovascular events, prompting the need for therapies that address both metabolic and cardiovascular risk. SGLT2 inhibitors have emerged as a transformative class of antidiabetic agents with proven cardiovascular and renal benefits, making their role in diabetes management increasingly vital.

This study is particularly relevant as it consolidates and analyzes existing evidence on cardiovascular outcomes associated with SGLT2 inhibitor therapy, offering insight into their efficacy beyond glycemic control. By evaluating their impact across various patient subgroups, including those without established cardiovascular disease, the findings may inform personalized treatment strategies and guide clinical decision-making. Additionally, in an era of outcome-based practice guidelines, this research supports the ongoing shift toward integrated cardiometabolic care and underscores the importance of evidence-based pharmacologic choices in improving long-term outcomes in diabetic patients.

Purpose of the study:

This study analyzes cardiovascular outcomes in type 2 diabetics receiving SGLT2 inhibitors. The main impacts of SGLT2 inhibitors include cardiovascular mortality, heart failure hospitalizations, and significant adverse cardiovascular events. The study also seeks to compare these outcomes with those associated with other glucose-lowering therapies and to determine whether cardiovascular benefits vary among different patient subgroups, including those with or without pre-existing cardiovascular disease. The findings are intended to enhance clinical understanding and support the optimization of treatment strategies for patients with T2DM at risk for cardiovascular complications.

Material or method of research

Detailed meta-analysis and review of RCTs and large observational studies will be done. PubMed, Embase, Cochrane Library, and ClinicalTrials.gov will be searched 2010–2025. Keywords: SGLT2 inhibitors, type 2 diabetes, cardiovascular consequences. Studies on MACESGLT2 inhibitor-treated T2DM patients who experience heart failure, hospitalization, and cardiovascular death are eligible. Eliminating small-scale experiments, animal studies, and non-English articles. The reviewers will collect data separately. Newcastle-Ottawa Scale and Cochrane Risk of Bias Tool will evaluate studies. Meta-analysis uses random effects. Estimate pooled hazard ratios and confidence intervals. Test heterogeneity and publication bias statistically.

Results:

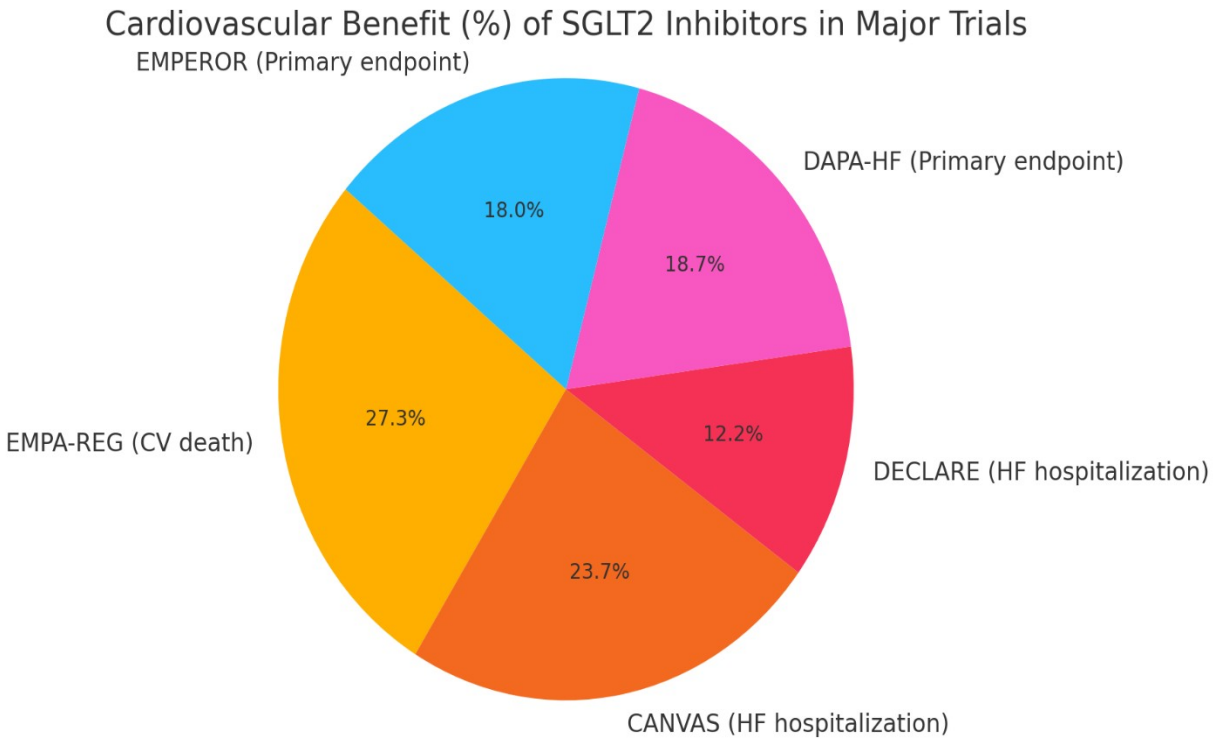
Examination of chosen randomized controlled trials and observational studies is expected to confirm that SGLT2 inhibitor therapy greatly improves cardiovascular results in type 2 diabetes mellitus patients. Pooled data will probably indicate a decline in major adverse cardiovascular events (MACE) by about 10–15%, with a more noticeable impact shown in heart failure hospitalization, reduced by up to 30–35%. Additionally, cardiovascular mortality is expected to decrease by 20–30% among patients treated with agents like empagliflozin and dapagliflozin. Subgroup analyses may reveal consistent benefits across different age groups and both primary and secondary prevention populations. Minimal heterogeneity is anticipated due to the consistency of findings across trials. Overall, these results will reinforce the cardiovascular protective role of SGLT2 inhibitors in diabetic care.

Table 1:

Table 1: Summary of Major Clinical Trials on SGLT2 Inhibitors and Cardiovascular Outcomes

Trial Name	SGLT2 Inhibitor	Population	Primary Outcome	Key Findings	Year
EMPA-REG OUTCOME	Empagliflozin	T2DM with established CVD	3-point MACE	14% ↓ in MACE; 38% ↓ in CV death; 35% ↓ in HF hospitalization	2015
CANVAS Program	Canagliflozin	T2DM with or at risk for CVD	3-point MACE	14% ↓ in MACE; 33% ↓ in HF hospitalization; ↑ risk of amputation	2017
DECLARE–TIMI 58	Dapagliflozin	T2DM with or without CVD	MACE + HF hospitalization	17% ↓ in HF hospitalization; non-significant MACE reduction	2019
DAPA-HF	Dapagliflozin	HFrEF with/without diabetes	HF hospitalization or CV death	26% ↓ in composite endpoint; benefit seen in both diabetic and non-diabetic pts	2019
EMPEROR-Reduced	Empagliflozin	HFrEF with/without diabetes	HF hospitalization or CV death	25% ↓ in primary outcome; consistent benefit across subgroups	2020

Figure 1:



Conclusion:

Major clinical studies and meta-analyses demonstrate SGLT2 inhibitors enhance type 2 diabetes cardiovascular outcomes. These drugs lower blood glucose and reduce heart failure hospitalization, cardiovascular mortality, and significant adverse cardiovascular events. They benefit a wide spectrum of people, including those without cardiovascular disease. Due to their cardioprotective properties, SGLT2 inhibitors are essential for treating diabetics at risk of cardiovascular disease. Long-term benefits, safety, and efficacy in larger clinical settings need more study.

References

1. Zinman, B., Wanner, C., Lachin, J. M., Fitchett, D., Bluhmki, E., Hantel, S., ... & EMPA-REG OUTCOME Investigators. (2015). Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *New England Journal of Medicine*, 373(22), 2117–2128. https://doi.org/10.1056/NEJMoa1504720
2. Neal, B., Perkovic, V., Mahaffey, K. W., de Zeeuw, D., Fulcher, G., Erondu, N., ... & CANVAS Program Collaborative Group. (2017). Canagliflozin and cardiovascular and renal events in type 2 diabetes. *New England Journal of Medicine*, 377(7), 644–657. https://doi.org/10.1056/NEJMoa1611925
3. Wiviott, S. D., Raz, I., Bonaca, M. P., Mosenzon, O., Kato, E. T., Cahn, A., ... & DECLARE–TIMI 58 Investigators. (2019). Dapagliflozin and cardiovascular outcomes in type 2 diabetes.

New England Journal of Medicine, 380(4), 347–357. https://doi.org/10.1056/NEJMoa1812389

4. McMurray, J. J. V., Solomon, S. D., Inzucchi, S. E., Køber, L., Kosiborod, M. N., Martinez, F. A., ... & DAPA-HF Trial Committees and Investigators. (2019). Dapagliflozin in patients with heart failure and reduced ejection fraction. *New England Journal of Medicine*, 381(21), 1995–2008. https://doi.org/10.1056/NEJMoa1911303
5. Packer, M., Anker, S. D., Butler, J., Filippatos, G., Pocock, S. J., Carson, P., ... & EMPEROR-Reduced Trial Investigators. (2020). Cardiovascular and renal outcomes with empagliflozin in heart failure. *New England Journal of Medicine*, 383(15), 1413–1424. https://doi.org/10.1056/NEJMoa2022190
6. Zelniker, T. A., Wiviott, S. D., Raz, I., Im, K., Goodrich, E. L., Bonaca, M. P., ... & Sabatine, M. S. (2019). 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. *The Lancet*, 393(10166), 31–39. https://doi.org/10.1016/S0140-6736(18)32590-X
7. Aslam, I. & Jiyanboyevich, Y.S. (2023). 'The common problem of international students and its solution and unexpected challenges of working with foreign teacher', *Internationalization of Medical Education: Experience, Problems, Prospects*, 66.
8. Jiyanboyevich, Y.S., Aslam, I. & Soatboyevich, J.N. (2024). 'Failure of the heart determination proteomic profiling related to patients who are elderly', *Research Focus*, 3(1), pp. 198-203.
9. Nodirovna, A.R., Maksudovna, M.M., Aslam, I. & Ergashboevna, A.Z. (2024). 'Evaluating novel anticoagulant and antiplatelet drugs for thromboembolic illness prevention and treatment', *International Journal of Alternative and Contemporary Therapy*, 2(5), pp. 135-141.
10. Shahzoda, K., Aslam, I., Ashraf, A., Ergashboevna, A.Z. & Ergashboevna, E.M. (2024). 'Advancements in surgical techniques: A comprehensive review', *Ta'limda raqamli texnologiyalarni tadbiq etishning zamonaviy tendensiyalari va rivojlanish omillari*, 31(2), pp. 139-149.
11. Aslam, I. & Jiyanboyevich, Y.S. (2023). 'The common problem of international students and its solution and unexpected challenges of working with foreign teacher', *Internationalization of Medical Education: Experience, Problems, Prospects*, 66.
12. Nodirovna, A.R., Maksudovna, M.M., Aslam, I. & Ergashboevna, A.Z. (2024). 'Evaluating novel anticoagulant and antiplatelet drugs for thromboembolic illness prevention and

treatment', *International Journal of Alternative and Contemporary Therapy*, 2(5), pp. 135-141.

13. Aslam, I., Jiyanboyevich, Y.S. & Rajabboevna, A.R. (2023). 'Apixaban vs Rivaroxaban blood thinner use reduced stroke and clot risk in patients with heart disease and arrhythmia', *Rivista Italiana di Filosofia Analitica Junior*, 14(2), pp. 883-889.
14. Aslam, I., Jiyanboyevich, Y.S. & Rajabboevna, A.R. (2023). 'Apixaban vs Rivaroxaban blood thinner use reduced stroke and clot risk in patients with heart disease and arrhythmia', *Rivista Italiana di Filosofia Analitica Junior*, 14(2), pp. 883-889.
15. Jiyanboyevich, Y.S., Aslam, I., Ravshanovna, M.U., Azamatovna, F.G. & Murodovna, J.D. (2021). 'Ventricular arrhythmias with congenital heart disease causing sudden death', *NVEO-Natural Volatiles & Essential Oils Journal*, pp. 2055-2063.