Sodium-glucose cotransporter inhibitors reduce cardiovascular outcomes regardless eGFR range in patients with heart failure. Systematic review and meta-regression meta-analysis

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Background and aims: Due to the potential for attenuation of the beneficial effects of SGLT2i treatment in patients with both HF and CKD who have lower glomerular filtration rates, and the risk of acute kidney injury following SGLT2i initiation, we performed a meta-analysis and meta-regression to assess the impact of SGLT2i on composite cardiovascular outcomes in this patient population.

Methods: We conducted a systematic literature review to find RCTs that evaluated SGLT2i treatment efficacy in HF and CKD patients. We used a random-effects model (Mantel-Haenszel) for the meta-analysis. Results show odds ratios (ORs) with 95% confidence intervals and P values for the primary outcome risk and in subgroups based on baseline eGFR. All probability values were two-tailed and statistical significance was set at P < 0.05. We also investigated type of SGLT2i and year of publication as predictor variables.

Results: When compared to a placebo, SGLT2 inhibitors reduced the risk of primary cardiovascular outcomes by 27% (HR 0.73, [95% CI 0.63–0.85], I² = 32%) in patients with eGFR < 60 mL/min/1.73 m² and by 20% (HR 0.80, [95% CI 0.74–0.88], I² = 0%) in patients with eGFR > 60 mL/min/1.73 m². Patients with HFpEF had 28% risk reduction (HR 0.72, [95% CI 0.56–0.93], I² = 37.23%), and HFrEF had 21% (HR 0.79, [95% CI 0.70–0.89], I² = 0%). The meta-regression analysis showed that the type of SGLT2i was not a significant predictor of treatment effect (Q = 2.29, p = 0.51). None of the other predictor variables were significant also.

Conclusion: This meta-regression analysis suggests that SGLT2i is an effective treatment for reduce cardiovascular outcomes in patients with concurrent HF and CKD, independent of the type of SGLT2i or eGFR range. Regardless of differences in participants characteristics, patients with HFpEF had higher risk reduction when compared with patients with HFrEF (28% vs 21%), our hypothesis for this find is that competitive risk favors patients with lower eGFR even in higher ejection fraction extract, further studies are needed to confirm these findings. Limitations of this study include potential publication bias and the exclusion of non-English studies.

Forrest plot for composite outcome

Bubble plot for composite outcome