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Effect of sodium-glucose transport protein 2 inhibitors on all-cause mortality in patients with gout: A multi-center cohort study

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Abstract

Objective: To evaluate the effects of sodium-glucose transport protein 2 inhibitors (SGLT2i) on all-cause mortality risk in patients with gout, compared to SGLT2i non-users.

Methods: This retrospective cohort study spanning from January 2010 and August 2023 across three medical centers in Taiwan, examined gout patients with and without T2DM. Covariates such as age, gender, comorbidities, co-medications were controlled using propensity score matching. All-cause mortality was the primary outcome, analyzed using Cox proportional model and Kaplan-Meier methods to estimate the hazard ratios and overall survival in SGLT2i users and non-users. Subgroup analysis assessed individual SGLT2i (empagliflozin, dapagliflozin, canagliflozin), with sensitivity tests using insulin as comparators to validate findings.

Results: 15,304 gout patients were included in this study, and 906 SGLT2i users were matched to SGLT2i non-users. The incidence rate of mortality per 1000 person-years were 38.38 for gout patients with T2DM on SGLT2i, 57.31 for gout patients without T2DM using SGLT2i, and 149.29 for gout patients with T2DM not using SGLT2i. Canagliflozin (HR, 0.36; 95% CI, 0.14-0.93) and empagliflozin (HR, 0.56; 95% CI, 0.37-0.84) showed significantly lower mortality risk after multivariable adjustment. Mediation analysis revealed SGLT2i had a greater impact on serum uric acid (6.5%) than HbA1c (0.7%). Sensitivity tests comparing gout patients with T2DM on SGLT2i to insulin users confirmed a significantly lower risk of all-cause mortality (HR: 0.50; 95% CI: 0.33-0.76).

Conclusion: Patients with gout who received SGLT2i were associated with a lower risk of all-cause mortality than their counterparts who used insulin and other anti-hyperglycemic medications.

Keywords: SGLT2 inhibitor, gout, all-cause mortality, type 2 diabetes mellitus