LETTER TO THE EDITOR

Glucagon-like Peptide-1 Receptor Agonists and the Risk of Acute Kidney Injury: Alarming, or Not?

To the Editor:

We read with interest the 2 case reports of acute kidney injury (AKI) associated with semaglutide use, described by Leehey et al,[1] given the risks associated with AKI.[2,3] In light of the reported kidney benefits of glucagon-like peptide-1 receptor agonists (GLP-1RAs),[4,5] we investigated whether GLP-1RAs are associated with increased risk for AKI, pooling data from cardiovascular outcome trials that enrolled high- or very-high-risk individuals with type 2 diabetes mellitus.

We set as primary safety outcome the incidence of AKI. Two independent reviewers (DP and AB) extracted data from eligible reports using a pilot tested data extraction form. Differences were calculated with the use of risk ratio (RR) after implementation of the Mantel-Haenszel random effects formula. Statistical heterogeneity among studies was assessed by using I^2 statistics. Analyses were performed using RevMan 5.3 software. Discrepancies between reviewers were solved by discussion, consensus, or arbitration by a third senior reviewer (MD).

Pooled data from 7 cardiovascular outcome trials with GLP-1RAs provided a total of 55,943 patients. Risk of bias was low across all selected trials. GLP-1RA treatment resulted in a nonsignificant decrease in risk for AKI (RR = 0.96; 95% CI: 0.82 to 1.14; Fig 1). When restricting our analysis to the 2 dedicated semaglutide trials, we observed no difference (RR = 0.74; 95% CI: 0.49 to 1.13; I^2 = 0%).

Notably, the 2 patients described by Leehey et al[1] had CKD stage 3b-4, an understudied population in the relevant literature. Accordingly, while GLP-1RAs do not increase the risk for AKI on a population level, caution is likely prudent in administering to patients with advanced CKD, particularly given potential effects on volume status owing to adverse gastrointestinal events associated with treatment.[6] Close monitoring of such patients is always required, especially within the first months after initiation of a GLP-1RA.

Dimitrios Patoulias, MD, Aristi Boulmpou, MD, Christodoulos E. Papadopoulos, PhD, Michael Doumas, PhD

ARTICLE INFORMATION

Authors' Affiliations: Second Propaedeutic Department of Internal Medicine (DP, MD) and Third Department of Cardiology (AB, CEP), General Hospital "Hippokration," Aristotle University of Thessaloniki, Thessaloniki, Greece; and Veterans Affairs Medical Center, George Washington University, Washington, District of Columbia (MD).

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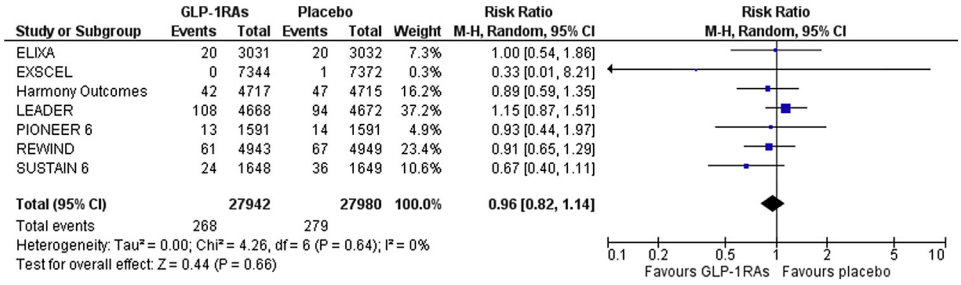

Figure 1. Effect of glucagon-like peptide-1 receptor agonists compared to placebo on the risk for acute kidney injury.

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