Cardiovascular Diabetology

MATTERS ARISING

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Potential benefits of GLP-1 receptor agonist in dialysis patients with type 2 diabetes: the need for comprehensive pharmacokinetic and hemodialysis analyses

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Abstract

The 2022 KDIGO guideline for diabetes management in patients with chronic kidney disease (CKD) had endorsed the use of GLP-1 receptor agonists (GLP-1RAs) for patients with CKD and type 2 diabetes who did not achieve optimal glycemic target with maximally tolerated metformin and sodium-glucose co-transporter-2 (SGLT-2) inhibitor. Our study revealed the potential benefits of GLP-1RAs in patients with dialysis-requiring acute kidney disease possibly owing to pleiotropic effects of the medicine. Nonetheless, pharmacokinetics and dialysis dose were omitted in our subgroup analyses. Herein, we would like to raise our concern regarding neglecting these important confounders in our analyses and the impact to the findings of the study.

Keywords GLP-1 receptor agonist, Type 2 diabetes, Dialysis, Pharmacokinetics

Main text

Our study reported potential effects of GLP-1RAs in patients with type 2 diabetes mellitus at dialysis initiation [1]. However, the omission of key confounders such as pharmacokinetics in dialysis-requiring patients and those at recovery stages of acute kidney injury, as well as critical aspects of dialysis management might cause substantial bias to the conclusion.

As rightly noted, the inherent limitations of the TriNetX platform preclude the inclusion of granular data such as dialysis dose, frequency, timing of drug administration, and cumulative exposure. We recognize that these variables could significantly influence mortality and cardiovascular outcomes, representing an important avenue for future research.

As a result, specific metrics like Kt/V values, drug clearance during dialysis, or the exact timing of drug administration are not comprehensively captured. Although the TriNetX platform delivers extensive observational data

This comment refers to the article available online at https://doi.org/10.1186/s12933-024-02364-2

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encompassing clinical events, diagnoses, medications used, and procedures, detailed elements of dialysis management and pharmacokinetic properties of GLP-RAs fall outside the current purview of its accessible data [2]. Regarding the absence of data on cumulative drug exposure, we stratified the patient cohort into long-term and short-term users based on their duration of use in our subgroup analysis. This approach aimed to assess cumulative drug exposure more effectively and help mitigate the restrictions arising from the lack of pharmacokinetic data for GLP-1RAs.

We fully acknowledge the limitations of our study and importance of exploring these key variables of GLP-1RAs on mortality and cardiovascular outcomes in dialysis patients with type 2 diabetes. All-inclusive databases are needed in future studies to incorporate factors such as precise dose, frequency, and evaluate drug clearance during dialysis, we stand by the potential benefits of GLP-1RAs as demonstrated using the current dataset. We also recognize that further research incorporating more comprehensive dialysis-specific data would enhance the precision and generalizability of these findings.

Sincerely,
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Acknowledgements
Not applicable.

Author contributions
All authors contributed to manuscript writing. All authors read and approved the final manuscript.

Funding
Not applicable.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 24 November 2024 / Accepted: 10 December 2024
Published online: 08 March 2025

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