Drug Design, Development and Therapy

Dovepress
Taylor & Francis Group

Open Access Full Text Article

RESPONSE TO LETTER

Competing Death and Absolute Benefit in Dexmedetomidine-Exposed Patients with Dialysis-Requiring Acute Kidney Injury [Response to Letter]

Kuo-Chuan Hung[1,2], I-Wen Chen[3]

[1]Department of Anesthesiology, Chi Mei Medical Center, Tainan, Taiwan; [2]School of Medicine, College of Medicine, National Sun Yat-Sen University, Kaohsiung, Taiwan; [3]Department of Anesthesiology, Chi Mei Hospital, Liouying, Tainan, Taiwan

Correspondence: I-Wen Chen, Department of Anesthesiology, Chi Mei Hospital, Liouying, Tainan, Taiwan, Tel +886 6 281 2811, Fax +886 6 283 3806, Email cheniwena60912@gmail.com

Drug Design, Development and Therapy downloaded from https://www.dovepress.com/
For personal use only.

Dear editor

We thank Wang et al for their thoughtful commentary on our study examining dexmedetomidine exposure and long-term outcomes in patients with dialysis-requiring acute kidney injury (AKI-D).[1] Their comments highlight important methodological considerations.

We agree that death may act as a competing event for renal outcomes such as progression to end-stage renal disease (ESRD) and eGFR decline. In our primary analysis, Cox proportional hazards models treated death as censoring, thereby estimating cause-specific hazard ratios. This approach addresses whether dexmedetomidine exposure is associated with the instantaneous risk of renal outcomes among patients who remain alive and under observation, but it does not directly estimate the cumulative probability of ESRD in the presence of competing mortality. Because dexmedetomidine exposure was associated with lower mortality, more patients in the dexmedetomidine group may have survived long enough to experience or be observed for renal endpoints. Conversely, control patients who died were censored and removed from the renal risk set. Under a Fine–Gray subdistribution framework, these deceased patients would remain in the risk set but could no longer develop ESRD, potentially attenuating the apparent renal benefit.[2] Therefore, the cause-specific hazard ratio for ESRD may overestimate the association when interpreted as an absolute clinical benefit. We acknowledge this as a valid limitation. The TriNetX platform provides large-scale, multi-institutional real-world data, but its integrated analytic tools do not currently support Fine–Gray competing risk regression. This limitation was not explicitly stated in our manuscript, and we appreciate the opportunity to clarify it.

Wang et al also suggest reporting risk differences, numbers needed to treat (NNTs), and safety outcomes to facilitate clinical interpretation. We agree that absolute effect measures and safety data are essential for evaluating net clinical benefit. However, because our study was observational and explicitly framed as associational, translating hazard ratios into NNTs requires caution. NNTs are most appropriately interpreted when a causal treatment effect can be assumed, because they attribute observed differences in outcome rates to the exposure itself. In our observational study, this assumption cannot be verified and may be affected by residual confounding.[3] Although approximate NNTs can be derived from reported absolute differences, presenting them as study-endorsed estimates could overstate therapeutic certainty, particularly in critically ill AKI-D patients with substantial heterogeneity and residual confounding.

We fully agree that future prospective randomized trials should incorporate competing risk analyses, absolute risk measures, and safety endpoints, including bradycardia, hypotension, and vasopressor escalation. Our study was intended to generate preliminary evidence and inform future trial design, rather than to justify immediate changes in sedation

https://doi.org/10.2147/DDDT.S623708
Received: 11 May 2026
Accepted: 11 May 2026
Published: 14 May 2026

© 2026 Hung and Chen. This work is published and licensed by Dove Medical Press Limited. The full terms of this license are available at https://www.dovepress.com/terms.php and incorporate the Creative Commons Attribution – Non Commercial (unported, v4.0) License (http://creativecommons.org/licenses/by-nc/4.0/). By accessing the work you hereby accept the Terms. Non-commercial uses of the work are permitted without any further permission from Dove Medical Press Limited, provided the work is properly attributed. For permission for commercial use of this work, please see paragraphs 4.2 and 5 of our Terms (https://www.dovepress.com/terms.php).

practice. Interpreted within this associational framework, we believe our findings contribute to the ongoing evaluation of dexmedetomidine in this high-risk population.

Funding

There is no funding to report.

Disclosure

The authors declare no conflicts of interest in this communication.

References

1. Hung KC, Chang LC, Chang YJ, Lai YC, Lin CM, Chen IW. Association of dexmedetomidine exposure with long-term mortality in patients with dialysis-requiring acute kidney injury: a propensity score-matched retrospective cohort study. *Drug Des Devel Ther*. 2026;20:598443. doi:10.2147/DDDT.S598443
2. Austin PC, Lee DS, Fine JP. Introduction to the analysis of survival data in the presence of competing risks. *Circulation*. 2016;133:601–609. doi:10.1161/CIRCULATIONAHA.115.017719
3. Root AA, Smeeth L. NNTs and NNHs: handle with care. *Br J Gen Pract*. 2017;67:133. doi:10.3399/bjgp17X689797

Dove Medical Press encourages responsible, free and frank academic debate. The contentTxt of the Drug Design, Development and Therapy 'letters to the editor' section does not necessarily represent the views of Dove Medical Press, its officers, agents, employees, related entities or the Drug Design, Development and Therapy editors. While all reasonable steps have been taken to confirm the contentTxt of each letter, Dove Medical Press accepts no liability in respect of the contentTxt of any letter, nor is it responsible for the contentTxt and accuracy of any letter to the editor.

Drug Design, Development and Therapy

Dovepress
Taylor & Francis Group

Publish your work in this journal

Drug Design, Development and Therapy is an international, peer-reviewed open-access journal that spans the spectrum of drug design and development through to clinical applications. Clinical outcomes, patient safety, and programs for the development and effective, safe, and sustained use of medicines are a feature of the journal, which has also been accepted for indexing on PubMed Central. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit http://www.dovepress.com/testimonials.php to read real quotes from published authors.

Submit your manuscript here: https://www.dovepress.com/drug-design-development-and-therapy-journal

https://doi.org/10.2147/DDDT.S623708