Title

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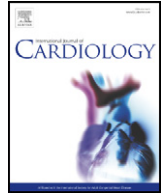
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Reply to "Is mean platelet volume a prognostic marker for hemodialysis patients?"

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We appreciate the comments from Drs. Zeng, Jiang, and Wang [1] regarding our original research study, "Mean Platelet Volume and Mortality Risk in an Incident Hemodialysis Cohort" [2]. In response to their first point, we agree that, given the observational study design, our findings of an association between incrementally higher mean platelet volume (MPV) levels and increasingly higher mortality risk may not have a causal interpretation, and due to data limitations, some confounders (e.g., certain comorbidities and medications) could not be accounted for. However, it should be noted that our study is the first to examine longitudinal MPV levels and mortality in a US-based nationally representative cohort of hemodialysis patients on a large unprecedented scale, with the objective of motivating future studies that will confirm associations, explore underlying mechanisms, and determine whether MPV-related death risk is modifiable with therapeutic interventions. In addition, the availability of detailed and granular patient-level data in our study allowed us to account for many key confounders such as markers of inflammation and nutrition (e.g., serum albumin as a negative acute phase reactant and nutritional index, normalized protein catabolic rate as a marker of protein intake, and serum creatinine as a proxy of muscle mass [3]) in sensitivity analyses. Notably, among the various medications that may modify MPV levels that are relevant to the hemodialysis population, we observed robust associations between high MPV level and mortality across strata of erythropoietin stimulating agent use [4–6].

The authors also highlighted concerns about missed opportunity to gain insight into mechanistic pathways underlying the high MPV−mortality association given the lack of cause-specific mortality data. However, given that cause-of-death is typically non-adjudicated in clinical data sources (i.e., collected as a part of routine patient care as opposed to research purposes), there may be a tendency towards an over-reporting of cardiovascular deaths and subsequent outcome misclassification [7,8]. Thus, we selected all-cause mortality as a more robust outcome of interest in our study.

Finally, in response to concerns about heterogeneous methodologic approaches used across various hospitals and centers that may influence MPV levels, all laboratory data were collected in the ambulatory setting and were measured in a single laboratory using uniform techniques, reducing the likelihood of measurement bias. Furthermore, any resultant misclassification of MPV levels would likely be non-differential, rendering our findings conservative.

Given that routinely-used hematologic indices such as platelet count may be inadequate metrics of thrombotic vs. bleeding propensity in dialysis patients, MPV has appeal as a widely-available, simple, and economical marker for assessing platelet reactivity [9]. However, further studies are needed to confirm findings, and well-designed interventional studies that lower MPV levels may provide insight into the causal implications of MPV upon the cardiovascular health and survival of dialysis patients.

Conflicts of interest and financial disclosures

None of the authors declare any relevant conflicts of interest.

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