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Verantwortliche/r des Verfahrens – Responsabile del procedimento: C. Wiedermann

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RESPONSE TO PEER-REVIEW REPORT

Name of journal: World Journal of Nephrology
Manuscript NO: 33527
Title: Causal relationship between hypoalbuminemia and acute kidney injury
Reviewer's code: 00502999
Reviewer's country: Argentina
Science editor: Xiu-Xia Song
Date sent for review: 2017-03-13
Date reviewed: 2017-03-21

COMMENTS FROM REVIEWER 1 AND RESPONSES

Comment #1:
The review article by Wiedermann CJ et al is interesting. Issues that could improve the manuscript: The authors must address before Conclusions the limitations of this metaanalysis, as such. Mainly, that most of the papers are restospective, the heterogeinity of the populations under consideration, that a uniform definition of AKI does not exist throughout the papers studied, and last but not least, the usual fact that we employ creatinine to assess and define AKI. We must address this important issue, and authors could suggest that besides RCTs in this field are mandatory, other AKI biomarkers should be employed to assess the relationship between hypoalbuminemia and AKI (like N-GAL, cystatin, TIMP-2, IL-18, KIM-1, GMP7, and so forth). Which were the scores employed in the included studies to define AKI?: RIFLE, AKIN, KDIGO 2012, ATKI 2013?. If so (and probably yes), then this must be commented and discussed.
Response: The following paragraph has been inserted after the discussion section taking into consideration all aspects of the reviewer's comments:

> ***LIMITATIONS***
> *Limitations of this review include the fact that most of the included studies were observational with patient populations in the various clinical settings that are heterogeneous. In addition, definitions of AKI were often creatinine-dependent and based on different classification systems for AKI including RIFLE, AKIN, and KDIGO.*

As additional limitation, the following sentence was added:

As the systematic search of the literature was restricted to PubMed (MEDLINE), additional studies may be missing.

Comment #2:
In the Introduction: Line 4, first paragraph: and decreased urine output. Please add and/OR decreased...
Response: "and/or" has been inserted.

Comment #3:
In the Introduction, please briefly refer to the impact of AKI on forthcoming CKD. This is very important.
Response: We agree with the reviewer that mentioning the impact of AKI on forthcoming CKD is very important. In the Introduction section it therefore says:

AKI is an acute systemic disease with major consequences for other organs besides the kidney, and is associated with significant short-term effects (e.g., fluid, electrolyte, and acid-base abnormalities, uremic toxin accumulation, cytokine elevation, systemic inflammation) and long-term adverse outcomes (e.g., myocardial infarction, chronic kidney disease, end-stage renal disease, mortality)[2, 3]. Need for dialysis and transplantation are increased, as is length of hospital stay[4, 5].

Comment #2:
Replace poorer by worse. ARF to be replaced by AKI. Please, this term is not employed any more.
Response: "poorer" has been replaced by "worse". ARF has been replaced by AKI in the text whenever possible, i.e. when not used as a term in the original publications. In the summary tables, however, ARF was left in place when it was an original outcome parameter.

COMMENTS FROM REVIEWER 2 AND RESPONSES

Reviewer 2 had no comments.

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