

LETTER

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Assessing preoperative plasma growth-differentiation factor-15 for prediction of acute kidney injury in patients undergoing cardiac surgery

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See related research by Heringlake et al. <http://ccforum.biomedcentral.com/articles/10.1186/s13054-016-1482-3>

With great interest, we read the recent article published by Heringlake et al. [1] assessing whether preoperative plasma GDF-15 independently predicts postoperative AKI in patients undergoing elective cardiac surgery. Many factors in this study were done well. Other than strict inclusion and exclusion criteria of patients, the authors had also tried to control most of the known risk factors that can affect AKI. We thank the authors for their endeavor to validate that preoperative plasma GDF-15 independently predicts postoperative AKI in patients undergoing elective cardiac surgery. Nevertheless, other than the limitations described in the discussion, we note that several important issues of this study were not addressed.

First, preoperative aspirin therapy was not included in the data analysis. Actually, preoperative aspirin therapy is common among patients undergoing cardiac surgery for primary or secondary prevention of myocardial infarction, stroke, and death. Preoperative aspirin therapy in cardiac surgery has been associated with decreased overall morbidity, mortality, and cardiac surgery-associated acute kidney injury [2].

Second, patients receiving valvular heart surgery or coronary artery bypass graft surgery were included in the study. However, some patients may use contrast agents

before surgeries. The preoperative contrast angiography or ventriculography is independently associated with increased risks of postoperative adverse renal events [3]. Therefore, contrast angiography or ventriculography should be included in the data analysis.

Third, it was unclear whether serum creatinine levels applied in the diagnosis of postoperative AKI had been adjusted based on the perioperative fluid balance. Moore et al. [4] showed that using Acute Kidney Injury Network criteria for diagnosis of AKI, if not adjusting serum creatinine levels for fluid balance, can underestimate the severity and incidence of AKI and can confuse the association of AKI with postoperative adverse outcomes.

Finally, when assessing the association of preoperative plasma GDF-15 with postoperative AKI in patients undergoing cardiac surgery, the available literature shows that postoperative complications including anemia, low cardiac output syndrome, hypoalbuminemia, and sepsis are independent risk factors of AKI after cardiac surgery [5]. We are concerned that not taking postoperative covariates into account would have biased the true effect of preoperative plasma GDF-15 on the occurrence of postoperative AKI in this study.

Authors' response

M. Heringlake, E. I. Charitos, K. Erber, A. E. Berggreen, H. Heinze and H. Paarmann

We thank Dr Zhang et al. for their interest in our work [1]. The authors raised concerns that our findings might be confounded by several variables not addressed specifically in our publication.

We are of course aware that every tool used for preoperative risk stratification must have relevant limitations, especially if aiming for the prediction of a multifactorial complication like cardiac surgery-associated acute kidney injury (CSA-AKI). However, we took the greatest care to take into account as many preoperative factors as possible.

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Zhang et al. criticized that preoperative treatment with aspirin was not included in our analyses. However, the incidence of AKI in patients preoperatively treated with aspirin was not different ($p = 0.720$) from the AKI incidence in patients not being treated with aspirin. Consequently this variable was not entered into the multivariate analyses.

We are also aware of the association between immediate preoperative radio contrast medium exposure and postoperative AKI [6]. To omit this potential confounder we focused only on elective surgery, and excluded urgent patients from the analysis; at least in our institution, elective patients are rarely subjected to an immediate preoperative contrast agent exposure.

We admit that not taking into account the postoperative fluid balance may have lead to underestimation of AKI incidence and severity. Several studies, including that by Moore et al. [4] cited by Zhang et al., have shown that adjusting creatinine levels to fluid balance and body weight will increase the probability to detect clinically significant AKI. However, precise data on fluid balance were not available for all patients and thus we could not adjust postoperative creatinine levels accordingly. Nonetheless, the current definitions of AKI [7] do not urge making such adjustments; and thus our findings are clearly valid according to current AKI criteria (based on creatinine).

We of course agree with Zhang et al.'s comment "that not taking postoperative covariates into account would have biased the true effect of preoperative plasma GDF-15 on the occurrence of postoperative AKI". However, as stated in our manuscript [1], a tool for preoperative risk stratification will hardly be capable to predict the unpredictable: bleeding anemia (due to poor surgery!), unexpected low cardiac output syndrome (e.g., due to inadequate cardioplegia), postoperative hypoalbuminemia (due to excessive need for crystalloid fluids), and sepsis.

Taken together the authors' comments do not alter our statement that preoperative plasma GDF-15 is an independent predictor of postoperative AKI in patients undergoing elective cardiac surgery and improves the predictive ability of the Cleveland Clinic Acute Renal Failure score.

Abbreviation

AKI: Acute kidney injury

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Authors' contributions

FX and HCC carefully read the manuscript of Heringlake et al., analyzed their methods and data, suggested comment points, drafted this manuscript, and are responsible for this manuscript. WZ carefully read the manuscript and analyzed their methods and data, and revised the comment points and this manuscript. All authors read and approved the final manuscript.

Authors' information

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Competing interests

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Consent for publication

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Ethical approval and consent to participate

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