

LETTER

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Does ulinastatin really reduce incidence of acute kidney injury after cardiac surgery?

Fu-Shan Xue*, Gao-Pu Liu and Chao Sun

See related research by Wan et al. <http://ccforum.biomedcentral.com/articles/10.1186/s13054-016-1207-7>

In a retrospective analysis by Wan and colleagues [1], propensity score matching analysis showed that ulinastatin administration was associated with a decreased incidence of acute kidney injury (AKI) after cardiac surgery. Paradoxically, patient outcomes, including intensive care unit (ICU) length of stay, in-hospital length of stay, and mortality, were not significantly different between the ulinastatin and control groups, although AKI has been significantly associated with increased morbidity and mortality after cardiac surgery [2].

An issue with this study is that it did not report cardiovascular medicine administration. It has been shown that preoperative statin is associated with a reduced risk of postoperative AKI and mortality in patients undergoing elective cardiac surgery [3]. However, preoperative use of renin-angiotensin system inhibitors has been associated

with a 28 % increase in AKI after cardiac surgery and this effect is independent of intraoperative and postoperative hypotension, suggesting a role for the changes in glomerular capillary pressure induced by these drugs [4]. Similarly, it was unclear whether the two groups were comparable with respect to types of cardiac surgery. The risk of AKI and mortality after cardiac surgery increases progressively with complexity of the planned procedure, i.e., the risk is lowest in patients undergoing coronary artery bypass grafting only, while it increases after valve replacement surgery and is greatest after combined coronary artery bypass grafting and valve procedures [5]. We are concerned that the lack of inclusion of these risk factors in the propensity score matching model would have biased the effect of ulinastatin administration on postoperative AKI and mortality in this study.

Authors' response

Xin Wan, Xiangcheng Xie, Yasser Gendoo, Xin Chen, Xiaobing Ji and Changchun Cao

We appreciate the valuable comments by Dr. Xue and colleagues regarding our article and agree that perioperative medications may in fact be involved in the development of AKI.

The protective role of statins remains a controversial issue. On one hand, they have been shown to possess anti-inflammatory properties by effectively reducing inflammatory cytokines. However, a systemic review containing seven randomized controlled trials did not find evidence that preoperative statin use is associated with a reduction in the incidence of AKI after cardiac surgery [6]. This issue has also been discussed in *Critical Care* [7].

In our study, we initially took medications into account, which included statins, phosphocreatine, non-steroidal anti-inflammatory drugs, hydroxyethyl starch,

and mannitol. Using multiple logistic regression analysis, our results showed no obvious protective effect of the phosphocreatine and statins in reducing the risk of AKI (data not shown). However, we found that ulinastatin played a protective role in the development of cardiac surgery-associated (CSA)-AKI after adjusting for statins and other factors. Therefore, we further performed propensity matching to confirm the result.

To date, the risk factors for AKI have been well studied [8]. We do agree that the risk of developing AKI is associated with the types of cardiac surgery and the complexity of the operation, which includes variables such as different cardiopulmonary bypass duration, hypothermia, mean artery pressure, transfusion, hematocrit, and so forth. These cardinal possible risk factors were considered and included in our study design, thus making the two groups relatively comparable. In addition, because this is a retrospective study, other medications which may also have had an impact on the development of AKI, such as antibiotics, diuretics, steroids, angiotensin converting enzyme

* Correspondence: xuefushan@aliyun.com

Department of Anesthesiology, Plastic Surgery Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100144, People's Republic of China

inhibitors/angiotensin-receptor blockers, and so forth, were not analyzed. We do acknowledge the possible existence of bias, and thus prospective, randomized, controlled trials with a large sample size and perioperative administration of ulinastatin are needed to confirm the reno-protective effect of ulinastatin in the development of CSA-AKI.

Abbreviations

AKI: acute kidney injury; CSA: cardiac surgery-associated; ICU: intensive care unit.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

F-SX carefully read the manuscript of Wan et al., analyzed their methods and data, suggested comment points, drafted this manuscript, and is the author responsible for this manuscript. G-PL carefully read the manuscript of Wan et al., analyzed their methods and data, and revised the comment points and this manuscript. CS read the manuscript of Wan et al. and helped to analyze their methods and data and revised the comment points. All authors have read and approved the final manuscript.

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