Peer Review File

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Reviewer Comments

Comment 1: This study population was biased because higher proportion of patients had severe AKI when compared to previous studies (for example, JASN January 2019, 30 (1) 170-181). Thus, this population does not seem representative of post-non cardiac surgery population.

Reply 1: Thank you for the question. In our study, the incidence of severe AKI (defined as AKI stage ≥2) after surgery was 22.2%, while in the study conducted by Park and colleagues, the incidence of critical AKI (defined as AKI stage ≥2 and AKI that consequently led to post-AKI death or dialysis) was 1.1% in the discovery cohort and 1.5% in the validation cohort, respectively. We thought there were two possible reasons. Firstly, compared to Park's study which included patients in general ward, our study mainly focused on critically ill patients following non-cardiac surgery who had more complex and severe perioperative conditions. Secondly, in our study, postoperative AKI and its severity was defined according to both serum creatinine and urine output criteria, while Park's study only used serum creatinine criteria which might underestimate the incidence of severe AKI.

Changes in the text: We added the above explanations in our discussion (see Page 13, line 268-278).

Comment 2: What timing did you measure serum creatinine after surgery? The timing should be prespecified to evaluate the utility of urine sediment for predicting AKI.

Reply 2: Thank you for your reminding. In our study, serum creatinine was examined at admission to SICU and daily at 6 am within 7 days after surgery.

Changes in the text: We added the time for serum creatinine measurement after surgery (see Page 8, line 171-172).

Comment 3: Please clarify how many patients had CKD.

Reply 3: Thank you for the question. As shown in Table 2, 76 patients had a history of CKD accounting for 11.5% in the whole cohort. The number and percentage of CKD were 29 (8.0%), 25 (16.3%) and 22 (15.0%) in patients without AKI, with mild AKI and with severe AKI, respectively.

Changes in the text: The data of patients with CKD were shown in Table 2.

Comment 4: The sensitivity of UMS was very low and UMS did not seem to be useful in clinical situation. When and what situation do you think is best for measuring UMS after non-cardiac surgery?

Reply 4: Thank you very much for the question. Our study demonstrated that elevated UMS 6 and 12 hours after SICU admission was independently associated with postoperative severe AKI. Considering the limited time window for renal protection, we thought the time point for measuring UMS might be 6 hours after

surgery. Elevated UMS showed a high specificity (93.8%) and negative predictive value (79.5%), while its sensitivity (15.6%) and positive predictive value (41.8%) was low. To improve its usefulness in clinical situation, we further analyzed risk factors related to the development of postoperative severe AKI (Additional file 4: Table S4) and the results showed that age (y) [OR 1.026 (95% CI 1.010-1.042)], BMI (kg/m2) [OR 1.082 (95% CI 1.028-1.140)], preoperative albumin (g/L) [OR 0.956 (95% CI 0.919-0.994)] and intraoperative urine output (ml/kg.h) [OR 0.818 (95% CI 0.688-0.972)] were independently associated with severe AKI. Therefore, on one hand, urine microscopy early after non-cardiac surgery could be used as a measurement assisting severe AKI exclusion in patients with risk factors, such as higher age and BMI, preoperative hypoalbuminemia and intraoperative oliguria. On the other hand, urine microscopy could be combined with other more sensitive novel injury biomarkers to improve early AKI detection, such as neutrophil gelatinase-associated lipocalin and kidney injury molecule-1.
Changes in the text: We added Table S4 for analyzing risk factors of postoperative severe AKI. The results of analyzing risk factors of postoperative severe AKI were described in Page 12, line 245-250. The suggestions for measuring UMS were added in Page 16, line 334-345.

Comment 5: Please describe positive and negative predictive values of UMS.
Reply 5: Thank you for your reminding. The positive predictive values of UMS ≥3 and ≥1 6 hours after surgery for severe AKI were 50.0% (95% CI 25.5-74.5%) and 41.8% (95% CI 28.8-54.8%), and the negative predictive values were 78.4% (95% CI 75.2-81.6%) and 79.5% (95% CI 76.3-82.7%), respectively.
Changes in the text: We added the positive and negative predictive values of UMS (see Page 11-12, line 240-243).

Comment 6: Table 3. Was urine output measured at intra or postoperative period? In addition, there is a trend that patients with severe AKI had less fluid balance, which indicates that severe AKI were caused partly by pre-renal factor.
Reply 6: Thank you very much. In our study, urine output was measured at intra- or post-operative period. As shown in Table 3, patients with severe AKI had significantly reduced intraoperative and D0 (the day of surgery) urine output. Furthermore, although severe AKI patients had more positive D0 fluid balance, there was a trend that they received less fluid balance during surgery. Therefore, pre-renal factor might partly contribute to the development of severe AKI. Urine microscopy examination was very helpful in differentiating structural AKI from those functional AKI. A purely pre-renal AKI often resulted in urinary sediment that was bland or characterized by hyaline casts, while the presence of RTECs or RTEC/granular casts usually indicated tubular structural injury.
Changes in the text: We added the data of D0 fluid balance and urine output in Table 3, and above analysis in our discussion (see Page 15, line 315-319, 321-325).

Comment 7: If you test inter-observer error, please describe.

Reply 7: Thank you very much. The urine microscopy in our study was examined by specially assigned and experienced investigators from clinical laboratory. As an important part of urinalysis in our hospital, there is a strict protocol for quality control, including inter-observer variability. Specifically, the department of clinical laboratory will conduct inter-observer comparison every 6 months. In which, 5 urine sediment samples with at least 3 abnormal are prepared, and then casts and cells are examined and averaged under at least 20 low power fields (LPF) and 10 high power fields (HPF), respectively. Taking the results from specialist in urine microscopy as reference, the following criteria are adopted. When casts are ≤10 /LPF or >10 /LPF, the difference of results should be <3 /LPF or <5 /LPF, respectively; when cells are ≤10 /HPF, between 10 and 100/HPF or >100 /HPF, the difference of results should be <3 /HPF, <10 /HPF or <20 /HPF, respectively. Furthermore, the urine microscopy of our clinical laboratory is also qualified by external quality assessment from National Center for Clinical Laboratories twice a year and International Organization for Standardization 15189 reassessment every two years. Therefore, we did not perform additional test for inter-observer variability in this study.

Changes in the text: We added the quality control description in the section of Methods (see Page 7, line 140-152).