# The predictors of sepsis-related acute kidney injury

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Sepsis-related acute kidney injury (AKI), involving hemodynamic, microcirculatory, and inflammatory mechanisms, contributes to the major cause of morbidity and mortality in critically ill patients.[1] Therefore, an early identification of any independent factor associated with worse outcome and prompt offering of optimal and goal-directed therapy, called as precision medicine (a revolutionizing advance for the therapy of various kinds of diseases), in which individualized therapies are offered to patients based on the specific genomic and cellular alterations accompanied their disease process, may decrease the morbidity or mortality rate.[2,3] In fact, two items (sepsis and AKI) should be clarified first, since both might be independent; might be correlated with each other, and one might be the end of the other. The definition of sepsis, reported in 2016 is a life-threatening organ dysfunction caused by as dysregulated host response to infection, represented by an increase in the Sequential (Sepsis-related) Organ Failure Assessment (SOFA) score of 2 points or more.[4] The evaluation items of SOFA include the respiratory system ($PaO_2$ [partial pressure of oxygen]/$FiO_2$ [fraction of inspired oxygen] ratio), coagulation (platelet count, $10^3$/μL), liver (bilirubin, mg/dL), cardiovascular system (mean arterial pressure, mmHg, and administration of vasopressors), central nervous system (Glasgow Coma Scale score), and renal system (serum creatinine, mg/dL, or urine output, mL/day), and all are scored ranged from 0 to 4.[4] The predictive validity for in-hospital mortality of SOFA was not significantly different from that derived from the more complex Logistic Organ Dysfunction System but was superior to that from Systemic Inflammatory Response Syndrome, supporting the use of SOFA in clinical criteria for sepsis.[5,6] Therefore, we believe that scoring system, which combines many parameters, may be a more reliable tool to predict the outcome of patients with sepsis.

AKI is defined principally by changes in serum creatinine (sCr) concentrations and categorized into stages defined by the degree of increase in sCr, as patients with AKI are not in the steady state and their concentrations of sCr inadequately reflect the real renal function (e.g., glomerular filtration rate); therefore, for clinical studies evaluating diagnostics and therapeutics, clinical adjudication of AKI is essential and preferred.[7] Based on the aforementioned, it may not be easy to use one point to calculate the data to predict the outcome of patients with AKI.

Aforementioned findings raise our interest to read the recent one article entitled "Relationship between platelet/lymphocyte ratio and prognosis of patients with septic acute kidney injury: A pilot study" published in the last November issue of the *Journal of the Chinese Medical Association*.[8]

Similar to our previous doubts about the value of using the parameters obtained from simple peripheral blood test in the prediction of outcomes of diseases,[9–11] although some are successful,[12,13] this publication should be read very carefully and their conclusion should be inspected. The following is our explanation.

First, statistical significance should be carefully interpreted whether this "significance" is clinically meaningful, since we do not believe that it can be a reflective of clinical significance. Statistical significance only indicates the reliability of the study results, and it is highly influenced by sample size.[14] If the sample size was big enough, even small treatment effects can appear statistically significant. We recommend that only clinical significance can be applied in clinical practice. Clinical significance is a reflective of "the extent of change," whether the change makes a real difference to subject lives, how long the effects last, consumer acceptability, cost-effectiveness and ease of implementation.[14] Unfortunately, nearly all physicians who conduct any clinical research prefer their interpretation of their results with the statistical significance, which can be directly transferred as being clinically important. The above-belief is based on the fact that many people equate "significance" with its literal meaning of "importance".[14] We should be kept in mind to avoid this misinterpretation.

Second, in clinical research, we often use the "patient-reported outcome measures (PROMs)" to provide a somewhat objective measurement of patient progress with respect to their management. In fact, PROMs are particularly valuable to demonstrate how healthcare interventions may affect various aspects of a personal quality of life and serve as a mechanism to monitor the therapeutic effectiveness.[15]

In the current study by Chen et al,[8] the authors tried to evaluate the role of subgroups of complete blood counts test in the prediction of outcome of patients with sepsis-related AKI, and they found that mechanical ventilation, platelet count, platelet/lymphocyte ratio, and arterial blood lactate concentration have a correlation with worse outcome of patients with sepsis-related AKI, and further multivariate analysis also showed that only mechanical ventilation and platelet/lymphocyte ratio were an

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independent factor associated with mortality in patients with sepsis-associated AKI.[8] Furthermore, Spearman correlation analysis of four parameters showed that either platelet/lymphocyte ratio or platelet counts were strongly correlated with outcomes of patients with sepsis-related AKI.[8] Although the success of publication in their article, we do not think that the finding of the current study can be used in clinical practice. To evaluate specific items, which are not included in the original SOFA, such as platelet/lymphocyte ratio, the baseline analysis should include all items of the SOFA. We found that the authors missed some of important items, for example, urine output, serum bilirubin level, the administration of vasopressors (dopamine, dobutamine, epinephrine, norepinephrine, etc.), Glasgow Coma scale. They hinted the possibility of selection bias. In addition, some data may be misinterpreted, as noted by audience.[16] That is why we recommended that the finding of Dr. Chen's article should be carefully interpreted.

Finally, we totally agree with Ranganathan's reminding that audience should keep in mind that interpretation of results from any study should be taken into consideration by looking at the actual therapeutic efficacy with confidence interval and should not be limited on the statistical significance.[14] In addition, if the statistical significance cannot be reflected by clinical significance, its application for clinical practice needs much evidence.

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