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Letter to the Editor

Citrulline and metabolomics in acute kidney injury

Dear Editor,

We have very much appreciated the article by Sun et al. [1], regarding the application of metabolomics to recognize the early patterns of acute kidney injury (AKI). Although they define the article a "pilot study", they report on a very important issue and promising methodology. Our question may be too simple, given the advanced conception of their study, however, we would like to ask whether they evaluated the significance of citrulline. This amino acid was not mentioned in the article [1], perhaps because it was not considered in the measurements, or because it performed less well than other metabolites. Our question stems from the circumstances that citrulline metabolism and kidney function are tightly interrelated, and that the superiority of increased citrulline levels, compared to increased blood urea nitrogen or creatinine levels, has repeatedly been claimed in the assessment of chronic renal failure (at least in the presence of integer small intestine, which is the largest source of circulating citrulline) [2–6]. Conversely the role of citrulline in AKI is less well ascertained [6–8] at least to our knowledge. The findings by Sun et al. [1] were generally consistent with our own experience on plasma amino acids. However, in measurements from a closely monitored patient with post-traumatic sepsis, not only we found an overall direct correlation between citrulline and creatinine ($r = 0.52$, $p < 0.001$) but, during the onset of AKI, a steady increase in citrulline anticipated by about 36 h both increase in creatinine and contraction of urine output. This might support a role of citrulline as an early marker of AKI, although we could not verify the phenomenon in other less closely monitored patients. If true, this would also help to better fit the general aims of the study performed by Sun et al. [1], and better explains the purpose of our letter. We congratulate once more the authors for their important investigation.

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