Is creatinine alone a suitable marker for acute kidney injury in critical care?

A standardized definition of acute kidney injury is of benefit in identifying populations at risk of acute kidney injury and as an endpoint in trials of its prevention or treatment. Retrospective observational studies of acute kidney injury frequently rely on functional criteria which are based on changes in serum creatinine concentrations. However, the utility of serum levels of creatinine is complicated by various confounders (Liang and Palevsky, 2018).

Creatinine alone is sufficient

Udeh et al (2018) reported an association between hyperoncotic albumin exposure and acute kidney injury in a retrospective sample of postoperative shock patients from a database of critical care patients from a single American centre. To assess the impact of albumin, patients who received a 25% albumin preparation during the first 48 hours of shock resuscitation in the intensive care unit were identified. A total of 11 512 perioperative (mostly cardiac surgery) patients with shock were included. Subsets of 3600 were selected for analyses after propensity score and matching on demographics, comorbidities and >30 treatment variables.

As assessed 48 hours after intensive care unit admission, there was increased occurrence of acute kidney injury (defined by changes in serum creatinine concentration) in shock patients in the intensive care unit who had been exposed early to hyperoncotic albumin. The results of the study were interpreted as confirming the nephrotoxic potential of hyperoncotic albumin (Udeh et al, 2018).

Dr Christian J Wiedermann, Associated Researcher, Institute of Public Health, Medical Decision Making and HTA, University of Health Sciences, Medical Informatics and Technology, Hall, Tyrol, Austria (christian.wiedermann@ext.umit.at)

Other markers are needed as well

As volume resuscitation may lead to confounding changes in creatinine concentration independent of renal function, randomized controlled trials using standardized definitions of acute kidney injury in a reliable manner are therefore of relevance, particularly when investigating the nephrotoxic potential of hyperoncotic albumin. Volume resuscitation with administration of hyperoncotic albumin exerts higher osmotic pressure relative to human plasma and could limit organ damage in shock states by achieving haemodynamic goals with smaller fluid volumes and avoiding adverse consequences of hypervolaemia (Zampieri and Hjortrup, 2018).

For albumin infusion in patients with severe sepsis and septic shock, randomized controlled trials have revealed no evidence of attributable renal harm including acute kidney injury (Wiedermann and Joannidis, 2015). This is difficult to reconcile with the results of observational studies reporting an increased risk of acute kidney injury associated with albumin administration for resuscitation in patients with shock and those who have undergone cardiac surgery.

In an international multicentre controlled trial by Mårtensson et al (2018), 330 low-risk hypotensive patients were randomized to receive 20% or 4–5% albumin preparations in the first 48 hours after intensive care unit admission, mostly after elective surgical procedures. The net effect of the trial intervention was a 570 ml lower fluid balance in patients receiving 20% albumin – 450 ml less fluid was given and there was an increase of 3 g/litre in albumin levels while having a similar urinary output. No sign of increased acute kidney injury was seen in the 20% albumin group (Mårtensson et al, 2018).

Conclusions

The definition and staging of acute kidney injury in the study by Udeh et al (2018) and the assessment of renal function as a secondary outcome parameter in the study by Mårtensson et al (2018) were both based on changes in serum creatinine concentrations. Confounders of serum creatinine concentrations include rhabdomyolysis after prolonged surgery, drugs, and changes in volume distribution after acute volume overload which may all affect the definition of acute kidney injury, particularly in high-risk patients with postoperative shock, independently of true changes in renal function (Liang and Palevsky, 2018).

The findings of Mårtensson et al (2018) not only support the safety of further exploration of resuscitation with 20–25% albumin in larger randomized trials but also indirectly invalidate the definition and staging of early acute kidney injury in patients with postoperative shock exclusively by using serum creatinine concentrations. **BJHM**

Liang KV, Palevsky PM. 2018. Definition and classification of acute kidney injury. In: Waikar SS, Murray PT, Singh AK, eds. Core Concepts in Acute Kidney Injury. New York (NY): Springer: 13–22.

Mårtensson J, Bihari S, Bannard-Smith J et al. Small volume resuscitation with 20% albumin in intensive care: physiological effects. Intensive Care Med. 2018 Nov;44(11):1797–1806. https://doi.org/10.1007/s00134-018-5253-2

Udeh CI, You J, Wanek MR et al. Acute kidney injury in postoperative shock: is hyperoncotic albumin administration an unrecognized resuscitation risk factor? Perioper Med (Lond). 2018 Dec;7(1):29. https://doi.org/10.1186/s13741-018-0110-y

Wiedermann CJ, Joannidis M. Nephroprotective potential of human albumin infusion: a narrative review. Gastroenterol Res Pract. 2015;2015:1–8. https://doi.org/10.1155/2015/912839

Zampieri FG, Hjortrup PB. Moving albumin into the small volume resuscitation era. Intensive Care Med. 2018 Nov;44(11):1967–1969. https://doi.org/10.1007/s00134-018-5313-7

Anaesthetic and critical care dilemmas are coordinated by **Dr Yasser Mandour**, Anaesthetic Registrar (ST7), Royal Free London NHS Foundation Trust, London and **Dr Anna Petsas**, Specialist Registrar in Anaesthesia and Intensive Care, Guy's and St Thomas' Hospital, London