AKI biomarkers: what's new in 2019?

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Acute Kidney Injury (AKI) is a clinico-biological syndrome that affects up to 75% of critically ill patients. It encompasses the entire spectrum of acute renal dysfunction, from minor alterations of glomerular filtration rate to the need of renal replacement therapy (RRT). AKI is also a strong risk factor of increased morbidity and mortality. Indeed, the short-term mortality rate of critically-ill patients with AKI requiring RRT reaches 50-60%. Importantly, diagnosis of AKI is currently made based on two functional criteria (serum creatinine and urine output), according to the KDIGO classification. Because it is well-known that these 2 criteria exhibit many limitations, a lot of attention has been paid over the last two decades on the development of new molecules that could perform better not only for AKI prediction but also for AKI etiology and prognosis.

Dozens of biomarkers have been proposed, assessed, studied in animal works and in humans (many different clinical settings in adults and children). Millions of data have been reported in more than 2000 publications referenced on Pubmed. Although some of these "new" biomarkers have shown very good performance for AKI prediction (e.g TIMP2-IGFBP7, NGAL, proenkephalin A 119-159), none of them is currently widely used in daily clinical practice. The explanation for this paradigm seems to be at least double. First, many clinicians have strongly argued that knowing in advance AKI is imminent, or will be developing within the next few hours, does not help them much. Indeed, these doctors usually explain that they already do everything possible in their practice to prevent AKI! In fact, it is today clearly demonstrated that, in reality, doctors do not act as they pretend to act or as they think they act and do not correctly follow guidelines and recommendations. Thus, it seems wise to say that we all could do much more in our practice to prevent AKI (e.g. more hemodynamic monitoring, less exposure to nephrotoxic agents). Second, the cost of these AKI biomarkers (as compared to serum creatinine) has also been identified as a significant barrier for their wide acceptance in daily clinical practice. Importantly, medical literature has recently reopened the debate. Two major publications recently reported that prevention of surgery associated AKI was possible when urinary biomarker Tissue Inhibitor of MetalloProteases 2 – Insulin-like Growth Factor Binding Protein 7 (TIMP2-IGFBP7) was used to identify patients at high risk for postoperative AKI. In those high-risk patients, the implementation of a "KDIGO bundle" led to a major decrease of AKI frequency and severity. This was observed in cardiac surgery patients and in major non cardiac surgery patients (1,2). Moreover, in sepsis, the leading cause of AKI in the ICU, proenkephalin A 119-159 level at ICU admission is strongly associated with major adverse kidney events (MAKEs) at day 7, persistent AKI and worsening renal function (3).

To conclude, it is in 2019 definitively untrue to state that "new" AKI biomarkers are just useless for clinical practice. In fact, it is probably just a matter of time before international experts make some clear recommendation on how to precisely use them in daily clinical practice. Taking these considerations to the extreme, one could very seriously imagine that some "damage" biomarkers will be one day part of a future new definition of AKI. Only time will tell…

Le Professeur Thomas RIMMELÉ abordera ces considérations lors de la session Rein, le jeudi 12 décembre 2019, entre 09h00 et 10h30.

References

1. Meersch et al. Intensive Care Med 2017
2. Gözce et al. Annals of surgery 2017
3. Hollinger et al. Kidney Int Rep 2018