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EDITORIAL

Predictions are difficult…especially about AKI

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Predicting AKI

Acute kidney injury (AKI) has been recognised as a major public health problem. Identifying patients at high risk of AKI and diagnosing AKI early are major goals worldwide. The definition of AKI is based on oliguria and elevated serum creatinine levels, two functional markers that are notoriously imperfect [1, 2]. Oliguria is neither sensitive nor specific [1, 3]. It can occur as result of renal injury but may also simply reflect an adaptive physiological response to both intracellular dehydration and hypovolemia [1]. Indeed, only a small proportion of patients in the intensive care unit (ICU) with oliguria have a sustained drop in glomerular filtration rate that leads to a rise in serum creatinine [1]. Serum creatinine is a late marker of renal function. Even when looking at a small rise in serum creatinine of 0.3 mg/dl, which would classify as AKI stage 1 according to current Kidney Disease/Improving Global Outcomes (KDIGO) criteria, acute deterioration in renal function may not be noticeable for >24 h, especially in critically ill patients with fluid accumulation and reduced creatinine generation [4]. These limitations and delays in diagnosis may explain why results from various intervention trials were negative and therapies for AKI are still lacking [5].

Numerous attempts have been made to identify high-risk patients and diagnose AKI earlier, ranging from the search for biomarkers to the development of scoring systems and the introduction of "AKI sniffers". Both functional biomarkers and markers of injury have been identified which detect subclinical insult or facilitate the diagnosis of AKI early [6]. Unfortunately, following initial enthusiasm, it has become clear that most biomarkers have important shortcomings and limited utility at the bedside [7, 8]. There are several potential explanations for their disappointing performance in clinical studies, including lack of a gold standard to define AKI, inclusion of patients with already overt AKI and absence of relevant patient outcomes. Clinical prediction scores to identify patients at risk of AKI have been developed with variable success in different cohorts, such as patients undergoing cardiac surgery or those being treated in the emergency department [9]. In addition to alerting clinicians and warning patients, they may prove to be useful in selecting patients for future prevention or intervention studies or for identifying those in whom biomarker testing should be undertaken. However, in the ICU, AKI scores usually have a limited role since most patients are considered to be at intermediate risk, especially following emergency or cardiac surgery [10]. Last, "AKI sniffers", although useful in alerting physicians earlier of a deterioration in renal function, have yet to prove their role in improving the process of care or clinically relevant outcomes [11].

In a recent article published in *Intensive Care Medicine*, Flechet et al. report the development of an electronic AKI prediction calculator [12]. In a post hoc analysis of the EPaNIC dataset, the authors analysed the data of 4490 patients with the aim to develop and validate a clinical model to predict the onset of AKI during the first 7 days in the ICU. Patients with AKI at ICU admission were excluded. AKI was defined as any stage of AKI according to the serum creatinine criteria of the KDIGO definition. The patients were divided into a development cohort and a matched validation cohort, and four models were developed using baseline parameters and characteristics at admission, during the first day in the ICU and after 24 h of ICU stay. The performance of these models proved to be fair to good in predicting subsequent development of

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AKI [9]. Not surprisingly, models that included kinetic data performed the best [8]. Interestingly, and in keeping with previously published data, the biomarker neutrophil gelatinase-associated lipocalin measured on admission to ICU performed only modestly in predicting AKI and was not superior to clinical prediction models [13].

The data were thoroughly analysed, interpreted and discussed, and the online programme has been made publicly available. Undoubtedly, this is major step forward towards the global aim of recognising AKI early and improving the outcome of patients with AKI. However, the enthusiasm needs to be tempered slightly by important limitations. First, the majority of patients (>80%) included in the database were patients admitted after surgery, in two-thirds of cases following cardiac surgery. Therefore, the application of these results to more general patient populations will need to be explored in future studies. In addition, the diagnosis of AKI was based only on the serum creatinine criteria of the KDIGO definition due to lack of hourly urine output data. Since previous studies demonstrated that up to one-third of ICU patients may develop AKI according to urine output criteria alone without a rise in serum creatinine [14], it is possible that a significant number of patients were misclassified. This may also explain the surprisingly low number of patients with AKI on admission to ICU [15]. However, the authors did not completely ignore changes in urinary output. Although they did not use urine output as an endpoint to define AKI, urine output and its slope were included in the day 1 and day +1 model. Thus, urinary output is an important component of the calculator. Finally, repeat prospective validation studies are necessary before the "predictor" can be adopted outside the research arena.

Despite these limitations, the authors need to be congratulated. They embarked on an area that has been insufficiently studied but has potential to be as interesting as biomarkers, a field that has enjoyed excessive but imperfect research. In doing so, they succeeded in developing an AKI risk prediction model that deserves to be investigated further. The next step towards personalized medicine would be a combination of biomarker assessment and an individualised prediction tool (Fig. 1). In isolation, risk scores tend to give an overall probability for an incidence or insult at population level but are usually not sufficient to determine an individual patient's risk. Biomarkers reflect pathophysiological processes which may translate into overt AKI in some patients, but the indiscriminate measurement of biomarkers is neither useful nor affordable. Furthermore, their performance is strongly dependent on the patient cohort, and a change of endpoint prevalence in the population of interest is likely to influence the diagnostic performance of the test as much as the clinical relevance. Once validated, AKI prediction scores like the one developed by Flechet and colleagues [12] may serve as powerful tools to select populations of interest for biomarker testing and future intervention studies.

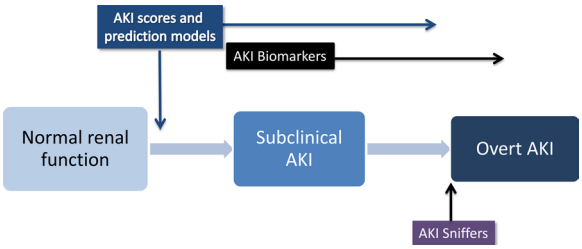

Fig. 1 Diagnostic tools for early detection of acute kidney injury (*AKI*)

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Compliance with ethical standards

Conflicts of interest
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