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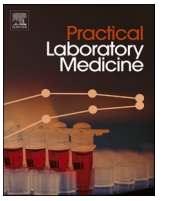

Advances in laboratory detection of acute kidney injury

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It has been a decade since the publication of the 2012 Kidney Disease Improving Global Outcomes (KDIGO) guideline on acute kidney injury (AKI) that established a universal definition for the disease and provided helpful guidance to practitioners caring for adults and children at risk for or with AKI [1]. The time since that seminal publication has brought significant advances in how we think about and detect AKI; with the emergence of novel structural and functional AKI biomarkers, development of automated alerts to help expedite detection of the disease, new creatinine-based definition proposed by leading laboratory organizations like the AACC Academy [2], and the evolution of machine learning tools for AKI prediction. In this special issue, my goal was to summarize the state of these advances and highlight the most important developments in this field that can help improve our ability to detect this silent and deadly disease.

Acute kidney injury represents a sudden deterioration in kidney function, usually within 48 hours, that occurs in about 15% of hospitalized patients and over 50% of those in the intensive care unit, and can lead to serious complications, including irreversible kidney damage and death [3]. It is defined by the Kidney Disease Improving Global Outcomes (KDIGO) 2012 guidelines based on a rise in serum creatinine or fall in urine output [1]. However, that definition has been challenged in recent years because it failed to account for the analytical and biological variability of creatinine [2], and it needed updating to account for the changes we see with structural biomarkers that have emerged since. In this issue, Hasson et al. [4] review what we know about these emerging biomarkers, including Cystatin C, urine neutrophil gelatinase associated lipocalin (NGAL) and the urinary product of tissue inhibitor metalloproteinase (TIMP-2) and insulin growth factor binding protein-7 (IGFBP7), including how they have been used to delineate AKI phenotypes. In their review, Hasson et al. [4] focus on those markers that are closest to clinical practice and that have already received regulatory approval in the U.S. or Europe. However, other unapproved biomarkers, such as proenkephalin or interleukins 6 (IL-6), IL-8 and IL-18, are also being evaluated for their ability to detect AKI, which is why meta-analyses like the one provided by Yousefifard et al. [5] are essential to understand how well these are performing and if they hold any promise for clinical care. In the case of urinary IL-18 and serum IL-6 and IL-8, their meta-analysis shows that while levels of these markers are higher in AKI patients compared to the control group, their sensitivity and specificity is poor, which questions their diagnostic value [5]. While Lima et al. [6] demonstrated in a small subset of liver transplant patients (n\xA0=\xA057) that proenkephalin may hold promise for greater accuracy and earlier rise than creatinine in patients with severe AKI.

Shifting our attention to creatinine, an old marker, but one that keeps demonstrating its increased value over time as our understanding of AKI evolves. In this issue, Gorelik et al. [7] use large-data analysis to demonstrate how monitoring day-to-day changes in creatinine among inpatients can help identify radiocontrast-induced nephropathy. While Ivica et al. [8] review the performance of using electronic alerts (e-alerts) based on changes in serum creatinine measured in the clinical laboratory, and their ability to improve

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clinical outcomes. They nicely summarize the problems with the current approaches used by institutions who have tried implementing e-alerts but had unfavorable outcomes, and then provide key recommendations to improve their performance [8].

Urine is another important testing matrix when evaluating AKI, with Tran et al. [9] demonstrating the importance of measuring urine albumin, dipstick blood and urine uromodulin to differentiate glomerular from tubulointerstitial diseases. While Hoenig et al. [10] used a case-based approach to highlight the importance of using manual urine microscopy in patients with AKI to improve clinical care.

Other interesting developments reported in this special include: 1) the potential association of high vancomycin trough concentration with AKI during combination therapy of piperacillin/tazobactam and vancomycin that would require careful monitoring of vancomycin concentrations to prevent AKI progression and deserves confirmation in larger trials, as reported by Saito et al. [11], and 2) the effect of acute changes in glomerular filtration rate, as happens during AKI, on common biochemical tests, as reported by Jones and Chung [12]. Interestingly, Jones and Chung show that out of the 28 common biochemistry tests they investigated, seven had significant changes while 21 did not. These were serum urea, phosphate, urate, parathyroid hormone, troponin T, B-natriuretic peptide (BNP) and NT-proBNP. This has significant implications for clinical teams interpreting results involving AKI patients, so they do not misinterpret blood test results involving these analytes.

In summary, this special issue dedicated to the advances in laboratory detection of AKI demonstrates how far we have come in the last decade. However, significant challenges for the adoption of new biomarkers, e-alerts and new creatinine definitions remain. Ultimately, it will all come down to their ability to improve clinical outcomes, with many of these studies currently ongoing. Hopefully, the author insights provided within this issue will help inform current and future studies so we can better detect, predict and ultimately prevent AKI. The emergence of artificial intelligence tools for that purpose also provides hope that we may make more concrete progress towards these goals in the next decade [13].

Declaration of competing interest

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