ACUTE KIDNEY INJURY
Timing of biomarker increases in acute kidney injury

A study reported in the *Journal of the American College of Cardiology* has shown the timing of elevation of predictive biomarkers in acute kidney injury (AKI).

As an increase in serum creatinine level is a delayed marker of AKI in the acute setting, numerous studies have investigated various potential early biomarkers of AKI to enable earlier intervention. Urinary levels of neutrophil gelatinase-associated lipocalin (NGAL), interleukin (IL)-18, liver fatty acid binding protein (L-FABP) and kidney injury molecule (KIM)-1 have all been shown to be increased early after AKI, but most studies have only investigated these biomarkers individually.

Krawczeski and colleagues set out to investigate the timing of elevation of each of these biomarkers in children who developed AKI following cardiac surgery. The researchers analyzed data from 220 patients aged <18 years who had undergone cardiac surgery with cardiopulmonary bypass (CPB). Urine samples for biomarker analysis were taken immediately before initiation of CPB and at 2 h, 6 h, 12 h and 24 h after CPB. The primary outcome was the development of AKI, defined as a ≥50% increase in serum creatinine level from the preoperative baseline level within 48 h after surgery.

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AKI occurred in 60 patients. Patients who developed AKI were younger and had lower baseline serum creatinine levels than those without AKI. The researchers found that urinary levels of each of the four biomarkers increased significantly at some point after initiation of CPB in patients with AKI. Significant differences between children with and without AKI were seen after 2 h for NGAL, after 6 h for IL-18 and L-FABP, and after 12 h for KIM-1. A stepwise increase in urinary levels of each biomarker was seen with worsening severity of AKI for all biomarkers, apart from IL-18 in children with pRIFLE-F (pediatric-modified Risk, Injury, Failure, Loss, and End-stage renal disease: 'Failure'). Urinary NGAL level had the best predictive ability up to 12 h, although at 24 h it was not superior to IL-18 or KIM-1. Adding the biomarkers to a clinical model of age and CPB time was found to improve prediction, and using combinations of biomarkers further improved the performance of predictive models.

"The application of biomarker technology to create a bedside AKI "panel" could allow clinicians the ability to pinpoint the timing of insult to the kidney and perhaps direct therapeutic interventions," state the authors.

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Original article Krawczeski, C. D. *et al.* Temporal relationship and predictive value of urinary acute kidney injury biomarkers after pediatric cardiopulmonary bypass. *J. Am. Coll. Cardiol.* **58**, 2301–2309 (2011)