Even Stage 1 AKI Increases CKD Risk

Even in mild cases with fast recovery, acute kidney injury (AKI) developing in the hospital is a strong risk factor for chronic kidney disease (CKD) at follow-up, reports a study in *The American Journal of Kidney Disease*.

Using Veterans Health Administration data for 2011, the investigators identified nearly 105,000 hospitalized patients with normal baseline kidney function, no diagnosed kidney disease, and at least 2 inpatient serum creatinine measurements. With varying follow-up times, the risk of CKD associated with AKI was analyzed. The analysis included not only the stage of AKI, but also the pattern of recovery: within 2 days (fast), 3 to 10 days (intermediate), and no recovery within 10 days (slow or unknown).

Ninety-one percent of AKI episodes were stage 1; recovery occurred within 2 days in 71% of cases. By one year, CKD had developed in 18.2% of patients: 31.8% of those with AKI versus 15.5% without AKI. Among patients with stage 1 AKI, risk of CKD increased with time to recovery. Adjusted relative risk ratio for CKD stage 3 or higher was 1.43 for fast, 2.00 for intermediate, and 2.65 for slow/unknown recovery. The relative risks were about the same on subgroup and sensitivity analyses.

In this cohort of veterans, inpatient AKI is associated with an elevated risk of developing CKD during follow-up, the risk is significant even for the large group of patients with stage 1 AKI, and increases further with longer time to recovery. The authors discuss the implications for postdischarge follow-up of patients with inpatient AKI [Heung M, et al. Acute kidney injury recovery pattern and subsequent risk of CKD: an analysis of Veterans Health Administration data. *Am J Kidney Dis* 2016; 67:742–752].

New Equations Can Estimate Residual Kidney Function

Residual kidney function (RKF) in dialysis patients can be estimated by equations based on serum measures of endogenous filtration markers, avoiding the need for prolonged timed urine collections, reports a study in *Transplantation*.

Closely supervised 24-hour urine clearance values were obtained in a cohort of 44 dialysis patients in Baltimore. The researchers developed dialysis-specific equations to estimate urinary urea clearance, based on serum endogenous filtration markers. They then validated the equations in 826 patients from an external cohort of Dutch dialysis patients.

Median urinary urea clearance values were 2.6 mL/min in the development cohort and 2.4 mL/min in the validation cohort. During 24-hour urine collection, concentrations of most serum filtration markers increased over time, with the exception of β-trace protein (BTP).

The equations developed in the Baltimore cohort showed low bias in the Dutch cohort. Compared to an equation using urea plus creatinine, precision was higher for BTP and β2-microglobulin (B2M) equations, while accuracy was higher for BTP B2M, and cystatin C equations. For detection of a measured urinary urea clearance of 2 mL/min or greater, area under the receiver operator characteristic curve was 0.821 for the BTP equation, 0.850 for the B2M equation, and 0.796 for the cystatin C equation (compared to 0.663 for the urea plus creatinine equation).

Residual kidney function is strongly associated with survival in dialysis patients, but currently must be measured in timed urine collections. The new equations, based on serum filtration markers, can estimate RKF with good performance and diagnostic accuracy.


HLA Mismatch Still Linked to Decreased Allograft Survival

Even in more recent periods, HLA mismatches show a linear association with the outcomes of kidney allograft survival, concludes a study in *Transplantation*.

The analysis included more than 189,000 first adult, deceased-donor, kidney-only transplants performed in the US from 1987 through 2013. Number of HLA mismatches was evaluated for associated-with-kidney-allograft survival, with adjustment for recipient and donor characteristics.

In nearly 995,000 years of follow-up, HLA mismatch was significantly related to allograft survival. In the fully adjusted model, hazard ratio for allograft failure increased in linear fashion with each additional HLA mismatch: from 1.13 with 1 mismatch to 1.98 with 6 mismatches (compared to zero mismatches). The effect of HLA mismatch remained significant after considering the increasing success of kidney transplantation in recent years. Nearly all mismatch categories showed equal effect on the risk of transplant failure, independent of locus.

There are conflicting reports as to the importance of HLA matching as a determinant of kidney allograft survival. The new analysis shows a significant linear relationship of hazard ratios for allograft failure with the number of HLA mismatches—even at a time of better transplant success rates. The investigators conclude that their results “reinforce the importance of optimizing HLA matching to further improve survival in renal allografts in the future” [Williams RC, et al. The risk of transplant failure with HLA mismatch in first adult kidney allografts from deceased donors. *Transplantation* 2016; 100:1094–1102].

Rosuvastatin Linked to Increase in Postoperative AKI

For patients undergoing heart surgery, treatment with rosuvastatin doesn’t reduce the rate of adverse outcomes, but is associated with an increased risk of postoperative acute kidney injury (AKI), according to a randomized trial in *The New England Journal of Medicine*.

The Statin Therapy in Cardiac Surgery (STICS) trial included 1922 patients undergoing elective coronary artery bypass grafting and/or aortic valve replacement. All were in sinus rhythm and not taking antiarrhythmic drug. Patients were randomly assigned to receive rosuvastatin 20 mg/d or placebo, starting up to 8 days before surgery and continuing until 5 days afterward.

The 2 primary outcomes were atrial fibrillation developing within 5 days after surgery (based on Holter electrocardiographic monitoring) and myocardial injury developing within 120 hours (based on troponin T measurement). The wide range of secondary outcomes included AKI, based on Acute Kidney Injury Network criteria.

Postoperative atrial fibrillation occurred in 21% of patients in the rosuvastatin group and 20% in the placebo group. Troponin I release was also similar between groups; primary outcomes were no better with rosuvastatin in any patient subgroup.

Most secondary outcomes were also no different with rosuvastatin versus placebo. However, plasma creatinine increased to a greater extent with rosuvastatin, and remained elevated up to 5 days after surgery. Rates of any AKI at 48 hours were 24.7% with rosuvastatin and 19.3% with placebo. While most cases of AKI were stage 1, there was also a significant excess of stage 2 or 3 AKI (1.8 percentage points).

The STICS results question the recommendation to use perioperative statins to prevent atrial fibrillation and other complications after cardiac surgery. The findings also raise concern about an increased risk of AKI in patients assigned to rosuvastatin. The researchers write, “Given the lack of good evidence of beneficial effects of perioperative statin therapy... the adverse effects on renal function warrant careful consideration” [Zheng Z, et al. Perioperative rosuvastatin in cardiac surgery. *N Engl J Med* 2016; 374:1744–1753].