

leads to vitamin D deficiency. To determine whether vitamin D deficiency is associated with survival in people with renal failure, Wolf *et al.* studied US patients as they began chronic hemodialysis; 60% were classed as having moderately low serum levels of vitamin D, while 18% had extremely low levels.

In a nested case-control analysis, 175 consecutive patients who died within 90 days of beginning dialysis were compared with 750 patients who survived for this period. No patients were receiving vitamin D supplements. Lower serum levels of both forms of vitamin D—but especially of 25-hydroxyvitamin D—increased the risk of early death, independent of standard nutritional factors, residual renal function, comorbidities and other known predictors of mortality in patients on dialysis, as well as biomarkers of mineral metabolism. A survival advantage was conferred by *ad hoc* treatment with activated vitamin D.

The authors suggest that patients with kidney disease should be screened for vitamin D deficiency, and that a randomized controlled trial should be performed to prove that supplementing deficient dialysis patients improves survival.

Original article Wolf M *et al.* (2007) Vitamin D levels and early mortality among incident hemodialysis patients. *Kidney Int* 72: 1004–1013

Higher serum creatinine paradoxically associated with better survival in AKI

Small increases in serum creatinine level are associated with marked increases in mortality. Paradoxically, some studies have indicated that higher serum creatinine concentrations are associated with a greater likelihood of survival of patients with acute kidney injury (AKI).

Cerdá and colleagues studied 134 critically ill patients with AKI who required continuous renal replacement therapy (CRRT). Multivariate logistic regression analysis detected a relationship between a higher serum creatinine level on CRRT initiation and improved survival (odds ratio 1.438; 95% CI 1.034–1.999). Adjusting for the degree of preadmission chronic kidney disease (CKD; defined by glomerular filtration rate estimated with the MDRD equation) reduced the significance of the association, and adjusting for disease severity (Liano score)

eliminated the association altogether; however, adjusting for nutritional status and fluid volume status had no effect.

The authors propose several possible mechanisms for the association of higher serum creatinine levels with better patient survival in AKI. The hypothesis that is best supported by the current analysis is that patients with pre-existing CKD suffer less-severe acute renal damage before requiring initiation of CRRT in a critical care setting than do people without CKD, and as a result have better survival. They propose three other theories that warrant investigation. Firstly, lower serum creatinine level when CRRT is commenced might indicate fluid overload, which is associated with a poor prognosis in AKI. Secondly, serum creatinine levels might not increase rapidly in AKI patients with fluid overload and a low muscle mass, leading to delayed initiation of CRRT and worse outcomes. Thirdly, higher serum creatinine concentrations (indicative of well-nourished patients with appropriate muscle mass) might indicate better health status.

Original article Cerdá J *et al.* (2007) In severe acute kidney injury, a higher serum creatinine is paradoxically associated with better patient survival. *Nephrol Dial Transplant* 22: 2781–2784

Pre-emptive management of polyomavirus BK in pediatric kidney transplant recipients

Polyomavirus BK-associated nephropathy (PVAN) in renal allograft recipients is sometimes controlled through a reduction in the level of immunosuppression. Screening for BK viremia could identify patients at high risk of developing PVAN who might benefit from pre-emptive minimization of immunosuppression, but there is concern that early immunosuppression reduction will induce acute rejection.

A recent study investigated pre-emptive immunosuppression reduction in 62 pediatric kidney transplant recipients followed up for a median of 24 months. Polymerase chain reaction was used to detect BK virus in blood and urine samples taken at regular intervals after transplantation. Doses of maintenance immunosuppressants were tapered in a step-wise manner in viremic patients with increasing viral loads. Renal biopsies were performed to evaluate PVAN presence in viremic patients.

BK viremia was detected in 39 (63%) patients at a median of 3 months (range 1–24 months) after transplantation. BK viremia was detected in 13 (21%) patients at a median of 3 months (range 1–18 months) after transplantation. Pre-emptive reduction of immunosuppression resulted in viremia clearance in all 13 patients, taking a median of 2 months (range 1–8 months). Viremia was cleared in 12 of the 13 viremic patients during the study, taking a median of 8 months. At last follow-up, no PVAN had been detected. Pre-emptive immunosuppression tapering did not cause any cases of acute rejection.

Original article Ginevri F *et al.* (2007) Prospective monitoring of polyomavirus BK replication and impact of pre-emptive intervention in pediatric kidney recipients. *Am J Transplant* 7: 2727–2735

Individualized dosing of MMF is superior to fixed dosing in renal transplant patients

Mycophenolate mofetil (MMF) at a fixed dose of 2 g/day has been approved for the prevention of kidney allograft rejection in adults. The complex pharmacokinetics of MMF mean that actual exposure to the active metabolite of the drug (mycophenolic acid or MPA) can vary substantially between patients and in the same patient over time

Le Meur *et al.* recently developed an accurate model for determining MPA exposure. They have now applied this model during a 12-month, open-label, multicenter study.

Renal transplant recipients on an immunosuppressive regimen of basiliximab, ciclosporin (low target levels), gradual corticosteroid withdrawal and MMF were randomized to receive MMF at doses varied according to the Bayesian model or at fixed doses of 2 g/day ($n=65$ in each group). The target for MPA exposure was 40 mg.h/l. Doses of MMF in the concentration-variable group were individualized at 7 days, 14 days, 1 month, 3 months and 6 months after transplantation.

After 1 year, significantly fewer patients in the group assigned to individualized MMF dosing had experienced treatment failure (a composite end point of death, graft loss, acute rejection and discontinuation of MMF; 29% vs 48%, $P=0.03$). Variation in acute rejection rates accounted for the majority of this difference;

12% of patients in the concentration-variable group experienced an acute rejection episode, compared with 31% of those in the fixed-dose cohort. There were no differences in adverse event frequency between the two groups (>90% for both).

Original article Le Meur Y *et al.* (2007) Individualized mycophenolate mofetil dosing based on drug exposure significantly improves patient outcomes after renal transplantation. *Am J Transplant* 7: 2496–2503

Systematic review of ARB and ACE inhibitor use in kidney transplant recipients

Routine use of angiotensin-converting-enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs) is recommended in proteinuric nontransplant kidney disease patients, to reduce proteinuria and slow progression of chronic kidney disease. Data on use of these drugs in kidney transplant recipients, however, are limited. A recent systematic review analyzed data from 21 randomized controlled trials of ACE inhibitors or ARBs involving 1,549 kidney transplant recipients.

Pooled analyses showed that use of an ACE inhibitor and/or an ARB was associated with a greater decrease in glomerular filtration rate (GFR) than were control management strategies (weighted mean difference [WMD] -5.7 ml/min, 95% CI -8.7 to -2.8 ; $P<0.001$). Baseline GFR, duration of follow-up and time after transplantation did not influence the change in GFR. When analyses were restricted to studies with at least 12 months of follow-up, use of an ACE inhibitor and/or an ARB was associated with a significantly greater decline in proteinuria than were control strategies (WMD -0.47 g/day, 95% CI -0.86 to -0.08 ; $P=0.02$), but there was no difference in the degree to which potassium level changed. Use of either drug was associated with a greater decline in hematocrit than were control strategies (WMD -3.5% , 95% CI -6.1 to -0.95 ; $P=0.007$). Mean arterial blood pressure changes in patients on ACE inhibitors or ARBs were similar to those in controls.

Clinicians should consider the benefits and risks of ACE inhibitors and ARBs before prescribing them to renal transplant recipients.

Original article Hiremath S *et al.* (2007) Renin angiotensin system blockade in kidney transplantation: a systematic review of the evidence. *Am J Transplant* 7: 2350–2360