AKI: fluid overload and mortality

Several observational studies have shown a direct correlation between fluid overload and mortality in critically ill patients with acute kidney injury (AKI). Bouchard *et al.* (*Kidney Int.* doi:10.1038/ki.2009.159) have now reported results of a prospective, multicenter observational study of 618 patients that aimed to determine whether fluid overload (>10% increase in body weight) in critically ill patients with AKI is associated with increased mortality. After adjustment for severity of illness, patients who survived 60 days from enrollment were found to have had a significantly lower level of fluid accumulation at initiation of dialysis ($P = 0.01$) and dialysis cessation ($P = 0.002$) than non-survivors. Similarly, in patients with AKI who did not receive dialysis, those who survived had a lower level of fluid accumulation than non-survivors. Furthermore, a highly significant correlation between mortality and the proportion of dialysis days with fluid overload was found ($P < 0.0001$). Patients with AKI who were treated with continuous renal replacement were more likely to have a reduction in their level of fluid accumulation than those treated with intermittent hemodialysis. After adjustment for severity of disease, patients with AKI and with fluid overload at the time peak serum creatinine levels were recorded were less likely to recover renal function than those with AKI but without fluid overload.

Although results such as these await confirmation in prospective, randomized trials, several reasons exist as to how fluid overload might increase mortality in patients with AKI. Fluid overload in these patients frequently leads to hypoxia and institution of mechanical ventilation. Mechanical ventilation has been shown to be a very serious risk factor for mortality in patients with AKI. Infection is a major cause of mortality in AKI patients and the primary source of infection is the lungs, to an even greater extent than the urinary tract. Many patients with AKI are diagnosed as having adult respiratory distress syndrome (ARDS). Most of these patients, however, have pseudo-ARDS as documented by normal lung compliance and improved oxygenation with fluid removal by dialysis. Systemic hemodynamics remain stable as long as the rate of fluid removal does not exceed the rate of mobilization of interstitial fluid into the vascular compartment. A randomized study by the ARDS clinical trials network (*N. Engl. J. Med.* 354, 2564–2575 [2006]) demonstrated that pulmonary function in critically ill patients was worse in those treated with a liberal fluid management strategy (that is, to achieve a mean central venous pressure of ~12 mmHg) than in those who were treated with a conservative strategy (that is, to achieve a mean central venous pressure ~8 mmHg). Moreover, fewer patients in the conservative strategy group required dialysis than in the liberal strategy group ($P < 0.06$). Thus, no evidence was found to suggest that the liberal approach to fluid management (~8 l positive fluid balance) 'protected' the kidney. As prolonged prerenal azotemia can progress to acute tubular necrosis, prolonged pseudo-ARDS that requires mechanical ventilation can no doubt progress to bona fide ARDS secondary to infection, barotrauma and oxygen toxicity, which could lead to the development of 'stiff lungs'.

What is frequently not recognized is that cardiac function can also be profoundly impaired by fluid overload. Increased venous return can cause cardiac dilatation, increased ventricular wall stress, and functional tricuspid and/or mitral insufficiency. Many patients with AKI already have impaired cardiac function because of the myocardial depression that occurs with increased levels of circulating cytokines, such as tumor necrosis factor. While it is well known that depletion of extracellular fluid volume (ECF) can delay recovery from AKI, cardiac dysfunction in the presence of ECF volume expansion also can delay or prevent recovery from AKI. Another frequently unrecognized factor that can delay recovery from AKI in patients with fluid overload is an increase in renal venous pressure. Increases in renal venous pressure can decrease renal perfusion pressure, increase interstitial pressure and activate the renin–angiotensin system—all of which can contribute to delayed recovery of renal function in patients with AKI.

Thus, there are reasons to believe that fluid overload is not just a marker, but rather a pathological factor of the high mortality (50–70%) of critically ill patients with AKI. Prospective, randomized clinical trials will be needed to confirm this possibility. Until such studies are available, however, the avoidance of fluid overload in patients with AKI on the basis of knowledge of body weight changes and cumulative fluid balance should be standard of care for these patients.

doi:10.1038/nrneph.2009.138

> "...no evidence was found to suggest that the liberal approach to fluid management ... 'protected' the kidney"

Robert W. Schrier is the Editor-in-Chief of *Nature Reviews Nephrology*.

Competing interests
The author declares no competing interests.

© 2009 Macmillan Publishers Limited. All rights reserved