

## DIALYSIS

## Soluble CD14 predicts mortality in hemodialysis patients

Serum level of soluble CD14 (sCD14) is associated with inflammation and is an independent predictor of mortality in patients on hemodialysis, according to two new studies conducted in the US and Sweden.

Inflammation is thought to contribute to the increased risk of mortality in patients with end-stage renal disease (ESRD); however, the etiology of unprovoked inflammation in these patients is unknown. One potential source of inflammation in patients on dialysis is subclinical endotoxemia, which may induce the production of proinflammatory cytokines. The molecule CD14 is upregulated by very low levels of endotoxin and is an effector of endotoxin signaling. To investigate the association between subclinical endotoxemia and mortality in patients with ESRD, Dominic Raj and colleagues assessed serum levels of a soluble form of CD14 (sCD14) in patients on hemodialysis.

In one study, Raj and colleagues investigated sCD14 levels in participants of the Nutritional and Inflammatory Evaluation in Dialysis Study, in Los Angeles, CA, USA. The 310 individuals who were included in this study had been on hemodialysis for at least 8 weeks and were followed for up to 33 months. The researchers found sCD14 levels correlated

with levels of the proinflammatory markers tumor necrosis factor and interleukin 6. Indicators of nutritional status, such as BMI and body fat, correlated negatively with sCD14 level. During follow up, 71 (23%) of patients died. Risk of mortality increased with increasing sCD14 level; patients in the highest tertile of sCD14 level had a twofold higher risk of death than those in the lowest tertile (hazard ratio [HR], 2.59; 95% CI, 1.39–4.83;  $P < 0.05$ ).

In a second study, Raj and colleagues investigated levels of sCD14 and endotoxin in 211 patients undergoing hemodialysis in Stockholm or Uppsala, Sweden. In a univariate analysis, sCD14 levels correlated with endotoxin levels and with levels of inflammatory markers such as C-reactive protein and fibrinogen. In addition, sCD14 levels correlated negatively with surrogates of muscle mass. Overall, 78 (36%) patients died during the mean follow-up of 31 months. As in the previous study, patients in the top tertile of sCD14 level had a twofold greater risk of death than those in the lowest tertile (HR, 1.94; 95% CI, 1.13–3.32;  $P = 0.01$ ).

The researchers say that these studies demonstrate an association between sCD14 level, markers of inflammation, nutritional status and risk of death in patients on hemodialysis. They hope to continue their investigations in a larger



cohort to investigate the association between subclinical endotoxemia and cardiovascular end points in patients with ESRD.

*Susan J. Allison*

**Original articles** Raj, D. S. *et al.* Association of soluble endotoxin receptor CD14 and mortality among patients undergoing hemodialysis. *Am. J. Kidney Dis.* **54**, 1062–1071 (2009) | Raj, D. S. *et al.* Soluble CD14 levels, interleukin 6, and mortality among prevalent hemodialysis patients. *Am. J. Kidney Dis.* **54**, 1072–1080 (2009)