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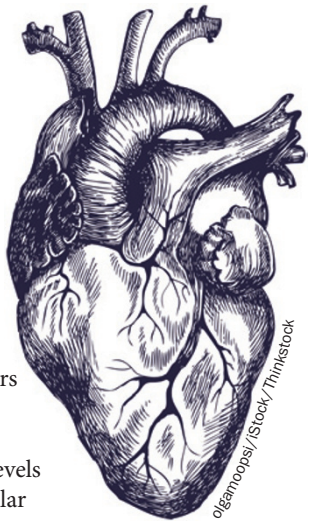
CHRONIC KIDNEY DISEASE

Paradoxical association between serum IL-10 levels and risk of cardiovascular events



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New data from a prospective study suggest that serum levels of the immunoregulatory cytokine IL-10 are associated with increased risk of cardiovascular events in patients with chronic kidney disease (CKD). This finding is somewhat surprising given the reported anti-inflammatory, antithrombotic and anti-atherosclerotic effects of IL-10.

To investigate the relationship between IL-10, inflammation, kidney function and cardiovascular events, Mehmet Kanbay and colleagues analysed levels of IL-10, the proinflammatory cytokine IL-6, markers of inflammation (high-sensitivity C-reactive protein [hsCRP] and pentraxin-3 [PTX-3]) and flow-mediated dilatation (FMD; a surrogate measure of endothelial function) in 403 patients with CKD stages 1–5. Patients were monitored until the occurrence of fatal or nonfatal cardiovascular events, including stroke, myocardial infarction and peripheral vascular disease.

The researchers report that 31 fatal and 98 nonfatal cardiovascular events occurred during the mean follow-up period of 38 months. Levels of IL-10, IL-6, hsCRP and PTX-3 were significantly higher among patients with lower estimated glomerular filtration rates than in those with less-severe CKD. Moreover, patients with serum IL-10 levels greater than the median had significantly higher levels of inflammatory cytokines, greater numbers of fatal and nonfatal cardiovascular events, and significantly lower FMD (indicating greater endothelial dysfunction), than those with lower IL-10 levels. The frequency of diabetes mellitus was also increased in the high IL-10 group.

"Paradoxically the incidence of cardiovascular events was higher among patients with high serum levels of IL-10 than among those with lower levels," explains Kanbay. "This finding seems contradictory given data from experimental studies that suggest an anti-inflammatory or anti-atherosclerotic role of IL-10."

The researchers speculate that the association between IL-10 levels and cardiovascular events in patients with CKD might reflect a compensatory anti-inflammatory response to a proinflammatory milieu rather than an adverse effect of IL-10. "Studies are needed to investigate why some patients with CKD are able to upregulate IL-10 and shut off the proinflammatory cascade and others can't do this," concludes Kanbay.

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