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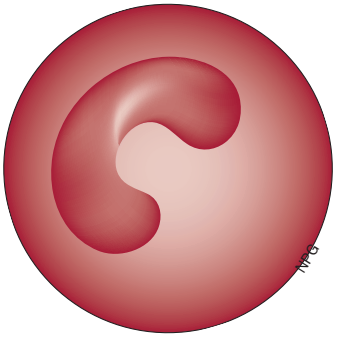
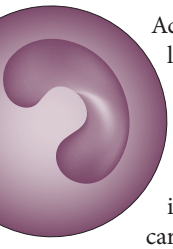


CARDIOVASCULAR DISEASE

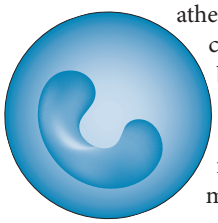
Monocytosis, atherosclerosis and increased cardiovascular risk in mild renal dysfunction



According to new data, high plasma levels of cystatin C—a marker of mild renal dysfunction—are associated with reduced levels of high-density lipoprotein (HDL) cholesterol, high monocyte counts and increased intima–media thickness at the carotid bifurcation (an area of low shear stress that is prone to plaque formation). Based on these findings, Anjali Ganda and colleagues suggest that monocytosis and atherosclerosis might contribute to the increased risk of cardiovascular events in patients with mild renal dysfunction.

To investigate their hypothesis that mild renal dysfunction might be associated with monocytosis and low HDL-cholesterol levels, the researchers analysed monocyte counts, cystatin C levels and fasting HDL-cholesterol levels in 4,757 individuals with no history of myocardial infarction or stroke, including 992 participants with mild renal dysfunction (defined as those in the top quintile of cystatin C levels [mean cystatin C level of 0.99 ± 0.18 mg/l]). In their cross-sectional analysis, they found that increased cystatin C levels (indicating worse renal function) were significantly associated with lower HDL-cholesterol levels and higher monocyte counts (both $P<0.001$ [ANOVA]).

In a subset of the study population ($n=752$), the researchers also investigated the levels of several amino acid metabolites that are associated with low HDL-cholesterol levels and insulin resistance. They found that high levels of some of these metabolites were independently associated with monocytosis after adjustment for traditional risk factors.



Finally, the researchers analysed the atherosclerosis end point of cross-sectional carotid bulb intima–media thickness in 3,134 individuals. They found that increased monocyte counts and mild renal dysfunction were independently associated with increased intima–media thickness at this location ($P=0.02$ and $P<0.01$, respectively).

Dr Ganda concludes that individuals with mild renal dysfunction have "a high-risk metabolic signature" characterized by high levels of circulating monocytes, low HDL-cholesterol levels and increased concentrations of branched chain and aromatic amino acid metabolites that are associated with insulin resistance. "Our results strongly suggest that accelerated atherosclerosis is at least partly responsible for the increased risk of cardiovascular disease in individuals with mild renal dysfunction," she says.

Ellen F. Carney

Original article Ganda, A. *et al*. Mild renal dysfunction and metabolites tied to low HDL cholesterol are associated with monocytosis and atherosclerosis. *Circulation* doi:10.1161/CIRCULATIONAHA.112.000682