Uric acid, endothelial dysfunction and atherosclerosis

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Recent years have shown a considerable increase in interest in the association of uric acid and cardiovascular disease. In many ways the nearest analogy is with homocysteine. As with the latter there is a consensus that elevated levels indicate greater cardiovascular risk. But, again as with homocysteine, it is much less clear whether uric acid is merely a marker for risk or actually a pathogenetic factor. Again in both cases a complicating factor is that increased serum levels parallel decreased renal function. However, there are important differences. Uric acid has been identified as one of the most important water-soluble anti-oxidants in the circulation. It has therefore been proposed that hyperuricemia is a compensatory mechanism for the oxidative stress associated with atherosclerosis and with hypertension. Although an appealing concept it does not explain why the highest levels of uric acid, independent of renal dysfunction, are associated with the worse cardiovascular outcomes. A possible explanation, at least partially, might be that in some circumstances uric acid may become pro-oxidant, as is seen with ascorbic acid and vitamin E. If this is the case uric acid may be directly damaging to the endothelium and therefore can promote atherogenesis and hypertension. Another aspect of this controversy is whether uric acid should be regarded in itself as a therapeutic target: should levels be deliberately reduced and if so how? This talk will outline the current evidence for these ongoing debates.