

Testosterone and atherosclerosis in aging men: purported association and clinical implications.

[Jones RD](#), [Nettleship JE](#), [Kapoor D](#), [Jones HT](#), [Channer KS](#).

Academic Unit of Endocrinology, Division of Genomic Medicine, Hormone & Vascular Biology Group, The University of Sheffield, Sheffield, UK. R.D.Jones@sheffield.ac.uk

Two of the strongest independent risk factors for coronary heart disease (CHD) are increasing age and male sex. Despite a wide variance in CHD mortality between countries, men are consistently twice as likely to die from CHD than their female counterparts. This sex difference has been attributed to a protective effect of female sex hormones, and a deleterious effect of male sex hormones, upon the cardiovascular system. However, little evidence suggests that testosterone exerts cardiovascular harm. In fact, serum levels of testosterone decline with age, and low testosterone is positively associated with other cardiovascular risk factors. Furthermore, testosterone exhibits a number of potential cardioprotective actions. For example, testosterone treatment is reported to reduce serum levels of the pro-inflammatory cytokines interleukin (IL)-1 β and tumor necrosis factor (TNF)- α , and to increase levels of the anti-inflammatory cytokine IL-10; to reduce vascular cell adhesion molecule (VCAM)-1 expression in aortic endothelial cells; to promote vascular smooth muscle and endothelial cell proliferation; to induce vasodilatation and to improve vascular reactivity, to reduce serum levels of the pro-thrombotic factors plasminogen activator inhibitor (PAI)-1 and fibrinogen; to reduce low-density lipoprotein-cholesterol (LDL-C); to improve insulin sensitivity; and to reduce body mass index and visceral fat mass. These actions of testosterone may confer cardiovascular benefit since testosterone therapy reduces atheroma formation in cholesterol-fed animal models, and reduces myocardial ischemia in men with CHD. Consequently, an alternative hypothesis is that an age-related decline in testosterone contributes to the atherosclerotic process. This is supported by recent findings, which suggest that as many as one in four men with CHD have serum levels of testosterone within the clinically hypogonadal range. Consequently, restoration of serum levels of testosterone via testosterone replacement therapy could offer cardiovascular, as well as other, clinical advantages to these individuals.

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