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The role of androgen receptors in atherosclerosis

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Abstract

Male disadvantage in cardiovascular health is well recognised. However, the influence of androgens on atherosclerosis, one of the major causes of many life-threatening cardiovascular events, is not well understood. With the dramatic increase in clinical prescription of testosterone in the past decade, concerns about the cardiovascular side-effects of androgen supplementation or androgen deprivation therapy are increasing. Potential atheroprotective effects of testosterone could be secondary to (aromatase-mediated) conversion into oestradiol or, alternatively, to direct activation of androgen receptors (AR). Recent development of animal models with cell-specific AR knockout has indicated a complex role for androgen action in atherosclerosis. Most studies suggest androgens are atheroprotective but the precise role of AR remains unclear. Increased use of AR knockout models should clarify the role of AR in atherogenesis and, thus, lead to exploitation of this pathway as a therapeutic target.

Introduction

The burden of cardiovascular disease (CVD) is undisputed, accounting for approximately a third of global deaths (17.5 million people in 2012) (WHO, 2012). Atherosclerosis leads to the development of coronary heart disease (CHD) which accounts for more than 40% of these deaths (WHO, 2012). Rupture of atherosclerotic plaques may lead to thrombotic events, such as stroke and myocardial infarction, which, if not fatal, cause significant morbidity.