Increased blood pressure, vascular inflammation, and endothelial dysfunction in androgen-deficient follitropin receptor knockout male mice.

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Abstract

The relationship between testosterone, vascular function, and blood pressure remains unclear. Here we utilized a mouse model of andropause, follitropin receptor knockout (FORKO) male mice, which are testosterone-deficient, to investigate whether vascular function and structure are altered and whether this is associated with elevated blood pressure. Blood pressure was measured by radiotelemetry, and vascular function and structure were assessed in isolated pressurized mesenteric resistance arteries in wild-type (WT) and FORKO mice. Diastolic and mean arterial pressures were significantly higher in FORKO than in WT mice ($P < .05$). Resistance arteries of FORKO mice had greater media-to-lumen ratio (10.4 vs. 8.2; $P < .05$) and reduced relaxation responses to acetylcholine (Ach) (62% vs. 94% at Ach 10(-4) mol/L, $P < .05$) in pressurized preparations. N(omega)-nitro-L-arginine (L-NAME) reduced Ach-induced relaxation equally in both groups (45% to 46%), and plasma nitrite was lower ($P < .05$) in FORKO mice. However, the L-NAME-resistant relaxation was smaller in FORKO (16% vs. 48% at Ach 10(-4) mol/L, $P < .05$). In FORKO, expression of intracellular adhesion molecule-1 and vascular cell adhesion molecule-1 was enhanced by immunohistochemistry, and vascular estrogen receptors (ER)alpha/ERbeta expression ratio was decreased 5-fold by immunoblot analysis. Vasoconstrictor responses to angiotensin II were blunted, and angiotensin receptor 1 expression was decreased in FORKO mice. Our data indicate that in androgen-deficient FORKO mice, blood pressure is elevated and resistance arteries exhibit endothelial dysfunction, structural remodeling, and vascular inflammation. These phenomena may be related to reduced expression of ERalpha and/or to decreased testosterone levels and indicate that androgens may play an important role in modulating vascular function and regulation of blood pressure.