169 **A CRUCIAL ROLE OF NOX2-DERIVED OXIDATIVE STRESS IN AGEING-ASSOCIATED METABOLIC DISORDERS AND VASCULAR DYSFUNCTION**

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doi:10.1136/heartjnl-2013-304019.169

Ageing has been recognised to be a major risk factor for the development of cardiovascular disease and growing evidence suggests a role for oxidative stress. NADPH oxidase 2 has been reported to be a major source of reactive oxygen species (ROS) generation in the cardiovascular system, however, the role of this enzyme in age-related metabolic disorders and vascular diseases remains unclear. In this study we used age-matched wild-type (WT) and Nox2-deficient ($Nox2^{-/-}$) mice on a C57BL/6 background at young (3–4 month) and ageing (20-24 month) to investigate the role of Nox2 in age-related oxidative stress, metabolic disorders and vascular dysfunction. There was an age-related increase in blood pressure in WT mice (126 mmHg for young and 148 mmHg for ageing) ($P<0.05$); however the blood pressure remained at lower levels in $Nox2^{-/-}$ ageing mice. Compared with young WT mice, WT ageing mice had significantly high levels of fasting serum insulin and this was accompanied with delayed clearance of glucose ($P<0.05$) indicating insulin resistance. However, no indication of insulin resistance was found in $Nox2^{-/-}$ ageing mice. The endothelial function was examined using aortic rings in an organ bath. Compared to the young controls, there was a significant decrease in the endothelium-dependent relaxation to acetylcholine in WT ageing aortas (Emax 72% for young and 64% for ageing, $P<0.05$). However, endothelial function was well preserved in $Nox2^{-/-}$ ageing aortas (Emax 83% for young and 80% for ageing. The ROS production was then measured in aortic sections by DHE fluorescence and a significant increase was found in ROS production in WT ageing aortas as compared to WT young controls ($P<0.05$). However, there was a significantly lower level of ROS production ($P<0.05$) in both age-matched $Nox2^{-/-}$ aortas. In conclusion, Nox2-derived oxidative stress plays an important role in ageing-associated metabolic disorders and vascular dysfunction, and targeting Nox2 represents a valuable therapeutic strategy to treat these aging-related diseases.