Functional and Structural Modifications Associated with Hypertension, Obesity and Diabetes in the Resistance Vasculature

Jorge A. Castorena-Gonzalez

Dr. Luis A. Martinez-Lemus, Dissertation Supervisor

Abstract

Cardiovascular diseases are considered the leading cause of death nowadays. Hypertension, obesity and type-2 diabetes are deemed major risk factors for the development of cardiovascular diseases. In essential hypertension, one of the most important structural changes is the inward remodeling of the resistance arteries. I found that the mechanical properties of inwardly remodeled cremasteric-arterioles from rats are affected. Furthermore, it is the F-actin components of the cytoskeleton the ones that are strongly modified. In old spontaneously hypertensive rats, my results showed that, resistance arteries undergo hypertrophic inward remodeling; and, adrenergic-vasoconstriction and vasodilation pathways are impaired. In diet-induced-obesity, mice-mesenteric arterioles were observed to undergo remodeling of the extracellular matrix components. Obesity and type-2 diabetes have been associated with insulin resistance, endothelial dysfunction and arterial stiffening. Jejunal-submucosal arterioles from diabetic obese patients had a reduced vasorelaxation to insulin in comparison to obese non-diabetics, while acetylcholine-vasodilation was similar in both groups. Reduced amounts of the subunit-alpha of the insulin receptor and MMP-9 were found in diabetics as well. This suggests that, in type-2 diabetes, the presence of a blunted insulin-vasodilation response is a form of endothelial dysfunction that is not correlated with the body-to-mass index, but whose mechanism may be related with the activity of MMPs.