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Review article

Vascular biology of ageing—Implications in hypertension

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ABSTRACT

Ageing is associated with functional, structural and mechanical changes in arteries that closely resemble the vascular alterations in hypertension. Characteristic features of large and small arteries that occur with ageing and during the development of hypertension include endothelial dysfunction, vascular remodelling, inflammation, calcification and increased stiffness. Arterial changes in young hypertensive patients mimic those in old normotensive individuals. Hypertension accelerates and augments age-related vascular remodelling and dysfunction, and ageing may impact on the severity of vascular damage in hypertension, indicating close interactions between biological ageing and blood pressure elevation. Molecular and cellular mechanisms underlying vascular alterations in ageing and hypertension are common and include aberrant signal transduction, oxidative stress and activation of pro-inflammatory and pro-fibrotic transcription factors. Strategies to suppress age-associated vascular changes could ameliorate vascular damage associated with hypertension. An overview on the vascular biology of ageing and hypertension is presented and novel molecular mechanisms contributing to these processes are discussed. The complex interaction between biological ageing and blood pressure elevation on the vasculature is highlighted. This article is part of a Special Issue entitled: CV Ageing.

Contents

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1. Introduction

Clinical studies show a significant relationship between ageing and increased blood pressure, with advancing age being a major non-modifiable risk factor in the development of hypertension [1]. This is due, in part, to changes that occur in the vasculature, including endothelial dysfunction, vascular remodelling, increased vascular stiffness and inflammation. These functional and structural changes define the 'vascular phenotype' of hypertension, features that are also found during ageing [2] (Fig. 1). At the cellular level, there is endothelial cell damage, increased vascular smooth muscle cell growth, cell migration, inflammation, contraction, extracellular matrix deposition, fibrosis, and calcification [3].

Young patients with elevated blood pressure exhibit arterial changes similar to those in older individuals with normal blood pressure, and accordingly the concept of 'premature' or 'early' vascular ageing in hypertension has been proposed [4]. Hypertension accelerates age-related vascular changes, processes that are attenuated when blood pressure is normalised. The direct relationship between ageing and vascular health is evident in progeria syndrome, where patients exhibit accelerated ageing, endothelial dysfunction, accelerated atherosclerosis and die prematurely from complications of cardiovascular disease, such as stroke and myocardial infarction [5]. Considering the fact that the population is ageing and that the major chronic disease of ageing is hypertension and associated cardiovascular complications, the potential health and economic burden in our modern society is enormous. Accordingly it is important to understand how vascular function changes with ageing and how this impacts on hypertension, so that targeted strategies could be developed to prevent and repair damaged 'aged' arteries and thereby reduce the risk of hypertension and target organ damage. In the present review, we discuss the vascular changes that occur with ageing and during the development of hypertension and focus on some molecular mechanisms that underlie these vascular changes.

2. Structural and mechanical changes in the ageing vasculature

Physiological changes to the vascular wall are dynamic and occur throughout life [6,7]. Endothelial cell turnover occurs over years, whereas that of vascular smooth muscle cells seems to occur over a shorter time period. Many structural and mechanical alterations have been observed in the aged vasculature including increased intimal-to-media (IM) thickness, evidenced by the finding that the IM thickness of the carotid artery increases two- to three-fold between 20 and 90 years of age [8,9]. Subclinical IM thickening is strongly associated with ageing and is also a predictor of future cardiovascular events [8,9]. Both aortic length and circumference gradually increase with advancing age [10–12]. Associated with these structural alterations are mechanical changes, characterised by a reduction in compliance, reduced elasticity/distensibility and increased stiffness [8,9]. Stiffening of the large conduit arteries due to fracture of elastin fibres within the tunica media and collagenous remodelling, results in increased aortic pulse pressure and pulse wave velocity (PWV). Increased PWV, a non-invasive measure of vascular stiffness, increases in both sexes with ageing and is determined by the mean arterial pressure and the intrinsic stress/strain relationship (stiffness) of the arterial wall. As arterial wall stiffness increases, central systolic pressure increases and diastolic pressure decreases, leading to increased pulse pressure, an independent risk factor for future cardiovascular events [13]. Processes underlying these structural and mechanical changes involve growth and migration of vascular smooth muscle cells

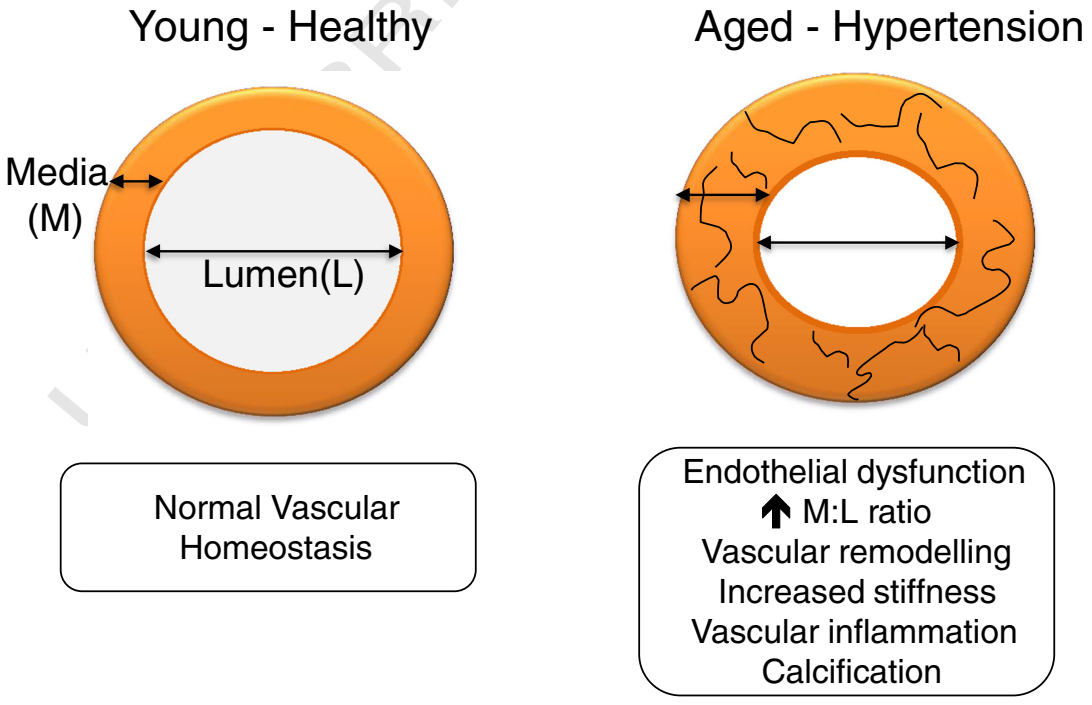

Fig. 1. Schematic demonstrating vascular changes that occur during ageing and with the development of hypertension. Vascular changes in hypertension mimic those found in arteries observed with ageing.

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