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# Elastic fibres and vascular structure in hypertension

Silvia M. Arribas [a,*], Aleksander Hinek [b], M. Carmen González [a]

[a] Departamento de Fisiología, Facultad de Medicina, Universidad Autónoma de Madrid, C/ Arzobispo Morcillo 2, 28029-Madrid, Spain
[b] Cardiovascular Program, The Hospital for Sick Children, University of Toronto, Toronto, Canada

**Abstract**

Blood vessels are dynamic structures composed of cells and extracellular matrix (ECM), which are in continuous cross-talk with each other. Thus, cellular changes in phenotype or in proliferation/death rate affect ECM synthesis. In turn, ECM elements not only provide the structural framework for vascular cells, but they also modulate cellular function through specific receptors. These ECM–cell interactions, together with neurotransmitters, hormones and the mechanical forces imposed by the heart, modulate the structural organization of the vascular wall. It is not surprising that pathological states related to alterations in the nervous, humoral or haemodynamic environment–such as hypertension–are associated with vascular wall remodeling, which, in the end, is deleterious for cardiovascular function. However, the question remains whether these structural alterations are simply a consequence of the disease or if there are early cellular or ECM alterations–determined either genetically or by environmental factors–that can predispose to vascular remodeling independent of hypertension. Elastic fibres might be key elements in the pathophysiology of hypertensive vascular remodeling. In addition to the well known effects of hypertension on elastic fibre fatigue and accelerated degradation, leading to loss of arterial wall resilience, recent investigations have highlighted new roles for individual components of elastic fibres and their degradation products. These elements can act as signal transducers and regulate cellular proliferation, migration, phenotype, and ECM degradation. In this paper, we review current knowledge regarding components of elastic fibres and discuss their possible pathomechanistic associations with vascular structural abnormalities and with hypertension development or progression.


*Keywords:* Elastin; Hypertension; Vascular structure; Stiffening; Extracellular matrix; Elastic fibres; Elastin gene defects; Elastin-derived peptides

*Abbreviations:* ACEI, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blockers; Ang II, angiotensin II; CCB, calcium channel blockers; EBP, elastin-binding protein; ECM, extracellular matrix; EMILINs, elastin microfibril interface-located proteins; ERK1/2, extracellular signal regulated protein kinase; FAK, focal adhesion kinase; IEL, internal elastic lamina; LOX, lysyl oxidase; MAGPs, microfibril-associated glycoproteins; MAP, mitogen-activated protein; MMPs, matrix metalloproteinases; NO, nitric oxide; ROS, reactive oxygen species; S-GAL, alternatively spliced variant of human β-galactosidase; SHR, spontaneously hypertensive rat; SHR-SP, stroke-prone spontaneously hypertensive rat; SMC, smooth muscle cells; SVAS, supravalvular aortic stenosis; TIMPs, tissue inhibitors of metalloproteinases; TGF-β, transforming growth factor β; WKY, Wistar Kyoto rat; WS, Williams Beuren syndrome.

**Contents**



* Corresponding author. Tel.: +34 91 497 5475; fax: +34 91 497 5478.
*E-mail address:* Silvia.Arribas@uam.es (S.M. Arribas).

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## 1. Introduction

The extracellular matrix (ECM), produced by numerous cell types, not only supports the proper organization and integrity of vertebrate tissues and organs, but also facilitates their basic functions and modulates response to pathological factors. Elastic fibres and laminae–particularly abundant in lungs, skin, and blood vessels–are the most complex ECM constituents. They are composed of elastin and multiple other heterogeneous components and they are mainly responsible for extensibility and resilience of tissues. In the circulatory system, the proper assembly and functioning of elastic fibres is absolutely crucial for maintaining a smooth and uninterrupted delivery of blood from the heart to organs and tissues. Knowledge of the nature and mutual interactions of different components of elastic fibres has expanded substantially in recent years (for review, see Kielty et al., 2002). This includes identification of other than mechanical functions of elastic fibres, such as the involvement of their particular components in cell signaling via surface receptors, which modulate cellular adhesion, proliferation, and phenotypic switch (Hinek, 1996; Dietz & Mecham, 2000; Brooke et al., 2003).

Structural and mechanical abnormalities leading to large artery stiffening (for reviews, see London & Cohn, 2002; Et-Taouil et al., 2003; Safar et al., 2003) and resistance artery narrowing (for reviews, see Intengan & Schiffrin, 2001; Mulvany, 2002; Schiffrin & Touyz, 2004) are two of the key features associated with essential hypertension. Both are known to contribute to the maintenance of hypertension as well as to the cardiovascular complications associated with it. In this context, ECM in general–and elastic fibres in particular–have been perceived for long as passive structural elements that are altered in response to sustained pressure elevation. However, the newly described engagement of elastic fibre components and their degradation products in the active cross-talk with vascular cells have raised the possibility that they might also actively modulate vascular remodeling in cardiovascular diseases. The fact that some genetic defects of elastic fibre components are accompanied by abnormal vessel structure and hypertension has given ground to the "fetal origins" hypothesis. This hypothesis postulates that an early embryonic defect constitutes the basis of the inevitable cardiovascular disease in adulthood (Barker et al., 1990; Martyn & Greenwald, 2001) and has raised the possibility that polymorphisms related to genes of elastic fibre components should be explored as causative elements in the development of essential hypertension (Brooke et al., 2003; D'Armiento, 2003; Faury et al., 2003).

The purpose of our review is to summarise current information on the possible linkage between impaired initial elastogenesis or increased destruction of elastic fibres with the pathophysiology and development of hypertension. Sections 2 and 3 present general information on the biology of elastic fibres in the vascular system and current concepts on hypertensive vascular remodeling. Following this, we describe known vascular abnormalities of elastic fibres associated with hypertension. In the last section, we discuss the possibility that early elastic fibre defects, either genetically or environmentally determined, can facilitate vascular remodeling and hypertension development.