



Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

Journal Home Page: <https://www.atlantis-press.com/journals/artres>

ARTERIAL STIFFENING: CAUSES AND CONSEQUENCES

Marina Cecelja

To cite this article: Marina Cecelja (2012) ARTERIAL STIFFENING: CAUSES AND CONSEQUENCES, Artery Research 6:4, 202–202, DOI: <https://doi.org/10.1016/j.artres.2012.10.005>

To link to this article: <https://doi.org/10.1016/j.artres.2012.10.005>

Published online: 21 December 2019

Career development lectures

ARTERIAL STIFFENING: CAUSES AND CONSEQUENCES

Marina Cecelja

St Thomas' Hospital, London, UK

Abstract: Increased arterial stiffness, as measured by pulse wave velocity (PWV), is increasingly recognised as an important predictor of future cardiovascular events. At present, the mechanisms leading to arterial stiffening and the processes underlying its association with cardiovascular disease remain unclear. One suggestion is that stiffening may be caused by atherosclerosis along the aorta, explaining its association with atherothrombotic cardiovascular events. However, other than age and blood pressure, there is little or no association between arterial stiffness and established risk factors for atherosclerosis. PWV is not increased in early stages of atherosclerosis, as manifest by intima-media thickening and presence of non-calcified atheromatous plaque, but is associated with presence of calcified plaque and calcification of the aorta. Furthermore, the correlation between PWV and vascular calcification is in the majority explained by common genetic factors. One consequence of increased large artery stiffness is an increase in pulse pressure, which, in older subjects, is the blood pressure components most closely correlated with cardiovascular events. Arterial stiffening increases early aortic pressure generated from ventricular contraction. However, this pressure wave can further be increased by an amount called the augmentation pressure, traditionally attributed to pressure wave reflection, which is associated with arterial tapering independently of PWV. Augmentation pressure is an important contributor to age-related increase in central PP, especially in women <50 years of age, and can be effectively reduced by nitrovasodilation independently of any change in arterial stiffness.

GETTING A GRIP ON ARTERIAL STIFFNESS: THE ASKLEPIOS STUDY

Ernst Rietzschel

Universitair Ziekhuis, Ghent, Belgium

Abstract: The ASKLEPIOS study started in 2002 with a medium-term goal of providing better understanding into the interplay between ageing, haemodynamics (and non-haemodynamic stresses) on the development of cardiovascular disease. The long-term goal is to focus on better risk prevention strategies.

The study cohort consists of a representative, random population sample of >2500 apparently healthy Belgian subjects, examined initially in 2002–2004 and currently undergoing re-examination after a 10-year interval (completion due Q4 2014). An overarching theme has been the study of time-integrative biomarkers, which reflect a cumulative – preferably lifecourse – risk factor burden. These include biomechanics-derived biomarkers (arterial stiffness, altered haemodynamics, cardiac remodeling), but also blood-borne ageing biomarkers (telomere length, DNA methylation) and imaging-based biomarkers (intima-media thickness and plaque accumulation). Asklepios, from the beginning, was (and is) a very close collaboration between clinicians and engineers. An important research focus has been the study of haemodynamics as complex time-varying phenomena, by combining pressure, flow and diameter or volume curves, an approach that is currently feasible in clinical practice datasets, using non-invasive tools.

In recent years, we better understand how subtle cardio-vascular dysfunctions, while asymptomatic at rest, become clinically relevant when heart and vessels need to effectively interact in order to perform an exercise. Therefore, in the current re-examination of our 2500 subjects, we are extending our characterization by not only studying the subjects at rest, but also whilst a haemodynamic load is imposed (by isometric handgrip), an approach – we believe – that will allow for an even more profound insight in this complex field.

CARDIOTROPHIN-1: A NEW KEY MOLECULE IN VASCULAR FIBROSIS, ARTERIAL STIFFNESS AND SENESCENCE

Natalia Lopez-Andres

Inserm U961, Nancy, France

Background: Cardiotrophin-1 (CT-1), a cytokine belonging to the interleukin-6 family, is increased in hypertension and in heart failure. We hypothesized that CT-1 excess promotes vascular fibrosis and dysfunction, whereas CT-1 deficiency influences lifespan by decreasing arterial stiffness.

Methods: CT-1 or vehicle were administered to Wistar rats for 6 weeks, and 29 month-old WT and CT-1-null mice were used. Vascular function was analysed *in vivo* using echotracking device and *ex vivo* employing a scanning

acoustic microscopy. Vascular histomorphology, senescence, metabolic, inflammatory and oxidative stress parameters were measured by immunohistochemistry, RT-PCR, Western Blot and ELISA.

Results: CT-1 treatment did not modify blood pressure levels. In CT-1-treated rats, the circumferential wall stress-incremental elastic modulus curve was shifted leftward and the acoustic speed of sound in the aorta was augmented, indicating increased arterial stiffness. Vascular media thickness, collagen and fibronectin content were increased by CT-1 treatment. The wall stress-incremental elastic modulus curve of old CT-1-null mice was shifted rightward as compared to WT, indicating decreased arterial stiffness. Media thickness and wall fibrosis were lower in CT-1-null mice. CT-1-null mice showed decreased levels of inflammatory, apoptotic and senescence pathways, whereas telomere-linked proteins, DNA repair proteins and antioxidant enzyme activities were increased. CT-1-null mice displayed a 5-month increased median longevity compared with WT.

Conclusion: CT-1 is a new potent vascular fibrotic agent able to induce arterial stiffness independently from blood pressure. CT-1 absence is associated with decreased arterial fibrosis, stiffness and senescence and increased longevity in mice likely through downregulating apoptotic, senescence and inflammatory pathways. CT-1 may be a major regulator of arterial stiffness with a major impact on the aging process.

Special guest lecture

STRUCTURAL PROTEINS AND ARTERIAL AGING

Michael J. Sherratt

Institute of Inflammation & Repair, Manchester Academic Health Science Centre, The University of Manchester, Manchester, UK

In common with most dynamic tissues, the mechanical properties of arteries are determined by the relative composition and architecture of key structural extracellular matrix (ECM) proteins including fibrillar collagens and elastic fiber components. Although it is apparent that age-related loss of ECM homeostasis leads to arteriosclerosis (vascular stiffening), which in turn is associated with the development of both fatal strokes and heart failure, the causative mechanisms and principal molecular targets remain poorly defined. Whilst there are many potential effectors of ECM degradation it is unclear how these mechanisms could drive selective molecular remodelling in the aging vasculature. Our data suggest that the preferential oxidation of cysteine-rich elastic fibre-associated components may play a key role in initiating and promoting tissue remodeling (and hence stiffening) in aging mammals. In complementary studies we are developing new micro-mechanical methodologies, which in combination with conventional histological approaches, are capable of localising arteriosclerotic changes to specific regions and hence molecular targets in aging and diabetic vessels.

McDonald lecture

THE REALITY OF AGING VIEWED FROM THE ARTERIAL WALL

Edward G. Lakatta, MD

National Institute on Aging, NIH, USA

Viewing the reality of aging from the arterial wall beings with the realization that arterial diseases, e.g. atherosclerosis and hypertension, are rampant in Western society and increase exponentially with advancing age. Progressive changes occur throughout life in the structure and function of central arteries in numerous species. These changes include diffuse intimal and medial thickening, and enhanced stiffening. Age-associated remodeling of the aortic wall of both animals and humans involves a proinflammatory profile of arterial cell and matrix properties. This profile features increased production of angiotensin II (Ang II) and downstream Ang II/AT₁ receptor signaling molecules, e.g., matrix metalloproteases (MMPs), calpain-1 and monocyte chemoattractant protein (MCP-1), transforming growth factor β 1 (TGF- β 1) NF κ B, TNF α , iNOS, and VCAM. Activation of calpain-1, MMPs, TGF- β , and NADPH oxidase within the arterial wall is increased, and nitric oxide bioavailability is reduced. Both invasive and proliferative capacities of early passage vascular smooth muscle cells (VSMC) isolated from the aged arterial wall are increased, and are linked to augmented Ang II signaling. This age-associated arterial proinflammatory secretory profile within the grossly appearing arterial wall and related structural/functional remodeling, is reproduced in young rats by chronic infusion of Ang-II.

A megacept emerges with the realization that in arteries of younger animals, in response to experimental induction of hypertension or early atherosclerosis or diabetes, parts of this proinflammatory profile within the arterial wall that have been studied to date are strikingly similar to the profile that occurs with advancing age.