ISSN: 2591-7951

Arteriosclerosis, hypertension and vascular ageing.

Cristina Florescu*

Craiova University of Medicine and Pharmacy, Romania

Accepted on December 01, 2017

Short Communication

Arteriosclerosis represents stiffening and ageing of the arteries. Stiffening is responsible for increased systolic and pulse pressure, which are major risk factors for stroke and heart failure. Stiffening is measured as an increase in pulse wave velocity and pulsatile flow to the target organs. In diabetic patients is commonly seen an increase in microvascular pressure.

Arteriosclerosis may result from a reversible functional component, like changes in vascular smooth muscle tone, or endothelial dysfunction. More frequently, arteriosclerosis is due to an irreversible structural component like elastin loss, collagen deposition, glycation of proteins in the vascular cell wall, or calcification of the vessels (especially in people with chronic kidney disease) [1].

At a cellular level, ageing can be determined by the length of telomeres. Telomeres are small segments of DNA located at the end of chromosomes that are essential for maintaining DNA integrity during replication. As cells age, telomeres shorten and their length can be used to age the cell [2]. An association between vascular disease and telomere shortening in leucocytes isolated from the aorta has previously been shown [3]. This change is systemically, not confined to the aorta, leucocyte DNA being a good indicator of vascular age.

Even after correction for age and gender, leucocytes from healthy individuals have longer telomeres than those isolated from people with vascular disease. Accelerated telomere shortening is also observed in patients at increased cardiovascular risk due to the increased age of the cell. Vascular ageing also develops as a result of oxidative stress, a change confirmed in preclinical studies with angiotensin II [2]. Exposure to angiotensin II, a powerful pro-inflammatory molecule, was linked with the generation of oxidative free radicals in vascular smooth muscle cells, damageing cellular DNA, particularly in the telomere region.

The renin-angiotensin system (RAS) has the effect of acceleration of ageing of the vessels.

In young individuals, arteries are often relaxed, existing a good coupling with the ventricle, and little pressure is needed to push the blood flow. With age, arteries stiffen, and this creates a highly resistive and low conductive system that requires higher pulse pressure to drive the flow, resulting in hypertension.

The mechanical strain present in the vessel wall is fundamental, causing the irreversible fragmentation of elastin and the deposition of collagen, leading to stiffening [1].

Endothelial dysfunction also plays a role in this process and the smooth muscle in the vascular wall will stiffen, this being a potentially reversible process. The stiffening is due to oxidative stress and the presence of reactive oxygen species (ROS) and oxidized low-density lipoproteins (LDL) in the sub intima.

The third process seen in the pathophysiology of arterial ageing involves post-translational modification of collagen with advanced glycation end products (AGEs). This change is particularly relevant in patients with diabetes [1].

All these processes lead to aortic stiffening, dilatation and wall hypertrophy and manifest as an increase in pulse wave velocity. Pulse wave velocity is typically 5 or 6 m/s at age 20 years, but will double throughout life and can be as high as 10-15 m/s at 70-80 years. This increase in pulse wave velocity can be predicted by age due to the accumulation of alterations and stiffening and distending of the aorta causing elevated BP [4].

Hypertension is a clinical manifestation of ageing that increases with advancing age. The majority of cases occur in people aged over 40 years, and from about 50 years systolic blood pressure (SBP) increases while diastolic blood pressure (DBP) decreases. This divergence leads to a widening of pulse pressure. Pulse pressure is a manifestation of stiffening of the aorta and arterial ageing. Pulse pressure also increases pulsatile flow causing stress in target organs. Most cases of hypertension are a result of ageing of the vascular cell wall. The majority of these individuals will typically present with isolated systolic hypertension or systolic-diastolic hypertension [5,6]. The incidence of isolated systolic hypertension increases from around 20% in untreated people with hypertension aged up to 40 years to 54% in those aged 50-59 years, to 87% in those 60-69 years, accounting for almost 95% of cases in those aged over 70 years [5].

A method to measure flow is magnetic resonance imaging (MRI), which can be used to assess compliance in the aorta and calculate impedance. Impedance indicates the pressure required to drive flow in the aorta and is a measure of the coupling of the ventricle to the aortic root. Increased impedance is fundamental to the development of heart failure in patients with hypertension and contributes to increased left ventricular afterload and left ventricular hypertrophy [7,8].

By the age of 50 years, the accelerated loss of aortic root compliance is almost complete, with very little change seen after 50 years [9], because most damage occurs in the first 50 years of life, when the aorta has already stiffened to the point at which systolic hypertension can develop. Any intervention that aims to reduce vascular age should be done before 50 years of age as this may prevent progressive aortic stiffening.

Due to these age-related differences, hypertension can be understand as two different entities; the first in younger patients and the second in older patients. The *steady* component (mean

pressure disease) is seen in younger patients and predominantly results from mean arterial pressure and DBP, that increase cardiac output and systemic vascular resistance. A pulsatile component (pulse pressure disease) develops in older patients due to increased pulse pressure (systolic pressure), aortic stiffening, and increased pulse wave velocity. A transition from the first state into the second occurs as a result of mean pressure increase and age-related damage to the aortic wall. This transition can be accelerated by inflammation, the presence of vascular risk factors and the effect of angiotensin II, which can increase fibrosis, cellular senescence, and ageing.

Age-related changes in pulse rate also occur: while the radial pulse pressure will double between 18 and 97 years, the aortic pulse pressure will quadruple. Once the vessels begin to age, the pressure that is experienced centrally increases dramatically. This rapid increase in pulse pressure may explain the increased rate of stroke and other pressure-dependent conditions seen in patients over 50 years.

In untreated hypertensive patients, aortic impedance and stiffening continue to increase systolic and pulse pressure. These processes augment the ageing process and lead to a range of deleterious effects such as cardiac remodelling and impaired ventricular and vascular coupling [10,11]. Arteria stiffness has also been linked with damage to the brain microvasculature, including subcortical and white matter infarcts, small vessel disease, and microvascular injury [12].

Finally hypertension will result in end-organ damages manifested as cardiac disease (including heart failure), cerebrovascular disease and chronic kidney disease. These manifestations appear due to changing haemodynamics associated with ageing, representing potential therapeutic targets. Treatment may reduce the development of these conditions or delay their progression and improve patient outcomes. The pathophysiology of arterial ageing can be accelerated by known risk factors for vascular and heart disease, such as hypertension, impaired glucose tolerance or diabetes, dyslipidaemia and smoking. Reducing these risk factors has the potential to delay arterial ageing, this concept needing further investigation.

References

1. Williams B. The aorta and resistant hypertension. J Am Coll Cardiol. 2009;53:452-4.
2. Herbert K, Mistry Y, Hastings R, et al. B. Angiotensin II-mediated oxidative DNA damage accelerates cellular senescence in cultured human vascular smooth muscle cells via telomere-dependent and independent pathways. Circ Res. 2008;102:201-8.
3. Wilson W, Herbert K, Mistry Y, et al. Blood leucocyte telomere DNA content predicts vascular telomere DNA content in humans with and without vascular disease. Eur Heart J. 2008; 29:2689-94.
4. Cecelja M, Chowienczyk P (2009) Dissociation of aortic pulse wave velocity with risk factors for cardiovascular disease other than hypertension: a systematic review. Hypertension. 2009;54:1328-36.
5. Franklin S, Jacobs M, Wong N, et al. Predominance of isolated systolic hypertension among middle-aged and elderly US hypertensives: analysis based on national health and nutrition examination survey (NHANES) IIII. Hypertension. 2001;37:869-74.
6. Williams B, Lindholm L, Sever P. Systolic pressure is all that matters. Lancet. 2008;371:2219-21.
7. Gottdiener J, Gay J, Maron B, et al. Increased right ventricular wall thickness in left ventricular pressure overload: echocardiographic determination of hypertrophic response of the 'nonstressed' ventricle. J Am Coll Cardiol. 1985;6:550-5.
8. Krzesinski P, Uzieblo-Zyczkowska B, Gielerak G, et al. Global longitudinal two-dimensional systolic strain is associated with hemodynamic alterations in arterial hypertension. J Am Soc Hypertens. 2015;9:680-9.
9. Redheuil A, Yu W, Wu C, et al. Reduced ascending aortic strain and distensibility: earliest manifestations of vascular aging in humans. Hypertension. 2010;55:319-326.
10. Kass D. Ventricular arterial stiffening: integrating the pathophysiology. Hypertension. 2005;46:185-93.
11. Lantelme P, Laurent S, Besnard C, et al. Arterial stiffness is associated with left atrial size in hypertensive patients. Arch Cardiovasc Dis. 2008;101:35-40.
12. Mitchell G, Van Buchem M, Sigurdsson S, et al. Arterial stiffness, pressure and flow pulsatility and brain structure and function: the age, gene/ environment susceptibility-Reykjavik study. Brain. 2011;134:3398-407.

***Correspondence to:**

Cristina Florescu
Craiova University of Medicine and Pharmacy
Romania
E-mail: tohaneanu67@yahoo.com