Subclinical Gender-specific Differences in Arterial Carotid Stiffness - A Review

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Abstract. Arterial stiffness is a complex and inevitable physiological process that affects the entire cardiovascular system. Among the various arterial structures, the carotid arteries play a pivotal role in supplying oxygenated blood to the brain. The aging process impacts both men and women differently, and recent research has shed light on the gender-specific differences in arterial carotid stiffness. This article aims to explore published reports on the underlying mechanisms and clinical implications of these disparities, providing valuable insights for future research.

Keywords: carotid artery, arterial stiffness, gender-specific differences, numerical simulation.

1 Introduction

Aging is an intricate process that influences all systems within the human body. The vascular system, in particular, undergoes significant changes with advancing age, leading to a higher risk of cardiovascular diseases. Arteries are elastic blood vessels that carry oxygenated blood away from the heart to the rest of the body. They have a natural elasticity that allows them to stretch and recoil as blood is pumped through them. As we age or due to certain health conditions, the arteries can become stiffer and lose some of their elasticity. This can lead to several adverse effects on cardiovascular health. Among the major arteries, the carotid arteries, located in the neck, are crucial for cerebral perfusion. Studies have suggested that the aging of these arteries follows unique patterns in men and women, leading to distinctive clinical outcomes [1, 2, 3]. To understand gender-specific differences in carotid arterial stiffness, it is essential to grasp the anatomy and function of these vessels. The carotid arteries bifurcate into the internal and external carotid arteries, supplying the brain with oxygen and nutrients while facilitating waste removal. Compliance and distensibility are vessel wall properties of large arteries. Arterial compliance, defined as the absolute change in volume per unit of pressure ($\Delta V/\Delta P$), reflects the buffering capacity of an artery; a decrease in compliance increases cardiac afterload and the risk of cardiac hypertrophy. Arterial distensibility, defined as the relative change in volume per unit of pressure ($[\Delta V/V]/\Delta P$), reflects mainly the elasticity of the wall and is considered a determinant of strain on the vessel wall. A local decrease in distensibility might be associated with an increased risk of arterial wall damage, an important feature in atherosclerotic disease [4, 5]. Preservation of distensibility might be important in protecting the arterial wall against damage at a particular site. Arterial stiffness refers to the reduced ability of arteries to expand and contract in response to changes in blood pressure. Numerous factors contribute to arterial pathologies, and the mechanisms underlying gender disparities are multifaceted. Structural differences between males and females contribute to variations in arterial stiffness. Women typically have smaller arteries and a higher proportion of elastin fibers in the arterial walls, which enhances arterial compliance. In contrast, men tend to have larger arteries and a higher collagen-to-elastin ratio, leading to increased arterial stiffness. Hormonal influences, such as estrogen and testosterone, have been implicated in modulating vascular function differently in men and women [6]. Moreover, genetic factors, lifestyle choices, and systemic inflammation play significant roles in determining arterial health in both genders [7]. A comprehensive search of electronic databases was conducted to identify relevant studies published in the last decade. Studies involving human subjects and assessing carotid arterial stiffness in relation to gender were included.

2 Underlying mechanisms and disparities

The term large arteries, or large elastic arteries, refers to the aorta and carotid arteries. These large arteries have a very distensible wall and a high content of elastin protein. The main cause of arterial stiffness is the gradual accumulation of collagen and other structural proteins in the arterial walls, which results in decreased flexibility. The intima-media thickness (IMT) and plaque formation are crucial indicators of carotid arterial diseases.

In Fig. 1 a schematic representation of an healthy artery as compared with a stiffened artery. For healthy arteries, energy generated by distension of the arterial wall during systole is used during diastole to maintain blood flow and decrease pulse pressure downstream. For stiffened arteries, poor energy absorption results in higher pulse pressure, reduced flow during diastole, increased cardiac afterload, and end organ damage.

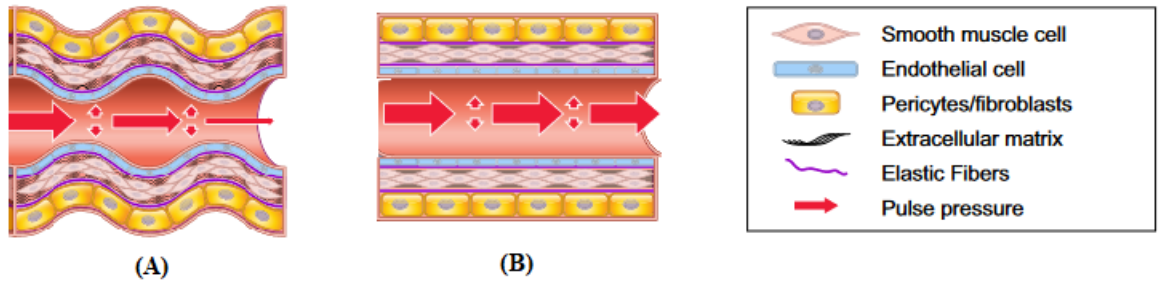

Figure 1. A schematic representation of (A) healthy artery and (B) stiffened artery.

Carotid stiffness can be quantified using various non-invasive techniques. One commonly used method is measuring the pulse wave velocity (PWV) or the time it takes for the arterial pressure wave to propagate between two points along the carotid artery. PWV is an established marker of arterial stiffness and is typically assessed by measuring the time delay between the R-wave on an electrocardiogram (ECG) and the arrival of the pulse wave at two different arterial sites. Carotid-femoral PWV (cfPWV) is the most widely utilized and accepted measurement. It involves recording pressure waveforms at the carotid and femoral arteries and measuring the time taken for the pulse wave to travel between these two sites. The distance between the two measurement points is also measured to calculate the PWV. Another method to assess carotid stiffness is the measurement of arterial distensibility or compliance. This can be achieved by using ultrasound imaging to measure the changes in arterial diameter during the cardiac cycle. By analyzing the changes in diameter and blood pressure, parameters such as arterial compliance, distensibility coefficient, or Young's elastic modulus can be calculated. These measurements provide insights into the arterial wall's ability to expand and contract in response to pressure changes.

Gender-related differences in carotid stiffness, specifically in the carotid arteries, have been observed in various studies. These differences can be attributed to a combination of hormonal, structural, and physiological factors. A few key factors that contribute to gender-related differences in carotid stiffness have been hormonal factors, structural differences, blood pressure patterns and age-related changes.

2.1 Hormonal factors

Sex hormones, such as estrogen and testosterone, play a significant role in vascular health and elasticity. High levels of testosterone, the primary male sex hormone, are associated with increased risk of cardiovascular calcification, whilst estrogen, the primary female sex hormone, is considered cardioprotective [8]. Estrogen has been found to have a protective effect on arterial stiffness by promoting arterial dilation and reducing collagen deposition in the arterial walls. In premenopausal women, higher levels of estrogen are associated with better arterial compliance and lower arterial stiffness compared to men. However, after menopause, when estrogen levels decline, women may experience an accelerated increase in arterial stiffness, leading to a catch-up effect with men.

2.2 Structural differences

The structure and composition of arterial walls can differ between genders. A number of studies have emphasized the relationship of short stature and risk of artery disease [9]. At every age, most women are of shorter stature and smaller size than most men. Height is related directly to arterial caliber and length as well as cardiac output through effects on stroke volume and heart rate. These parameters interact with the biomechanical properties of the large arteries to determine central pulse pressure. Generally, women tend to have smaller and more compliant arteries compared to men. This structural difference may contribute to lower arterial stiffness in women. Wall thickness, as well as arterial diameter, can be measured in superficial arteries using echo-tracking devices. These techniques allow direct visualization of small arterial wall segments, with direct evaluation of arterial geometry, and rely on acoustic characteristics of tissues to generate a cross-sectional image of the near and far walls of an artery thus permitting the measurements of arterial diameter and intima–media thickness.

Local mechanical properties are commonly reported using a variety of expressions relating distending pressure (P), diameter (D) or relative change in diameter ($S=\Delta D/D$) including stiffness (β-) index ($SI= ln(Psystolic/Pdiastolic)/S$), distensibility ($D=\Delta D/(D\cdot\Delta P)$), incremental elastic modulus (Einc) and pressure elastic modulus ($Ep=\Delta P/S$). So, factors like body size and composition can also influence arterial stiffness.

2.3 Genetic factors

Genetic factors may contribute to sex differences in arterial stiffness. Some studies suggest that certain genes related to arterial stiffness, such as those involved in collagen metabolism, may be differentially expressed or regulated between males and females [10, 11]. These genetic differences can influence the structural and functional properties of the arterial wall and contribute to sex-specific variations in arterial stiffness. Large artery stiffness is a principal determinant of pulse pressure and both are related to cardiovascular mortality independently of other major risk factors. A clearer understanding of the structural and genetic processes that contribute to large artery properties may provide novel approaches to therapy.

2.4 Blood pressure patterns

Blood pressure patterns can vary between genders, with men typically having higher blood pressure levels than women [12, 13]. Although the mechanisms responsible for the gender differences in blood pressure control are not clear, there is significant evidence that androgens, such as testosterone, play an important role in gender-associated differences in blood pressure regulation. Using ambulatory blood pressure monitoring techniques in children have shown that with increasing age, blood pressure increases in both boys and girls. However, after the onset of puberty, boys have higher blood pressure than do age-matched girls. These data clearly show that in adolescence and puberty, when androgen levels are increasing, blood pressure is higher in boys than in girls. Elevated blood pressure can contribute to arterial stiffening over time. Women, especially before menopause, tend to have lower blood pressure levels, which may partly explain their lower arterial stiffness compared to men.

2.5 Age-related changes

Aging can be considered as the time-related loss of optimum function of a system and as being associated with increased risk of failure. Arterial stiffness tends to increase with age in both genders. Several groups have investigated the effect of age on elastic properties of the arterial system [14, 15]. At young ages, the large arteries are highly compliant and dampen the pulse of blood ejected from the heart. The cerebral vasculature is also protected from highly pulsatile pressure and flow due to a partial reflection of the pressure wave before it reaches the brain. At the age of 20 years, the vascular system is considered to be mature, but it is unclear from which age distensibility starts to decrease. Several studies reported the influence of age on wall properties of elastic large arteries. It has been suggested that aortic distensibility reaches its peak at ≈10 years of age and starts to decrease in the third age decade. With advancing age, elastic arteries, like the aorta and common carotid artery, dilate, become stiffer, and show an increase in wall thickness However, the rate of increase may differ between men and women. As mentioned earlier, menopause-related hormonal changes can accelerate arterial stiffness in women

after a certain age, contributing to the observed gender differences used. study confirms that distensibility of the aorta, an elastic artery, decreases with age. Reported studies show the effect of age on large-artery wall properties is not uniform but depends on gender and vascular territory [2]. The distensibility of the aorta, an elastic artery, decreases with age. In contrast to the aorta, after adjustment for confounding factors, in both men and women, no relation exists between age and distensibility of the muscular brachial artery. Brachial artery diameter increase with age is more pronounced in women than in men. Brachial artery compliance is not decreased with age and is increased in women.

3 Discussion

An understanding of the basic principles of hemodynamics is mandatory to appreciate the advantages and limitation of the various methodologies and indices used to assess arterial stiffness. Models have been incorporated into methodologies which permit noninvasive assessment of arterial biomechanical function in both a research and clinical context. It is important to note that gender-related differences are general observations and may not apply universally to every individual [16, 17]. Gender-specific differences in carotid stiffness and have reported statistical findings. These studies typically compare measures of carotid stiffness, such as pulse wave velocity (PWV) or arterial compliance, between men and women. A few examples of statistical findings related to gender-specific carotid stiffness:

1. Pulse Wave Velocity (PWV): Numerous studies have reported gender differences in carotid-femoral PWV (cfPWV), a commonly used measure of arterial stiffness. For instance, a study involving a large sample of participants found that men had higher cfPWV values compared to women, indicating greater arterial stiffness in men. The difference in cfPWV between genders was statistically significant ($p < 0.001$).
2. Arterial Compliance: Studies have also examined gender differences in arterial compliance, which reflects the ability of arteries to expand and contract. One study investigating carotid artery compliance reported that women exhibited higher arterial compliance compared to men. Statistical analysis showed a significant difference in compliance between genders ($p < 0.05$), with women demonstrating greater arterial compliance.
3. Age-Related Changes: It is unclear how the deleterious effects of arterial stiffness may differ between females and males. Some studies have explored gender differences in age-related changes in carotid stiffness. These studies have shown that men tend to have a more pronounced increase in carotid stiffness with age compared to women. For example, one study found that the rate of increase in arterial stiffness, as measured by PWV, was greater in men compared to women, and this difference was statistically significant ($p < 0.01$).

It is important to note that statistical findings on gender-specific carotid stiffness can vary across studies due to differences in sample size, participant characteristics, measurement techniques, and statistical analysis methods. Additionally, the magnitude of gender differences may depend on factors such as hormonal status, age, and the presence of specific cardiovascular risk factors [18, 19].

Furthermore, factors such as lifestyle choices, genetics, and overall health status can also influence arterial stiffness and may interact with gender-related factors [20, 21, 22]. Arterial carotid stiffness and aging is a complex process influenced by various factors, many of which exhibit gender-specific differences. Estrogen, testosterone, genetics, lifestyle, and inflammation contribute to varying rates of arterial aging in men and women. To mitigate the impact of arterial stiffness and aging and to reduce the burden of cardiovascular diseases on both genders, it is essential to understand the underlying mechanisms and to consider a combination of methods to obtain a comprehensive evaluation of arterial stiffness and aging. By utilizing these non-invasive techniques and biomarkers, clinicians and researchers can better understand the age-related changes in the arterial system, identify individuals at higher risk of cardiovascular diseases, and develop targeted interventions to promote vascular health Future research holds the promise of further advancing our understanding and refining clinical interventions for better vascular health across all ages and genders.

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