Arterial Compliance in the Elderly: Its Effect on Blood Pressure Measurement and Cardiovascular Outcomes

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**KEYWORDS**
- Arterial stiffness
- Arterial compliance
- Elderly
- Pulse wave velocity
- Blood pressure
- Cardiovascular outcomes

“Longevity is a vascular question, which has been well expressed in the axiom that man is only as old as his arteries. To a majority of men death comes primarily or secondarily through this portal. The onset of what may be called physiological arterio-sclerosis depends, in the first place, upon the quality of arterial tissue which the individual has inherited, and secondly upon the amount of wear and tear to which he has subjected it.”

—Sir William Osler, 1898

More than 100 years since William Osler wrote the above statements, his ideas still hold true. The loss of arterial compliance as a result of the aging of human vasculature contributes to the age-dependent rise in isolated systolic hypertension and is an independent predictor of all-cause mortality and cardiovascular (CV) outcomes. In this article, we begin by providing a brief historical perspective of the study of the pulse wave. We then review the physiology of the normal arterial system, the effects of aging on the arterial system, and the different measures of arterial stiffness. Finally, we review the different studies that consider arterial stiffness in the elderly, its impact on hypertension and CV outcome, and current knowledge on how to prevent vascular stiffness.
HISTORICAL PERSPECTIVE

Interest in the human pulse dates back to as far as 1500 BC, when papyri from the ancient Egyptians described the link, albeit vaguely, between the arterial pulse and the function of the heart.\(^1\) The examination of the pulse was an integral part of traditional Chinese, Indian, and Greek medicine.\(^1\) Examination of the pulse then was more of an art than a science, with no way of objectively recording the human pulse, other than the physician’s sensing of it.\(^1\)

It was not until 1628, when William Harvey published his classic monograph *An Anatomical Essay on the Movement of the Heart and Blood in Animals*, that the modern era of understanding the CV system began.\(^2\) By proving that the arterial pulse was the result of cardiac systole, Harvey set the scene for physiologic knowledge of the arterial pulse and for its clinical applications.\(^1\)

The nineteenth century proved to be a golden era in the study of the human pulse, as the development of the sphygmograph by Étienne Marey and its refinement during the next few years by Mahomed, Broadbent, and Mackenzie ushered in the birth of sphygmocardiography, or the art of interpreting the shape of the arterial waveform.\(^3\) Mahomed noted important differences in the shape of the waveform with age and was able to differentiate normotensive patients from those with essential and renovascular hypertension.\(^1,3\) It was also in this century that Moens described the link between arterial elasticity and pulse wave velocity (PWV).\(^4\)

After the sphygmomanometer was introduced following the work of Scipione Riva-Rocci (1896) and Nicolai Korotkoff (1905), which enabled blood pressure (BP) to be recorded accurately, quickly, and noninvasively, sphygmography took a backseat in clinical practice. In the twentieth century, the development of easy-to-use mercury manometers by Otto Frank in contrast to the complex calculation required for PWV further overshadowed the use of pulse wave analysis in clinical practice.\(^1,4\)

In the latter half of the twentieth century, investigators noted that even with equivalent BP control some individuals developed CV disease and target organ damage, whereas others did not.\(^4\) These observations prompted considerations that there was likely to be more than just the measured excursion of the pulse (ie, the systolic and diastolic pressures) responsible for such findings. Vascular mechanics, including pulse contour analysis and arterial stiffness, have, in recent years, been demonstrated to play a role in the development of CV disease.\(^4\) Such observations, along with the development of devices that more easily estimate arterial stiffness and reflected wave characteristics, prompted the renewed interest and research in arterial stiffness and its relationship with CV outcomes.

NORMAL ARTERIAL FUNCTION

The arterial system is a branching network of elastic conduits (large arteries) and high-resistance vessels (small arterioles and capillaries). It has two important and interrelated functions: (1) the conduit function, providing sufficient amount of blood to various tissues of the body, and (2) the capacitance function, converting the intermittent, highly pulsatile flow from the left ventricle into a steady arterial blood flow at the level of the small arteries.\(^5\) The capacitance function is performed mainly by the large central arteries that are relatively rich in elastin and collagen and have a low wall-to-lumen ratio.\(^6\) The elastin fibers are responsible for the mechanical strength of the vasculature at low pressures, and the collagen fibers, at higher pressures.\(^7\)

During systole, a bolus of blood is ejected into the aorta, stretching the aortic wall; in the process, most of the systolic pressure is stored as elastic tensile energy within the wall, hence protecting the small arterioles and capillaries from the potential damage of
high-pressure flow. Close to the end of systole, when the left ventricle relaxes and can no longer oppose the tension in the aortic wall, blood begins to flow back into the heart until the aortic valve closes commencing diastole. Having nowhere else to go, the blood continues its passage through the systemic circulation (the coronary circulation included), largely propelled by the elastic energy stored during systole and a modest mean arterial pressure gradient favoring forward flow. Thus, the cushioning function, which stores energy in the elastic walls of compliant vessels such as the aorta, protects small arterioles from high-pressure damage and ensures continuous blood flow and oxygenation to target organs. It also minimizes cardiac work, by conserving energy and making the cardiac cycle as efficient as possible.

As blood flows out from the heart as a result of left ventricular systole, a propagation wave is generated, which accompanies the flow of blood from the heart to the periphery. This propagation wave is a composite of left ventricular ejection, properties of the blood (such as viscosity), and characteristics of the arterial tree. On arrival at branch points or sites of impedance mismatch, this pressure wave is reflected and returned to the heart. The final pressure wave, as seen by an invasive catheter, for example, is the sum of the forward and reflected waves. For maximal efficiency, wave reflection should not add to the pressure generated during systole. The reflected wave should ideally reach the heart during diastole, to sustain the diastolic BP and augment coronary perfusion during diastole.

Fig. 1 illustrates this concept.

AGING AND VASCULAR AGING

Aging has been associated with changes in the arterial system at different structural and functional levels. At the macroscopic level, an increase in lumen size as well as an increase in arterial wall thickening, mainly in the intima, are observed. At the molecular level, changes from aging consist of the following: (1) increased collagen content and cross-linking, (2) increased elastin fragmentation, and (3) decreased arterial compliance in the elderly.

![Aortic waveforms derived from radial artery-based tonometry.](image)

**A** 39 year old man

**B** 64 year old woman

Aortic Pulse Wave Velocity = 7.6 m/sec

Aortic Pulse Wave Velocity = 11.3 m/sec

Fig. 1. Aortic waveforms derived from radial artery-based tonometry. The yellow line represents summation waveforms of an outward traveling (green line) and backward traveling (red line). (A) An aortic waveform from a 39-year-old man with normal BP and a normal aortic PWV of 7.6 m/s. The backward traveling waveform arrives at the end of systole and contributes to the small rise in pressure at the incisura (green vertical line) when the aortic valve closes. This mostly diastolic pressure contribution aids in coronary perfusion. (B) A 64-year-old woman with an elevated aortic PWV of 11.3 m/s has a backward traveling wave that arrives earlier in systole contributing to additional systolic pressure. Note, too, the greater amplitude of the backward traveling wave on the right-hand side.
elastin content. Aside from these structural changes, functional changes are also observed in the form of age-associated deterioration in endothelial function. All of the above changes contribute to the observed increase in arterial stiffness that accompanies aging.

Arterial stiffness has a marked and progressive effect on the capacitance function. With arterial stiffness, the velocity of both the propagation wave and the reflected wave increases, resulting in an earlier arrival of the reflected wave back to the heart, encroaching upon systole. This causes an increase in systolic pressure and a decrease in diastolic pressure (leading to a widened pulse pressure). The end result is a higher workload for the heart, decreased coronary perfusion during diastole, and higher pressures that are transmitted to the end organs, such as the kidneys and the brain.

Increasing arterial stiffness also affects the conduit function. It does this by increasing blood flow during systole when shearing forces are higher.

PROXIMAL AND DISTAL ARTERIAL STIFFNESS

In a healthy arterial bed, the elastic properties of arteries are normally variable—with proximal arteries usually more elastic and distal arteries stiffer. Differences in the molecular, cellular, and histological structures of the arterial wall in different segments of the arterial tree account for this noted heterogeneity. Such heterogeneity on the vessel wall has important physiological and pathophysiological consequences.

Imagine a pressure wave propagated along an elastic tube without reflection sites. Eventually, this pressure wave will diminish in size and disappear. Imagine this same pressure wave propagated along an elastic tube with numerous branch points, each of these branch points serving as reflection sites. The pressure wave will get progressively amplified as it moves from central arteries to distal arterioles; the amplification would be even higher if the distal arteries are stiffer, because this would lead to a faster velocity of both propagated wave and reflected wave. This is known as the “amplification phenomenon," and it accounts for the higher amplitude of pressure wave in the peripheral arteries than that in the central arteries.

This amplification phenomenon is less pronounced in the elderly. In fact, when comparing arterial pressures between a 20-year-old and an 80-year-old, if we only look at their brachial systolic BPs (SBPs), only a 20% increase from 120 to 140 mm Hg is evident. However, looking more closely at their aortic pulse pressure, they typically change from 22 to 65 mm Hg, which is actually close to a 200% increase.

This shifting trend in using central pressure rather than peripheral brachial pressures to assess CV risk is not limited to the elderly population. In a population of more than 10,000 individuals aged 18 to 92 years, McEniery and colleagues recently showed that more than 70% of individuals with high normal brachial pressure had similar aortic pressures as those in individuals with stage 1 hypertension. Thus, using only brachial BP would miss the overlap of central aortic systolic pressures between those with brachial SBP < 140 and those with SBP ≥ 140.

Partly because of the reliance on brachial sphygmomanometer and cuff SBPs, the effects of aging on arterial function have been largely underestimated in the past. Hence, it is imperative that studies on vascular aging not only consider direct measures of vascular compliance and stiffness but also focus on central artery measurements as much as possible.

PULSE WAVE VELOCITY AND OTHER MEASURES OF VASCULAR COMPLIANCE

In the last 20 years, research on arterial stiffness, its measurement, and how it affects CV outcomes has expanded greatly. The assessment of arterial stiffness and compliance
can be grouped into three broad categories: (1) measurement of PWV, (2) measurement of arterial distensibility, and (3) assessment of peripheral arterial pressure waveforms.4

**Measurement of PWV**

PWV is defined as the speed of travel of the pressure pulse wave along a specified distance on the vascular bed and can be obtained from any vascular bed accessible to palpation.3,4,6,20,21 From a mathematical standpoint, PWV is defined using a formula called the Moens-Korteweg equation:

\[
PWV = \sqrt{\frac{E_h}{2\rho R}}
\]

where \(E\) is the Young’s modulus of elasticity of wall material, \(h\) is the wall thickness, \(\rho\) is the density of blood and, \(R\) is the inside radius of vessel.20 From this equation, it is evident that PWV is influenced by arterial compliance (which is in turn dependent on elasticity and wall thickness), blood density, and vessel radius. Simplistically stated, the stiffer the artery, the faster the PWV.

The technique of PWV measurement has been validated as simple to learn and reproducible.22–24 To measure PWV, pulse wave signals are recorded with pressure tonometers positioned over two arterial sites, such as the carotid and femoral arteries. Distances between the two sampling sites are measured (\(D\)). In order to determine the time elapsed (\(\Delta t\)) as the wave travels from the more proximal to the more distal site,

Fig. 2. Graphic of woman with neck and wrist segments of a PWV measurement device that records pulsations simultaneously at multiple sites (neck, wrist, thigh, etc). PWV is determined by dividing the distance between measurement sites by the time elapsed between the waveforms sensed at each site.
either two tonometers record the same pulse wave in series (such as the Complior) or a single tonometer records the time elapsed as the pulse wave travels to each site sequentially (such as the SphygmaCor). In the latter case, a timing reference, such as the tip of the QRS complex on the electrocardiogram, is used as a central starting point. PWV is then calculated as follows:

\[
PWV = \frac{D}{\Delta t}
\]

where \(D\) is the distance in meters, and \(\Delta t\) is the time interval in seconds. Figs. 2 and 3 illustrate this concept.

A number of limitations in this method should be emphasized.\(^\text{16}\) (1) Since PWV is largely influenced by the distance measured, small inaccuracies in measurement of distance, such as those in patients with abdominal obesity, would affect the absolute value of PWV. (2) The pressure wave may be attenuated and delayed in the presence of aortic, iliac, or proximal femoral artery stenosis, thus affecting the measured PWV. (3) The femoral pressure waveform may be technically difficult to obtain in certain patients (ie, obese patients or patients with peripheral artery diseases).

**Measurement of Arterial Distensibility**

Arterial distensibility is defined as the change in arterial diameter during systole relative to diastole.\(^\text{20}\) Decreased distensibility suggests arterial stiffening.

**Fig. 3.** Here PWV is measured by recordings made of waveforms (in sequence, instead of simultaneously as in Fig. 2) at two different sites of known distance. Since they are not simultaneous, to determine timing lapse at the sites, the tip of the QRS from a surface electrocardiogram is used (typically limb lead II) by averaging waveform times during 10 s of cardiac activity. Once distance is measured and average timing lapse is determined, the PWV is again calculated as distance divided by the delta (difference) in time between the points. In the example shown, it took an average of 70 msec for the waveform foot to be detected at the carotid site and an average of 136 msec for the waveform foot to be detected at the femoral site. The time elapsed is 66 msec.
Ultrasound and a simultaneously recorded BP have been used to measure distensibility and compliance using the following formulas:

Distensibility = \( \frac{\Delta V}{\Delta P \cdot V} \)

Compliance = \( \frac{\Delta V}{\Delta P} \)

where \( \Delta V \) is the change in volume, \( \Delta P \) is the change in pressure, and \( V \) is the volume of the vessel.\(^3\)

The use of this technique is limited to the larger and more accessible arteries and has mainly been used on the brachial, femoral, and carotid arteries and the abdominal aorta. Several images of the vessel wall are obtained per cardiac cycle; a computerized software and wall tracking are then used to compute the maximum and minimum wall areas and volume. Problems with this technique include the following: (1) limited resolution making small changes in vessel wall diameter difficult, (2) operator dependence, (3) concerns about reproducibility and (4) expense of equipment.\(^3\) Aside from these, the BP is usually obtained from a different site (brachial or finger) than the site being imaged by ultrasound, casting further doubts on the reliability of the distensibility and/or compliance measurements.\(^3\) Moreover, inherent differences in muscular arteries such as the brachial artery compared with more elastic arteries such as the aorta, which has a lower wall-to-lumen ratio, further make ultrasound as a measure of arterial stiffness unreliable. Because of all these limitations, the use of ultrasound to measure arterial distensibility has largely been limited to research settings.\(^3\)

![Aortic waveform derived from applanation tonometry from a 78-year-old woman. Her brachial BP of 120/72 mm Hg was entered into the computer program to calibrate the radial artery waveform. After recording 10 sec of radial artery waveforms of good quality, the software algorithm determined the central aortic pressure profile. In the aortic waveform provided, there is an inflection (first green dot on X-axis) at approximately 100 mm Hg (by the right-hand Y-axis calibration), which is labeled P1. The aortic pressure profile peaks at a value of 111 mm Hg (P2) delineated by the upper green line. The total excursion (or pulse pressure) of the aortic profile is 38 mm Hg (as noted by the lower value in the column of values to the left of the aortic waveform graphic; these values are the central aortic systolic, diastolic, mean, and pulse pressures (PP), reading top to bottom). The PP divided into the value of \( ?P \) (which is derived as the delta of peak systolic pressure P2 minus the P1 value; 11 mm Hg) is the Augmentation Index (AI).](image)
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<td>Stroke (63)</td>
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<td>2.28</td>
<td>1.05–4.96</td>
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Abbreviations: CI, confidence interval; CHD, coronary heart disease; ESRD, end-stage renal disease; HTN, hypertension; m/s, meters/second; n/a, not available.
**Assessment of Peripheral Arterial Pressure Waveforms**

As described earlier, the arterial pressure waveform is a composite of the forward propagation wave and reflected wave. In a healthy arterial tree, the reflected wave arrives back at the aortic root during diastole. Stiffer arteries generate higher PWVs, resulting in the reflected wave reaching the aortic root at the end of systole and augmenting the late systolic pressure (see Fig. 1, panel B). This results in a second systolic peak on the pressure waveform, also known as the inflection point. To estimate the effect of this reflected wave on the pulse pressure, a value called an augmentation index (AI) can be generated in the following fashion:

\[
\text{Augmentation index (AI)} = (P_2 - P_1) / pp
\]

where \( P_2 \) and \( P_1 \) are the peak systolic peak pressure and inflection pressure, respectively, and \( pp \) is the pulse pressure.\(^3,6,16,20\) A graphical depiction of the AI is shown in Fig. 4. The AI estimates vascular compliance, in that the stiffer the artery, the higher the AI.\(^3,6,16\) AI can be obtained by application of the transfer function to the pressure pulse obtained at the radial or carotid arteries by applanation tonometry.\(^6,16\)

First, in considering AI as a surrogate marker of arterial stiffness, it is important to recognize that in contrast to aortic PWV, which is the speed of wave travel and is thus a direct measure of arterial stiffness, AI is an indirect measure of arterial stiffness, as it is dependent on other factors aside from PWV.\(^16\) These include the amplitude of the reflected wave, the distance to the reflectance point (s), and the duration and pattern of ventricular ejection.\(^16\) Second, certain pathophysiologic conditions and drugs may change central pulse pressure and AI without necessarily changing PWV.\(^16,25,26\) Third, AI has been shown to be more sensitive to heart rate and height than PWV.\(^16\) Fourth, gender has been found to influence AI in that women have a higher AI than that of men.\(^27\) Finally, in the elderly population, aortic PWV was found to be a better measure of arterial stiffness than AI in at least 2 studies.\(^28,29\) Indeed, the position statement put forth by the European expert consensus on arterial stiffness is to not use AI and PWV interchangeably but to use AI coupled with PWV to determine the contribution of aortic stiffness to wave reflections.\(^16\)

**ARTERIAL STIFFNESS AND CARDIOVASCULAR OUTCOMES**

The largest amount of epidemiologic data with regard to arterial stiffness and its relationship to CV outcomes is that obtained via aortic PWV (carotid-femoral PWV). The first direct evidence that increased aortic stiffness is a strong and independent predictor of CV mortality was shown in a cohort of 241 hemodialysis patients followed prospectively by Blacher and colleagues in 1999.\(^30\) Subsequently, aortic stiffness has been shown to be an independent predictor of all-cause and CV mortalities, fatal and nonfatal coronary events, and fatal strokes in patients with uncomplicated essential hypertension,\(^31–33\) type 2 diabetes,\(^34\) end-stage renal disease (ESRD),\(^35,36\) elderly subjects,\(^37–39\) and the general population\(^40,41\) independent of other CV risk factors. The pertinent details of these studies are summarized in Table 1.

Worth special mention is a prospective study by Guerin and colleagues of 150 dialysis patients with hypertension.\(^36\) The patients’ BPs were lowered by targeting their dry weight; they were then randomly assigned to either an angiotensin-converting enzyme inhibitor ACE-I or a calcium channel blocker. Of the 150 patients, 59 died during the 4-year follow-up. The important observation that was made was that the aortic PWV of those who died during follow-up began at a higher average value and did not decline even with documented reduction in brachial BPs.
One possible explanation for this is the fact that aortic stiffness integrates the damage of CV risk factors on the arterial wall during a long period of time, whereas BP, glycemia, and lipids fluctuate over time, and their values, recorded at the time of risk assessment, may not reflect the true values damaging the arterial wall.\textsuperscript{4,16} Thus, lowering BP and lipid values and improving glycemia control in a few weeks may improve CV risk scores, but without attenuating arterial stiffness, which may take a longer period of time, or may be partially irreversible, an improvement in CV mortality may not actually be seen.\textsuperscript{16}

MODIFYING ARTERIAL STIFFNESS

A number of small studies have reported improvement in arterial compliance with several pharmacologic and nonpharmacologic interventions.

Dietary and lifestyle changes that have been shown to reduce arterial stiffness include the following: low-salt diet,\textsuperscript{42,43} moderate alcohol consumption,\textsuperscript{44} garlic powder,\textsuperscript{45} alpha-linoleic acid,\textsuperscript{46} fish oil,\textsuperscript{47} dietary isoflavins,\textsuperscript{48} and weight loss.\textsuperscript{49} Surprisingly, contradictory results have been found with aerobic exercise and arterial stiffness.\textsuperscript{49–51} Hormone replacement therapy has also been shown to have a positive effect on arterial stiffness.\textsuperscript{52,53}

Pharmacologic treatments that are able to reduce arterial stiffness include the following: antihypertensive medications (such as diuretics, ACE-I, angiotensin receptor blockers, beta blockers, and calcium channel blockers),\textsuperscript{54–61} medications for treatment of congestive heart failure (ACE-I, nitrate, and aldosterone antagonists),\textsuperscript{62,63} lipid-lowering agents,\textsuperscript{64} thiazolidinediones,\textsuperscript{65} sildenafil,\textsuperscript{66} and advanced glycation end-product breakers such as alagebrium.\textsuperscript{67}

SUMMARY

Aging is associated with a number of structural and functional changes that are thought to contribute to arterial stiffness. Increasing arterial stiffness has been associated with increasing central SBP and has been shown to be an independent predictor of all-cause mortality and CV outcomes. Sphygmanometric measurements of brachial SBP do not fully reflect central aortic pressure profiles and may thus be falsely reassuring. Measurement of aortic PWV is the best available noninvasive measure of aortic stiffness and correlates well with CV outcomes.

Numerous studies with pharmacologic and nonpharmacologic interventions have shown improvement of aortic PWV values. In spite of these studies, several questions remain unanswered: (1) Will improvement in arterial stiffness translate into improved CV morbidity and mortality? and (2) Will normalizing arterial stiffness be more effective at improving CV outcomes than the present standard of care? The study by Guerin and colleagues\textsuperscript{36} may have partially addressed the first question (at least in ESRD patients), but further studies need to be done to completely settle these issues.

REFERENCES


42. Avolio AP, Clyde KM, beard TC, et al. Improved arterial distensibility in normoten-
large elastic artery compliance in older adults with systolic hypertension. Hyper-
tension 2004;44:35–41.
44. Sierkman A, Lebrun CE, van der Schouw YT, et al. Alcohol consumption in rela-
tion to aortic stiffness and aortic pulse wave reflections: a cross-sectional study
in healthy post-menopausal women. Arterioscler Thromb Vasc Biol 2004;24:
342–8.
garlic intake on elastic properties of aorta in the elderly. Circulation 1997;96:
2649–55.
is improved with dietary plan-3 fatty acid from flaxseed oil despite increased LDL
47. McVeigh GE, Brennan GM, Cohn JN, et al. Fish oil improves arterial compliance
48. van der Schouw YT, Pijpe A, Lebrun CE, et al. Higher usual dietary intake of phy-
toestrogens is associated with lower aortic stiffness in postmenopausal women.
loss with or without exercise training on large artery compliance in healthy obese
50. Kingwell BA, Berry KL, Cameron JD, et al. Arterial compliance increases after
modify large artery compliance in isolated systolic hypertension. Hypertension
2001;38:222–6.
52. Rajkumar C, Kingwell BA, Cameron J, et al. Hormonal therapy increases arterial
weeks decreases arterial compliance in postmenopausal women. J Hypertens
54. Girerd X, Giannattasio C, Moulin C, et al. Regression of radial artery wall hyper-
trophy and improvement of carotid artery compliance after long term antihyper-
55. Asmar RG, Pannier B, Santoni JPh, et al. Reversion of cardiac hypertrophy and
reduced arterial compliance after angiotensin converting enzyme inhibition in
diuretic combination amiloride + hydrochlorothiazide on the vessel wall proper-
57. Ting CT, Chen CH, Chang MS, et al. Short and long-term effects of antihyperten-
sive drugs on arterial reflections, compliance and impedance. Hypertension
58. Mahmud A, Feely J. Reduction in arterial stiffness with angiotensin II antagonist is
type 2 diabetes independently of blood pressure lowering. Hypertension 2008;
51:1617–23.


