Original Paper

The Arterial Pulse Wave and Vascular Compliance

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For just over 1 century, we have relied on cuff sphygmomanometry to measure blood pressure at a peripheral (brachial) site. This measurement provides a quantitative snapshot of hemodynamic activity at 1 part of the arterial tree. Because the heart and brain are exposed to central (aortic) and not peripheral (brachial) pressure, it might be timely for nurses to start looking at alternative techniques to provide more meaningful information on central hemodynamics. The noninvasive technique of applanation tonometry allows such measurements to be performed quickly in the nursing clinic. By analyzing the pulse wave and calculating pulse wave velocity, the technique also assesses arterial "stiffness." This method of cardiovascular assessment further enables nurses to monitor the central effects of antihypertensive, lipid lowering, and other drug therapy over time. Prog Cardiovasc Nurs. *2009;24:53–58.*

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This review will highlight the importance and relevance of pulse wave analysis (PWA) that encompasses pulse wave velocity (PWV) and augmentation index (AI*x*)—both are measures of arterial compliance. This tool is particularly useful when investigating patients who are at risk of, or who have established, cardiovascular disease. The reason for adopting this noninvasive technique is that it provides *central* hemodynamic information that is unobtainable from conventional brachial artery (*peripheral*) recordings of blood pressure (BP) using a cuff sphygmomanometer. In addition, it assesses arterial "stiffness" as an independent risk factor for cardiovascular disease. Indeed, traditional risk factors all lead to the end result of arterial stiffness. In a preventative situation, PWA can detect early arterial stiffness, which can be halted or even reversed by appropriate intervention. In this paper, a historical background of mechanics and blood flow will be presented, followed by a review of PWA for monitoring arterial compliance and central hemodynamics. The accumulated evidence that emphasizes the importance of PWA in clinical practice will be addressed.

HISTORICAL BACKGROUND

Palpation of the arterial pulse is a fundamental sign in clinical practice, providing more information than merely the heart rate. In fact, the term "pulse" has been used incorrectly to denote the frequency of the heart beat. When the left ventricle ejects blood into the aorta, the elasticity of this vessel allows it to stretch. This is the start of the pulse wave, and is what is palpated during an assessment of the pulse. If the heart generates the *occasional* ineffective beat, it may not be detected at the radial artery. Likewise, if a *major* heart irregularity is present, palpation of heart beat frequency at the radial artery may not correspond to the actual rate of the heart. Nowadays, we assume the importance of hypertension in relation to cardiovascular disease. As long ago as 1827, William Bright diagnosed high BP on the "hardness" of the pulse.[1] A more scientific method for assessing the pulse called sphygmography[2] was developed by Dr Frederick Akbar Mahomed (Figure 1a). Sphygmography provided a qualitative illustration of the effects of medication on the arterial pulse, as well as providing a picture of the arterial waveform in hypertension and other diseases. Mahomed also used sphygmography to describe the effects of aging on arterial degeneration.[3] These effects were of great interest to the insurance companies, and were included in their estimation of risk.[4] Although the technique of sphygmography became well established in medical practice of the day, reported in journals and textbooks (Figure 1), it went out of favor with the introduction of the cuff sphygmomanometer in the early 20th century.[5,6]

Because diastolic, systolic, and pulse pressures (PP) are related to the physical properties of the elastic arteries, current attention has been redirected toward arterial stiffness, PWV, and altered wave reflection as independent risk factors for cardiovascular disease.[7–10] Comparable with Mahomed's 1874 work,[3] recent studies have shown an association between normal aging and arterial stiffness,[11,12] and between arterial stiffness and coronary artery

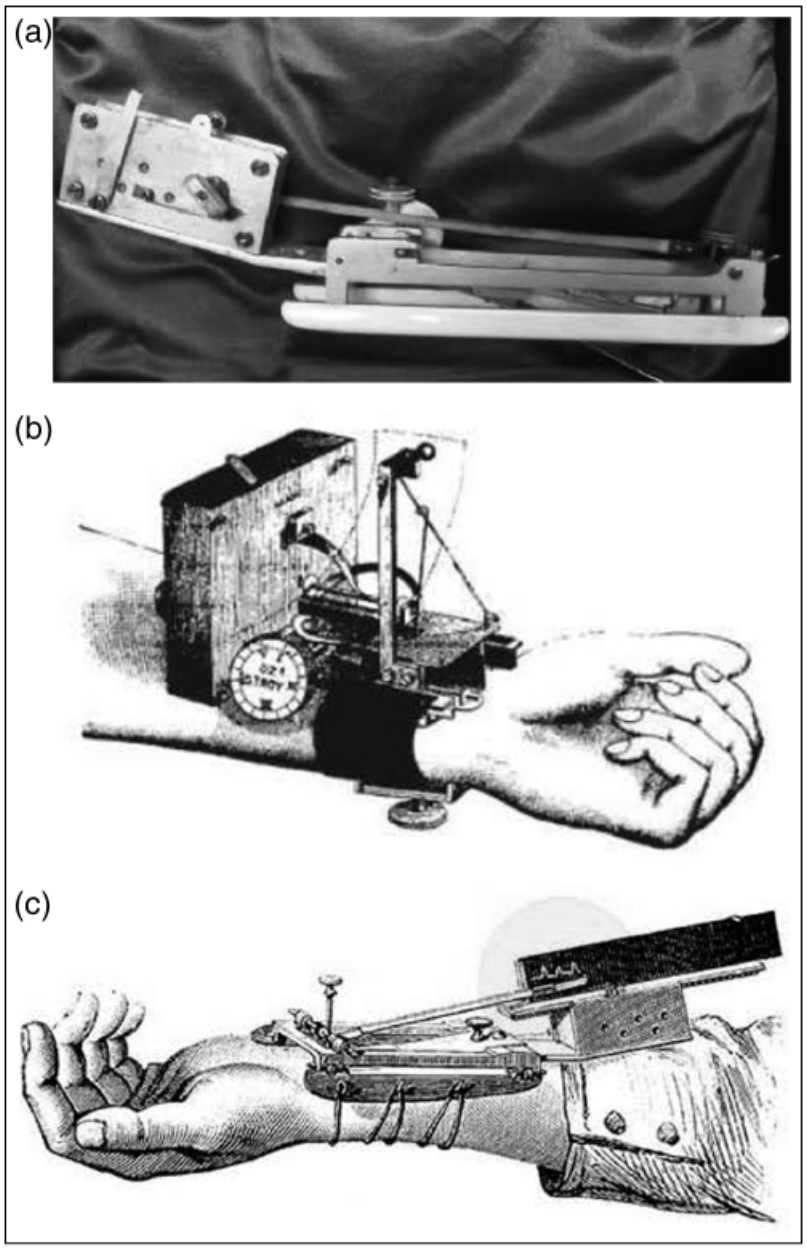

Figure 1. The figures depict the evolution of sphygmography technology in the late 1800s to the early 1900s, before the advent of the modern sphygmomanometer. (a) Sphygmomanometry instrument developed by Dr Mahomed in 1872 (Courtesy: University of Manchester Medical School Museum, 2008); (b) Sphygmomanometry device developed by Dr Dudgeon and used by Sir James MacKenzie in 1902 (Courtesy: Homéopathe International, 2001); and (c) Sphygmograph with arterial waveform recorded by a pen-recorder developed by Dr Marley in 1914 (Courtesy: Letzte Änderung: June 21, 2007).

disease,[10,13] myocardial infarction,[14] heart failure,[15] hypertension,[16,17] stroke,[18,19] diabetes mellitus,[20–23] renal disease,[24] hypercholesterolemia,[25] children with chronic kidney disease,[26] endothelial function,[27] inflammation,[28] and all-cause cardiovascular mortality.[16,29] Vascular damage is common to all of these conditions, with inflammation being a prerequisite, and leading to arterial stiffness. The central pathological processes involved are mainly structural, as we shall see, with endothelial dysfunction also playing a role. The focus on sphygmomanometry as developed by Mahomed and others at the beginning of the 20th century waned until about 50 years ago when MacDonald's seminal work on blood flow in arteries and arterial mechanics was published.[30] Since then, the advent of the microcomputer allowed Professors Michael O'Rourke and Wilmer Nichols to develop a 21st-century version of sphygmography.[31]

THE METHOD OF PWA AND PWV BY APPLANATION TONOMETRY TO ASSESS ARTERIAL COMPLIANCE

The technique of PWA using the SphygmoCor® Cardiovascular Management System (AtCor Medical, Sydney, Australia), which determines central aortic pressure and AI*x* and-PWV, has been used in many studies over the past decade.[7,30–32] Other devices are being manufactured increasingly, e.g., the oscillometric and capacitive method described by Cohn and colleagues.[33] PWA is used increasingly by nurses in the clinic and by research nurses in the research laboratory. Central (aortic) pressure can be measured and the AI*x* calculated, to yield an index of arterial stiffness. Gating or synchronizing the signals at two sites of the electrocardiogram (ECG) allows PWV to be measured. Thus, PWA provides an accurate, noninvasive, easily applied method with which to measure central pressures and two indices of stiffness, i.e., PWV and AI*x*. In applying the technique to a clinical situation, a high-fidelity micromanometer (SPT-301; Millar Instruments, Houston, TX) can be used to flatten but not occlude the artery in question, using gentle pressure. Because of its very high-frequency ultrasound specifications, this manometer is highly accurate and comparatively inexpensive. Other "array" micromanometers are available by Millar Instruments and other companies (e.g., model N-500, Nellcor Inc., Boulder, CO); however, these ma-

nometers are costly. When the artery underlying the skin surface is flattened using gentle pressure of the manometer, circumferential pressures within that point of the artery are equalized and an accurate pressure waveform can be recorded; this technique is termed applanation tonometry (Figure 2). Data are collected directly into a laptop computer. After 20 sequential waveforms are acquired, the integral software is used to generate an averaged peripheral and corresponding central waveform, which was then subjected to further analysis: determination of either AI*x* or PWV.

Physiological variations in the pulse wave and in PWV are seen at different sites of the arterial tree. Because the velocity of wave travel is faster in stiffer and smaller vessels, this structural alteration causes a progressive increase in the PWV along the arterial tree.[34] There is also a progressive increase in PP from the central aorta to the peripheral sites. This PP amplification is less evident with aging,[32] probably due to the increased aortic PWV, which is secondary to aortic stiffness. In healthy adults, the PWV is approximately 7.3 m/s from the heart to the radial artery and 8.0 m/s from the heart to the femoral artery.[32] The incident (forward) wave is reflected backward along the arterial system from peripheral reflection sites to the ascending aorta. A high level of arterial stiffness (decreased compliance) causes an increase in PWV and earlier return of the reflected wave to the ascending aorta.[34,35] Early return of reflected pressure waves adds to the amplitude of the incident wave during the systolic phase (Figure 2b). Thus, the augmentation in the systolic part of the ascending aortic pressure further increases systolic pressure and ventricular afterload. A PWV >8.5 to 9.0 m/s would be indicative of arterial stiffness.

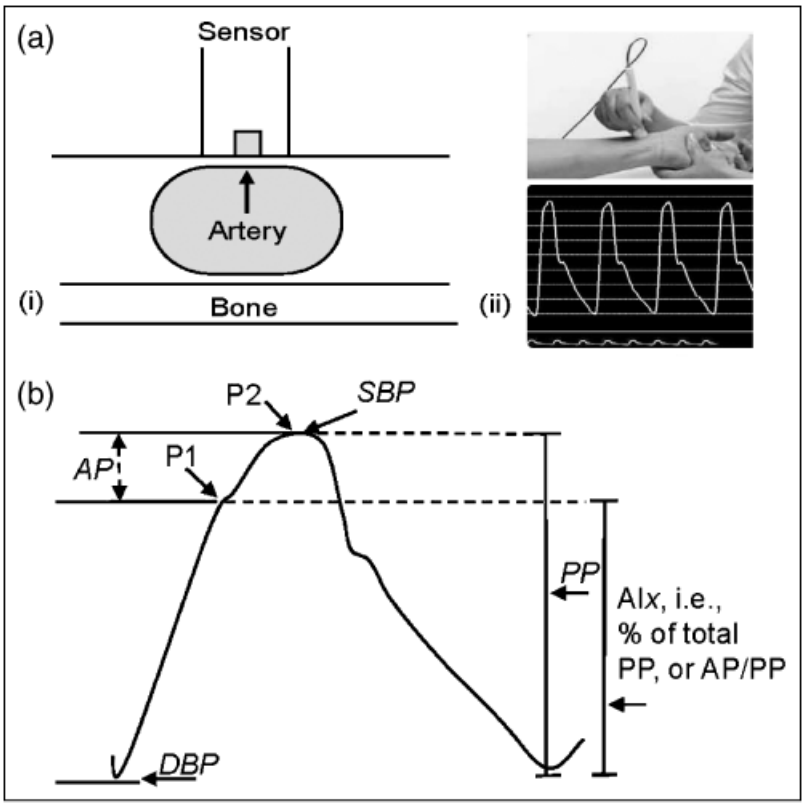

Figure 2. (a) Diagrammatic representation of the artery being "applanated" between the ultrasound sensor and the underlying hard structure—in this case, a bone. Actual applanation of the radial artery, with the wave form from the laptop screen shown below. Compare this with the more cumbersome devices in Fig. 1. (b) Definition of the augmentation index (AIx). The inflection point (P1) identifies the merging point of the propagated and reflected waves (the reflected wave arriving back sooner if arterial stiffness is present). AP, augmentation pressure; PP, pulse pressure; SBP, systolic blood pressure; and DBP, diastolic blood pressure.

RELIABILITY AND VALIDITY OF THE INSTRUMENT

It is important to determine the measurement of PWA and PWV with precision if they are used as indicators of arterial compliance. In other words, considerable reliance is placed on a single instrument, and we must be sure of its reliability and reproducibility, irrespective of the operator. The system's internal mathematical transfer factor, which converts peripheral data to corresponding central pressure data, has been shown to equate well with many invasive studies, and found to be highly accurate and reproducible.[9,36,37] The system has a built-in quality control that calculates the coefficient of variation (CV) for multiple waveforms, and will not accept sampling with a preset CV value of between $>1\%$ and $>5\%$. In addition, before each patient is studied, the machine engages in self-calibration based on the input of BP measurements taken with another device (our laboratory uses the well-validated Omron HEM-705CP semiautomated sphygmomanometer; Omron Corporation, Kyoto, Japan, but many other validated devices are available). AI*x* is defined as the difference between the first and the second peaks of the central arterial waveform, expressed as a percentage of the PP (Figure 2b). To determine PWV, pressure waveforms are recorded at 2 sites: the carotid and radial, or carotid and femoral arteries. Using the R wave of a simultaneously recorded ECG as a reference frame, the wave transit time is calculated by the system software. The surface distance between the 2 recording sites is

then measured, thus allowing PWV to be determined (velocity = distance/time). Like many other medical instruments, reliance on the accuracy and validity of this device is important if clinical decisions are made on the basis of its measurements.

WHY IS LARGE-ARTERY COMPLIANCE OF CLINICAL IMPORTANCE?

Historically, elevated peripheral vascular resistance is associated with essential hypertension. Reduced arterial compliance or distensibility and arterial stiffness are often used interchangeably by researchers. Mathematically and conceptually, they are different.[36] Compliance of an arterial segment represents the increase in its crosssectional volume for a given increase in pressure, which does not account for the diastolic dimension before distension begins. Distensibility is compliance normalized by arterial diameter. Stiffness is the reciprocal of distensibility.[34,38] Recently, this has been challenged because it ignores the pulsatile component,PP, of arterial pressure.[39] Arterial compliance is a principal determinant of BP. Compliance is pressure dependent, subject to arterial structural mechanics,[38,39] and also relies on the function of the vascular endothelium.[27] Ventricular ejection, interacting with the elasticity of the large arteries and the viscosity of the blood and wave reflection are 2 major determinants of the pulsatile component of BP. An increased PP reflects decreased arterial compliance (i.e., increased stiffness). Thus, elevated systolic blood pressure (SBP) and PP are now considered to be more reliable indicators of cardiovascular risk than diastolic blood pressure (DBP).[37,39–46] An increase in large-artery stiffness and a consequent increase in the amplitude of wave reflection result in a disproportionate increase in SBP and arterial pulsatility. This disproportionate increase in SBP increases PP, producing the phenomenon known as isolated systolic hypertension (ISH).[47] ISH is characterized by a widening PP, due to increased SBP and a normal DBP.[44,47] We know that arterial stiffness increases with aging,[3,11,12,38] which may account for ISH in the elderly. Given the changing demographics, especially the emergence of an increasingly aging population, we should be aware of PP in *all* patients, as elevations may point toward ISH.

THE CHARACTERISTICS OF LARGE ARTERIES AND PULSATILE FLOW

A reevaluation of these hemodynamic indicators of cardiovascular risk can be conceptualized by viewing large arteries as simple passive conduits. Large arteries cushion pulsatile flow generated by ventricular contraction during each cardiac cycle, transforming intermittent flow into a steady flow of blood in the periphery and reducing the pressure oscillations caused by the intermittent ventricular ejection.[38,45,46,48] The viscoelastic properties of the arterial wall determine the artery's ability to perform this cushion function. During systole, large arteries (e.g., the proximal aorta) expand to accommodate stroke volume (SV) and rebound during diastole to facilitate forward blood flow. When arterial compliance is decreased, less cushioning of SV occurs in the arterial bed during systole, and so a greater proportion of SV is forwarded to the periphery. Consequently, the amplitude of the arterial pulse wave during systole increases and diastolic pressure declines.[38,48]

One way to think about this reservoir or cushioning capacity is illustrated in the Windkessel model, which describes the recoiling of large arteries (Windkessel vessels). Windkessel in German means *elastic reservoir*.[49] The walls of large arteries (e.g., aorta, common carotid, subclavian, and pulmonary arteries and their larger branches) contain elastic fibers in their walls. These arteries increase their diameters when the BP increases during systole and decrease their diameters when the BP declines during diastole. The diameter changes result in the large arteries containing more blood during systole than during diastole. This additional blood is discharged peripherally during the next diastole. This compliance effect of the Windkessel prevents excessive increases in BP during systole. One result is a lower fluid mechanical load on the heart than otherwise would have occurred. Pressure wave reflections in the arterial system (a distributed system, as contrasted with a lumped system) can and do alter this effect.

The mechanical properties of the large arteries, the viscosity of the blood, the volume of blood being ejected from the heart, and the force of ventricular ejection are all important because impairments of or interruptions to any of these processes can lead to heart failure. We can detect possible anomalies by measuring arterial stiffness at an early stage in the disease process so that effective treatments can be considered.

COMPLIANCE AND THE ARTERIAL TREE

This cushioning effect of *large* arteries is affected by their structural mechanics, such as *compliance*. Arterial compliance also determines pressure wave travel and reflection in the rest of the arterial system. Thus, increased resistance in the periphery due to arterial stiffness causes earlier reflection of the pulse wave.[50] The incident wave, generated by ventricular ejection, moves away from the heart at a finite speed. The speed of pulse wave propagation (PWV) increases as arterial compliance decreases. The proximal aorta is relatively compliant to accepting the SV. As the aorta extends distally, it becomes less compliant. The compliance of the arteries also decreases with distance from the heart. Indeed, the observation was made >50 years ago that BP varies throughout the arterial tree.[51] Systolic BP in the *peripheral* brachial artery is approximately 5 to 30 mm Hg higher than in the *central* aorta. This keeps blood flowing in the forward direction as diastolic and mean pressures are slightly lower in the periphery. This is important because the heart and brain are exposed to aortic, not brachial, pressure. While

autoregulation of blood flow is a contributing factor to BP, it may be less responsive with *high* BP. This point is particularly pertinent to nurses who record the brachial BP routinely. In the management of cardiovascular patients, quick and easy measurements of *central* hemodynamics made by PWA (central PP, central BP, central AI*x*, ejection duration, subendocardial viability ratio [SEVR or Buckberg ratio], etc.,) may be of more value in the clinical setting, whether in the cardiovascular risk reduction clinic or in the heart failure unit.

CLINICAL TRIAL EVIDENCE FOR THE USE OF PWA

It has been generally accepted over the years that lowering of BP, irrespective of the particular antihypertensive agent used, results in better cardiovascular outcomes. However, there has been a recent paradox surrounding β-blockers that do lower BP, but that do not improve outcome.[52–55] Even in lowering BP, the selective β_1-adrenoceptor antagonist, atenolol, seems less effective than other agents,[54,55] despite an equivalent effect on brachial pressure, which may also explain why it also fails to improve outcome.[56] An explanation for the β-blocker inconsistency emerges from the recent Conduit Artery Function Evaluation (CAFE) study.[57] In this study, both brachial and aortic BPs were measured in a subset of 2199 patients from the Anglo-Scandanavian Cardiac Outcomes Trial (ASCOT) study.[58] Systolic and PPs in the aorta were 4.3 and 3.0 mm Hg lower, respectively, in patients randomized to a calcium-channel blocker (CCB) and an angiotensin-converting enzyme (ACE) inhibitor (amlodipine/perindopril) than those on a β-blocker and thiazide diuretic (atenolol/bendroflumethiazide), despite virtually identical reductions in brachial pressure. In addition, aortic PP was a significant independent determinant of total cardiovascular and renal events, even after adjusting for differences in brachial pressure. Thus, in hypertensive patients, having central hemodynamic information is more important than knowing about brachial pressure, taken with a conventional cuff sphygmomanometer. These results in the CAFE study may in part explain the results in the main ASCOT study: that patients assigned to atenolol/bendroflumethiazide did not do as well because they had higher aortic pressures than those receiving the CCB/ACE inhibitor treatment. However, most of the BP data from the randomized-controlled trials over the years have been based on brachial artery measurements. Reductions in brachial pressure have certainly led to improved patient outcomes. Nevertheless, CAFE is a start, and shows the value in assessing central pressures and of measuring arterial compliance in targeting specific, more effective treatment to individual patients. Serial assessment of arterial applanation tonometry also monitors the effect of treatment on compliance over time, showing, for example, that statins may "normalize" impaired distensibility, i.e., make stiff arteries more compliant again.[59] This is important for nurses in making the actual measurements, and also important in influencing which treatment to use, in accordance with the evidence-based clinical guidelines. Changes in arterial compliance have also been seen in patients with other, nonpharmacological treatments, such as hemodialysis[60] and renal transplant.[61]

SUMMARY

In summary, as arterial compliance decreases (stiffness increases), both the amplitude of the pressure wave generated by ventricular ejection and PWV increase, causing early return of the reflected pressure wave from the periphery to the aorta. The importance of applanation tonometry has been highlighted throughout this paper, and can be summarized by reiterating that it allows assessment of not only arterial stiffness by measuring pulse wave reflection and PWV, but it also provides more information on central hemodynamics than conventional brachial artery sphygmomanometry. Thus, the simple, noninvasive technique of applanation tonometry could be adopted more by nurses as part of the overall cardiovascular risk assessment in our hypertension, lipid, and risk-reduction clinics.

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