Review Article

Central Aortic Blood Pressure: An Evidence-based Approach

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Abstract

The conventional brachial blood pressure measurement remains as a principle tool to assess cardiovascular risks and monitor the effect of drug therapies. The convenience of measuring the blood pressure in the brachial artery and its cost-effectiveness made it a gold standard for measuring the blood pressure across the world. Even though the diastolic pressure and mean arterial pressure are close to constant throughout the arterial tree, the systolic pressure is not. The systolic pressure widely varies in different segments of the arterial system. This makes the measured brachial pressure inaccurate reflection of load in the central hemodynamics. All the major end organs such as the heart, brain, kidneys, and large arteries, which bear the brunt of hypertension, actually perceive the pressure on the central elastic arteries and certainly not on the brachial artery. Due to the complex mechanism of the presence of wave reflection, pulse pressure amplification, and arrival of the reflected wave to the aorta, the central aortic systolic pressure and brachial pressure were never identical. To add to this complexity, the drug has a differential effect on the brachial and central aortic pressure. In future, the management of hypertension will revolve around central blood pressure and central aortic pressure waveform analysis.

Key words: Central blood pressure, wave reflection, pressure amplification, arterial stiffness, cardiovascular events

Introduction

Hypertension is one of the major causes of cardiovascular death and disability across both developed and developing nations.[1] Blood pressure, measured in brachial artery over the forearm, has firmly established itself as a routine clinical tool in the cardiovascular risk assessment and managing hypertension. Predicting future cardiovascular events in asymptomatic individuals and patients with cardiovascular disease made brachial blood pressure not only a routine but also a superior clinical tool. In the past couple of decades, several studies have shown patients with diagnosed hypertension; if their brachial blood pressure is lowered by hypertension drugs, this can positively influence the future cardiovascular event rates. Inadvertently, all these successes with brachial blood pressure have left it unchallenged for more than 100 years and have been slowly accepted as a surrogate measure of pressure in the central elastic artery, such as central aortic blood pressure. When diagnostic cardiac catheterization came into practice in the late 1940s, it became increasingly evident that the pressure in the arterial tree was different at different segments of the artery due to arterial stiffness and wave reflections.[2] This questions the basic assumption that brachial pressure as a surrogate measure of central aortic blood pressure was not accurate. In many instance the difference between the central and brachial pressure vary widely from 20 to 40 mmHg.[3-5] Furthermore, the pressure in the central elastic artery, where all the major organs were exposed to, was never the reflection of pressure in the peripheral brachial artery. The future of blood pressure management will be based on the accuracy of measuring the central blood pressure noninvasively. Currently, there are a number of clinical data to show the superiority of central blood pressure over brachial pressure in predicting future cardiovascular events. Studies also showed targeting and reducing the central blood pressure results

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in greater reduction of cardiovascular events.

Historical Perspective

Historically for thousands of years, palpating the pulse in the radial artery was practiced in the Eastern countries including Greek, Egypt, China, and India. The palpation of the radial artery was done to assess the characteristics of the pulse. The change in pulse contour in health and in disease status was well recognized during these civilizations at a very early date. This practice reached western countries only in the 18th century. In the 1860s, palpation of the radial artery was advanced and the recording of this pulse waveform from the radial artery was made possible through a device called the sphygmograph [Figure 1].

Thus, the art of interpretation of the pulse waveform in different disease conditions had began and popularized.[6] One of the many pioneers Akbar Mahomed, the grandson of a Bengali Indian restaurant owner, who was considered as a visionary, wrote in 1871 in his paper "The pulse ranks first among our guides; no surgeon can despise its counsel, no physician shut his ears to its appeal…we should study the pulse in its marvelous changes of character and form." However, by the early 19th century, the sphygmograph was slowly replaced by the sphygmomanometer due to this new device's ability to quantify blood pressure in numbers. This new device was able to provide numbers for the two extreme measure of the waveform, namely systolic and diastolic pressure. This, indeed, revolutionized the management of hypertension, which was actively encouraged by the Life Insurance Companies as a risk assessment tool for its policyholders. This ultimately resulted in the shift from pulse waveform interpretation to systolic and diastolic numbers of interpretation. The waveform which carries remarkable information about the ventricular interaction with the vascular system, reflecting the compliance of the systemic vessels, was abandoned in favor of two simple numbers. From early 19th century to the 20th century, sphygmomanometer was unchallenged. Now, for the past two decades, there was a renewed interest among researchers and clinicians to move toward arterial waveform and arterial stiffness assessment rather than fully depending on brachial systolic and diastolic pressure. This derived central aortic blood pressure waveform noninvasively from peripheral artery is a more accurate reflection of the real pressure load on the major target organs of hypertension, namely
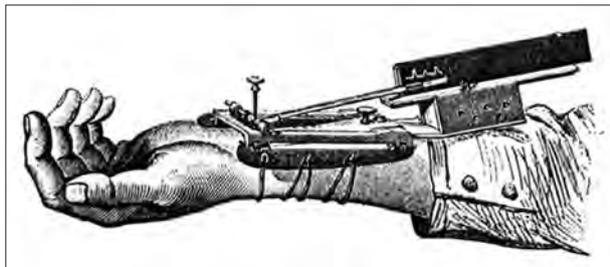

Figure 1: Sphygmograph original equipment, showing amplified pulse recorded in the smoked paper

the brain, kidneys, and heart. The forearm-based brachial blood pressure measure is devoid of the waveform which can provide crucial information on wave reflection and its effect on central hemodynamics. Newer devices can now derive central blood pressure noninvasively by applying a tonometer in the radial artery or by blood pressure cuff in the brachial artery as accurate as invasive measurement through cardiac catheterization.[7]

Effect of Wave Reflection on Central Aortic Pressure

In an arterial tree from the proximal aorta to the femoral artery, the pressure waveform contours and peak systolic pressure change throughout the vascular system. However, the diastolic and mean arterial pressure is relatively constant. In young individuals, the peak systolic pressure increases and the waveform contour changes significantly as the pressure waveform moves from the center to the periphery. In middle age and older individuals, the increase in peak systolic pressure is comparatively lower and the waveform contour changes also less significant as the pressure wave moves toward the periphery in the vascular system [Figure 2].

This change in the peak systolic pressure and wave contour is due to the wave reflection. This phenomenon of an increase in systolic pressure from the center to peripheral is called systolic pressure amplification. Sometimes, it is referred as pulse pressure amplification, which is defined as the ratio of peripheral to central pulse pressure. This systolic pressure amplification is not constant and can vary between individuals, and it is inversely proportional to arterial stiffness and vessel diameter. Many other factors such as age, gender, height, ethnicity, and heart rate affect it.[8-10] The reason for high systolic pressure amplification in the younger age group is due to compliant or lower stiffness in the arteries, leading to a slower travel velocity of the reflected wave. Hence, in the peripheral muscular brachial artery, since the reflective site is closer, the wave will arrive during the systolic phase, thereby increasing the brachial systolic pressure. Hence, the systolic pressure measured in the brachial artery is higher or amplified. However, by the time the reflected wave arrives at the central elastic aorta, it reaches later during the diastolic phase, so it will not contribute to an increase in systolic pressure. This explains why the central aortic blood pressure is always lower than the brachial blood pressure. This amplification of systolic and pulse pressure causes the overestimation of pressure by the sphygmomanometer in the younger age group patients (without arterial stiffness). Hence, in the younger age group, raised systolic pressure may not be a good indicator for risk assessment but raised diastolic pressure does.[11] In this group of patients, there are no clinical data available to substantiate the use of antihypertensive drugs, since published prospective data have shown that they do not proceed to systolic or diastolic hypertension in the near future.[12] Hence, this is a gray area, where brachial systolic pressure may not increase the risk of cardiac events since the corresponding derived central blood pressure may sometimes be normal. This was endorsed by the European Society of Cardiology/European Society of Hypertension 2013 guidelines.
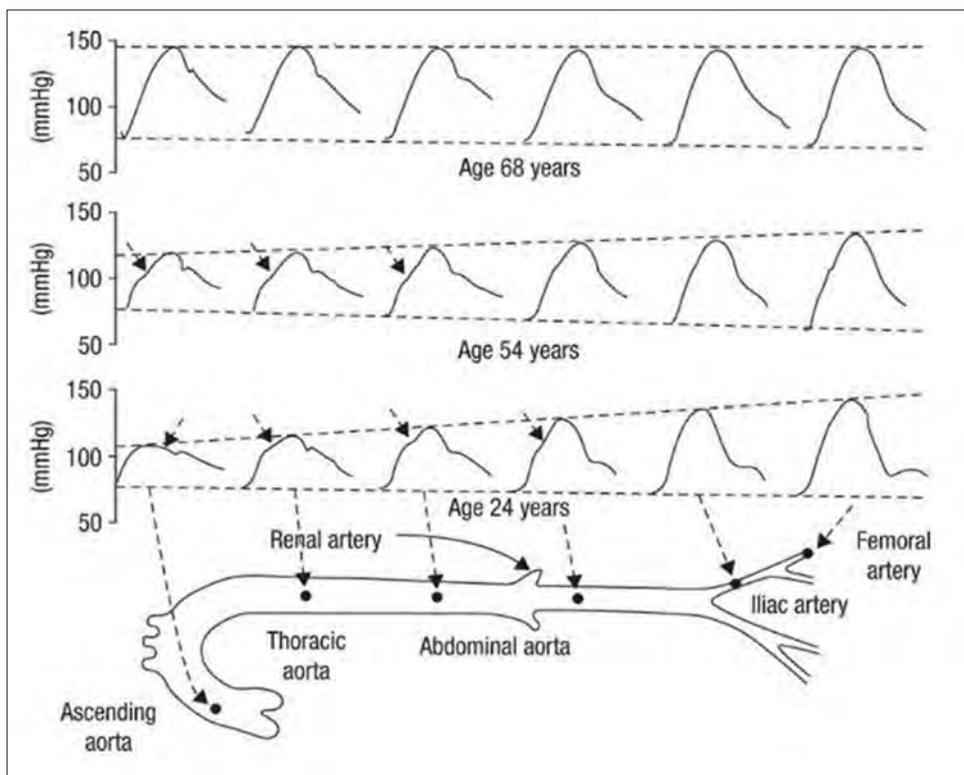
Figure 2: Systolic pressure amplification in different age groups from central aorta to peripheral femoral artery. Note, the pressure amplification is higher in younger age group when compared to older age group

Ventricular Vascular Interaction

When the ventricle contracts during systolic phase, it does not only eject the end diastolic volume into the aorta but also generate pressure wave that propagates along the vascular system. This forward travelling pressure wave moves through the large elastic artery, muscular artery, and the high resistance arterioles. Along the pathway, it gets reflected wherever there is impedance mismatch. The major reflective sites are the branching points of distal arteries and high-resistant arterioles. The velocity of this forward traveling and the reflected waves depends on resistance offered by these following pathways. A large elastic artery plays an important role of buffering the pulsatile blood flow due to the systolic and diastolic phase of the cardiac cycle. When advancing age is couples with cardiac risk factors, the calcification of aorta with loss of elasticity will contribute to increase in the forward and reflected wave velocity and widening of the pulse pressure due to loss of buffering function of the aorta. The muscular artery provides an increased resistance due to endothelial dysfunction, which leads to vasoconstriction and will increase the wave reflection. Finally, the smaller arterioles which are responsible for majority of peripheral vascular resistance due to vasoconstriction will lead to an increase in wave reflection velocity. All these segments of the vascular system contribute to the forward and reflected wave velocity and this may impact on the central aortic pressure. If the vascular system is a complaint, then the reflected wave comes to the central aorta when the ventricle is still at the diastolic phase. This provides additional advantage, as this wave can boost the coronary perfusion further and help to improve myocardial blood flow. If the vascular system is non -complaint or stiff, then the pressure wave travels with high amplitude and velocity, so it arrives at the central aorta, when the ventricle is still at the systolic phase. This is detrimental as the natural boost done by the reflective wave in boosting coronary perfusion is lost and also the early reflective wave can cause raise in central aortic systolic pressure and increase the left ventricular afterload. These changes in the central hemodynamic and reflective wave impact on central blood pressure make central aortic blood pressure a better reflection of ventricular-vascular interaction, which cannot be appreciated in brachial pressure.

Measuring Central Blood Pressure

The most direct and accurate method of measuring the central blood pressure in the ascending aorta can be done through an invasive catheter, tipped with a pressure sensor. This method cannot be applied for routine use of blood pressure measurement in hypertension management. However, the central blood pressure and waveform can be derived from the peripheral radial artery through a pressure sensor tipped applanation tonometer. The handheld tonometer is placed over the radial artery mildly flattening it over the underlying bone, and the intraarterial pressure is measured [Figure 3].

This pressure waveform using a validated generalized transfer function is used to estimate the central pressure waveform.[13] This derived central pressure waveform not only provides the central systolic, diastolic, and pulse pressure but also provides various indices which carry information on vascular status and ventricular ejection duration. The increase in central systolic pressure due to the reflected wave is called augmentation pressure. This reflects the ventricular load or the pressure; the ventricle has to generate to eject the blood into the aorta. The augmentation index is the ratio of augmentation pressure to the central pulse pressure and is usually expressed in percentage. Subendocardial viability ratio is the measure of myocardial supply divided by demand. Poor subendocardial viability ration can happen due to no diastolic augmentation, which occurs due to the absence of a reflected wave. This can precipitate subendocardial ischemia on exertion.

Central Blood Pressure in Patient Management

Patients with hypertension and blood pressure reduction measured in brachial artery *per se* are considered as the major determinant of reducing the cardiovascular events both in young and older patients. This outcome is not related to the choice of antihypertensive drugs used to reduce the pressure.[14] However, some of the published studies challenged this simplistic view as different antihypertensive drugs have shown to influence the outcome differently. When this was placed carefully on investigation, it was shown that the blood pressure reduction *per se* matters rather than the choice of antihypertensive drugs, but the difference in outcome is due to the differential effect of the hypertension drugs on aortic and brachial artery pressures. Hence, it is the ability of the drug to reduce the central aortic pressure, which determines the outcome. In ASCOT study, the amlodipine-/perindopril-based regimen is compared with

the standard atenolol-/bendroflumethiazide-based regimen.[15] Even though the brachial systolic pressure reduction is similar in both these regimens, the amlodipine/perindopril group has better reduction in all-cause mortality, stroke, non-fatal MI, and cardiovascular mortality. This trial was prematurely stopped due to significant increase in mortality in the atenolol-based regimen. The CAFE trial is a major substudy of the ASCOT trial, which was designed to answer why there is a difference in the clinical outcome between these two drug regimens, even though the reduction in brachial systolic pressure is similar in both of these drug arms.[16] It has been observed that the aortic systolic pressure and pulse pressure were around 4.3 mmHg and 3.0 mmHg lower in amlodipine-based treatment regimen. This reduction in the central pressures was the reason behind the observed differences in outcome. The same trend was previously shown in an another randomized double-blind study called REASON.[17] In this study perindopril and diuretic drug, indapamide combination is compared with the beta-blocker atenolol. The brachial blood pressure reduction was superior in perindopril based arm around 6 mmHg, but when the central aortic pressure is measured, it showed a much greater reduction in the perindopril arm when compared to the atenolol arm as much as 13 mmMg. When these patients are followed up for 1 year, the left ventricular mass regression was more pronounced in the perindopril treatment arm.[18] This shows that the ventricular load is dependent on the central aortic pressure and not on brachial pressure. Furthermore, in this study, it is very clear that the brachial pressure has significantly underestimated the efficacy of pressure reduction by perindopril/indapamide combination in the central aorta.

Beta-blockers in Hypertension

Cardioselective beta blocker especially atenolol has shown less effective in reducing central blood pressure when compared to
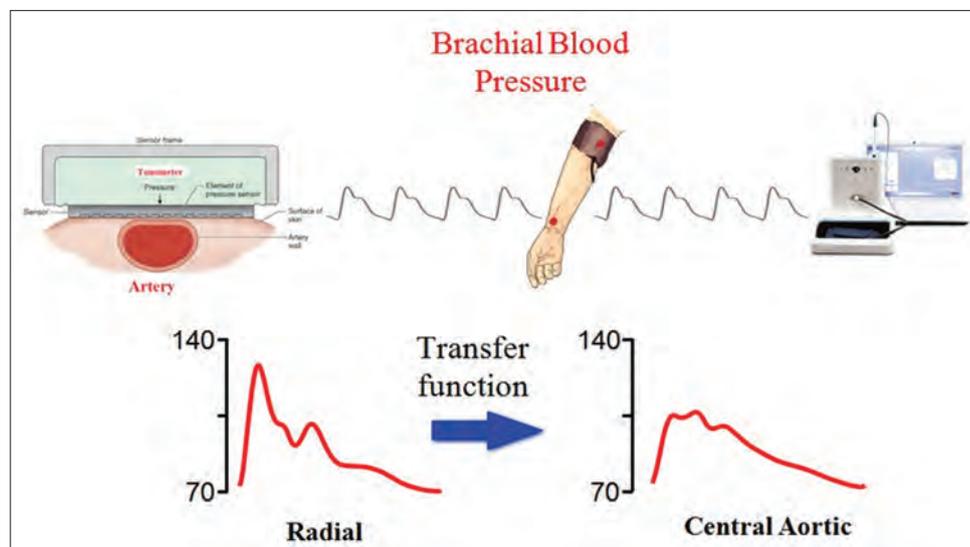
Figure 3: Applanation tonometer is used to derive the central aortic pressure by measuring intra-arterial pressure in the radial artery by applying validated general transfer function

other antihypertensive drugs. Still, Its brachial pressure reduction is comparable, which is evident from the above-mentioned trials. Atenolol failure to reduce the central blood pressure is possible due to the lack of vasodilatory property. Another main action of the beta-blockers, which may affect the central blood pressure reduction efficacy, is the reduction of heart rate. When heart rate decreases, it increases the systolic ejection duration, thereby allowing the reflective wave to fall on the systolic ejection time due to prolong systolic phase. This results in the augmentation of central pressure. Furthermore, beta-blockers reduce the cardiac output triggering compensatory increase in peripheral vascular resistance. These combined effects of reduced heart rate, cardiac output, and raised peripheral vascular resistance make cardioselective beta-blocker not a good drug of choice for primary hypertension. It has been postulated that this probably may not be a case if the beta-blocker has a vasodilatory effect. Arterial vasodilatation causes a decrease in amplitude and velocity of the reflected wave preventing central pressure augmentation due to the early arrival of the wave. A newer drug, Nebivolol, a different class of beta-blocker with vasodilatory effect when compared to another cardioselective beta-blocker metoprolol has shown to reduce the central blood pressure and left ventricular wall thickness better than metoprolol.[19] Even though the heart rate reduction is similar in both these groups, the reduction in central blood pressure is significant in the nebivolol group. This shows somehow the deleterious effect of reduction in heart rate on central pressure is offset by the vasodilatory effect. This shows that drugs such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, nitrates, and vasodilating beta-blockers will have a much-pronounced effect in central blood pressure.[20-24] This is predominantly due to its reduction in peripheral vascular resistance by vasodilating the arterioles and also moving the reflective site to the distal. This late arrival of the reflected wave may cause a reduction in the left ventricular myocardial demand or LV after load.

Central Pulse Pressure

In another pivotal study called strong heart, the relation of central and brachial systolic and pulse pressures toward outcome was studied in a larger sample size.[25] It is the pulse pressure which shows more significant when compared to the systolic pressure of both brachial and central. When mutual adjustments were made, it became clear that it is the central pulse pressure and augmentation index, which are the predictor of cardiovascular outcome than the brachial pulse pressure. Furthermore, the central pulse pressure and the augmentation index are strongly related to carotid intimal-medial thickness and carotid plaque score. When antihypertensive medication is added to this model, the predictive value of brachial pulse pressure becomes non-significant and only the central pulse pressure remains so as a sole predictor of outcome. This disappearance of the brachial pulse pressure predictive value after adding the hypertension

medication shows the lowering of the brachial systolic pressure higher than the central systolic pressure. In the subsequent analysis of Strong Heart study,[26] its shown that the central pulse pressure >50 mmHg possesses a greater risk for cardiovascular events and serves as a target for reduction by antihypertensive medications.

Conclusion

The treatment of hypertension, a modifiable cardiac risk factor, has shown to reduce the occurrence of future cardiovascular events. To measure and monitor the reduction of blood pressure, measuring brachial pressure at the arm has been practiced for more than a century without any change. Recent accumulating data have shown that the brachial systolic and pulse pressure may not be an accurate reflection of pressure in the central aorta. From a younger to an older age group, the central systolic and pulse pressure was never identical to the peripheral systolic and pulse pressure. These differences are attributed to pulse pressure amplification and due to the presence of strong wave reflection in the arterial tree. Antihypertensive drugs are also shown to have a differential effect in the peripheral and central systolic pressure. Many times, brachial blood pressure either underestimates or overestimates the blood pressure reduction in central hemodynamic and these may influence class of antihypertensive drugs used and cardiovascular outcomes. Newer concepts such as pulse pressure amplification, wave reflection, and augmentation index will be implemented in the future to manage hypertension effectively. The central pressure-based treatment strategy will help to better manage hypertension. However, in spite of the overwhelming evidences, its unlikely brachial blood pressure will be replaced sooner by central blood pressure. This is not due to the lack of evidence but due to the ease of using sphygmomanometer and the practice which lasted more than a century will be difficult to change, so it will be gradual.

Acknowledgment

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