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Review Article

Central Aortic Blood Pressure and Pulse Wave Velocity as Tools in the Hemodynamic Assessment of Hypertension

Isabella Tan[1], Mark Butlin[1], Fatemeh Shirbani[1], James R. Cox[1], Karen Peebles[2], Junli Zuo[1,3,4], Alberto P. Avolio[1]

[1]Department of Biomedical Sciences, Faculty of Medicine, Health and Human Sciences, Macquarie University, Sydney, Australia, [2]Department of Health Professions, Faculty of Medicine and Health Sciences, Macquarie University, Sydney, Australia, [3]Department of Hypertension, Ruijin Hospital North, Shanghai Jiaotong School of Medicine, Shanghai, China, [4]Department of Geriatrics, Ruijin Hospital North, Shanghai Jiaotong School of Medicine, Shanghai, China

Abstract

The effects of age on arteries are associated with stiffening of the artery wall, and this phenomenon is a major determinant of the age-related increase in isolated systolic hypertension. Arterial stiffness affects the speed of the arterial pulse which can be readily measured noninvasively. Alterations in arterial stiffness also affect the relationship between the conventionally measured blood pressure in the brachial artery and the pressure in the central aorta, which characterizes the pressure load on the ejecting ventricle. Central aortic systolic pressure is lower than peripheral systolic pressure and is affected by a range of hemodynamic factors, including heart rate. Devices are now available that can estimate central aortic pressure from the calibrated peripheral pulse waveform. Studies have shown that arterial stiffness, as measured by pulse wave velocity, and central aortic pressure can enhance the characterization of cardiovascular risk beyond the conventional measurement of brachial blood pressure. Although measurements of central aortic pressure and pulse wave velocity have provided a wealth of research and epidemiological data, there has been limited entry of these techniques in the routine clinical setting as well as in guidelines for treatment and management of hypertension. This review will address the current evidence of the use of central aortic pressure and pulse wave velocity for assessment of hypertension as a major cardiovascular risk.

Key words: Blood pressure, vascular stiffness, arterial pressure, hypertension, heart disease risk factors

Introduction

The hemodynamic assessment of hypertension, or "hard pulse disease" as it was once known,[1] has its roots in the late 19th century when Frederick Akbar Mahomed (1849–1884) used the sphygmograph to quantify the "hardness of the pulse."[2] By quantifying the amount of hold-down force necessary to obtain an ideal arterial pulse trace, Mahomed was able to describe both quantitatively, using measured force, and qualitatively, using pulse contour changes, the phenomenon of essential hypertension. However, perhaps due to the technical difficulties and the meticulousness required to operate the sphygmograph, this form of hemodynamic assessment did not gain traction in the medical field. It was not until some 25 years after the introduction of the Riva-Rocci method of using an occlusive cuff, together with the application of Korotkoff sounds, that routine measurement of blood pressure became a part of standard clinical care.[3] Since then, the hemodynamic assessment of hypertension, at least in clinical practice, has been based solely on two discrete numerical values – systolic pressure and diastolic pressure. From the first Build and Blood Pressure study conducted in 1959[4] that produced the first diagnosis threshold for hypertension diagnosis, to subsequent large epidemiological studies, such as the Framingham Heart Study[5] identifying the risks associated with hypertension, research evidence that informs clinical practice has all been based on measurements of brachial systolic and diastolic blood pressure. Furthermore, studies have shown that lowering brachial blood pressure in hypertensive individuals resulted in reduced cardiovascular events[6] and regression of left ventricular hypertrophy (LVH).[7] As such, despite the knowledge that brachial

Address for correspondence:
Dr Isabella Tan, Level 1, 75 Talavera Road, Macquarie University, Sydney, NSW 2109, Australia. E-mail: isabella.tan@mq.edu.au

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blood pressure is not the same as central aortic blood pressure, which represents the real pressure load on the heart, it has been clinically accepted that diagnosis and treatment of hypertension based on brachial blood pressure values would be sufficient. However, as differential effects on the heart of pharmacological antihypertensive treatments come to light despite achieving the same reduction in brachial blood pressure,[8] questions have been raised as to whether assessing central aortic pressure, which can now be readily measured non-invasively, would provide additional benefits in the diagnosis and management of hypertension. In addition, large artery stiffness, the major determinant of central aortic pressure and moderator between central and brachial blood pressure, is an established prognostic factor for hypertension.[9] Research in the past two decades has time and time again shown that large artery stiffness, as assessed by pulse wave velocity, is an independent risk factor for cardiovascular disease and events above and beyond the risk of hypertension itself,[10] yet routine measurement of pulse wave velocity in clinical practice is scarce. Evidently, this intricate relationship between central aortic pressure, large artery stiffness, and hypertension is currently underappreciated in clinical practice. This review will discuss the evidence supporting the use of central aortic pressure and pulse wave velocity in the hemodynamic assessment of hypertension and postulate why the clinical uptake of these measurements may have been slow despite this supporting evidence.

The Arterial Pulse, Central Aortic Pressure, and Pulse Wave Velocity

While current hemodynamic assessment of hypertension is mainly based on discrete numerical values of systolic and diastolic pressure, it cannot be forgotten that arterial pressure changes continuously within each cardiac cycle, forming the arterial pulse. As the heart beats, a train of arterial pulses travels from the aorta to the peripheral vessels and the pulse changes shape in the process, becoming narrower in the systolic portion and with systolic pressure increasing as the wave travels further away from the heart. Mahomed was the first to describe pulse contour changes between the central and peripheral arteries using tracings from the sphygmograph.[2] However, changes in the pulse contour were not specifically studied until the work of Kroeker and Wood,[11] in which arterial pulse waveforms were measured simultaneously in a central artery (the arch of the aorta or left subclavian artery) and a peripheral artery (brachial, radial, and femoral artery) using intra-arterial catheters. Kroeker and Wood observed that, while diastolic pressure and mean arterial pressure showed a small progressive decrease as the arterial pulse wave travelled from central to peripheral arteries, systolic pressure in the peripheral arteries was consistently higher than the central artery, with brachial, radial, and femoral systolic pressure at 109%, 112%, and 110% of central systolic pressure, respectively.[11] Later studies showed that this amplification of systolic pressure from the central to peripheral arteries varies greatly both within and between individuals depending on age, gender, height, and heart rate.[12] This phenomenon of systolic pressure amplification can be attributed to the nature of the arterial system, whereby vessels get stiffer further away from the heart. As the arterial pulse wave travels from the compliant central arteries to the stiffer peripheral arteries, the pulse wave is reflected toward the heart, resulting in a summation of a "forward" traveling pulse wave and a reflected "backward" travelling pulse wave. This leads to an augmented systolic pressure in the periphery, as the reflected wave generally meets the forward wave during systole due to the speed at which the arterial pulse wave travels, that is, pulse wave velocity. This pulse wave velocity is dependent on the stiffness of the arterial wall, and, as documented by Kroeker and Wood,[11] increases as the arterial pulse wave travels from the central to peripheral arteries, thus explaining, at least in part, the larger augmentation in systolic pressure in the peripheral arteries compared to central arteries. However, as central arteries stiffen with age, the difference between central and peripheral systolic pressure decreases, resulting in reduced systolic pressure amplification.[13]

Central aortic pressure, as opposed to brachial pressure, represents the true pressure load on the heart, as it is the pressure the heart must work against to expel the ventricular content (stroke volume). One of the main determinants of central aortic pressure is the compliance of the aorta. As blood is ejected intermittently from the heart, the aorta acts as a cushion and stores a portion of stroke volume during systole, which then is released during diastole. This ensures that blood flow reaches peripheral tissues in a continuous fashion with pulsatility minimized. A compliant aorta would store a larger proportion of the stroke volume during systole than would a stiffer aorta. Thus, given the same stroke volume, a stiffer aorta would result in a higher peak pressure during systole and lower pressure during diastole, resulting in an increase in pulse pressure. In addition, due to the reduction of the stroke volume stored during systole this will inherently this increase the in pulsatility which will continue throughout the vasculature. This will lead, leading to increased stress on small vessels that are not designed to accommodate pulsatile flow and ultimately result in end-organ damage, such as in the brain and kidneys.[14] In essence, an increase in large artery stiffness has both upstream effects on the heart (through increase in central aortic pressure) and downstream effects on end-organs (through increased pulsatility transmitted to small vessels). As such, it is not unreasonable to assume that measurement of central aortic pressure and large artery stiffness, the latter by way of pulse wave velocity measurement, can provide additive value in risk stratification beyond the assessment of hypertension with brachial blood pressure alone.

Evidence for the Use of Central Aortic Pressure and Pulse Wave Velocity in the Hemodynamic Assessment of Hypertension

Central Aortic Pressure

Hypertension is conventionally diagnosed using systolic and diastolic pressure values measured by brachial cuff sphygmomanometry. However, although the blood pressure

values present a cardiovascular risk and the condition is essentially asymptomatic, there are important progressive pathological sequalae such as LVH.[15] Hence, assessment of antihypertensive treatment is quantified by the effect of blood pressure lowering on regression of LVH. This was done in a major clinical trial comparing the effect of different pharmacological interventions on reducing brachial blood pressure and regression of LVH. The Losartan Intervention for Endpoint reduction in hypertension study (LIFE)[16] compared an angiotensin receptor blocker, losartan, against a beta blocker, and atenolol. The study showed that although both agents had similar effects in lowering brachial blood pressure after a 4-year follow-up, and both were associated with regression of LVH, losartan produced a greater degree of LVH regression, as assessed by reduction of Cornell voltage-duration product (10%) and Sokolow-Lyon voltage (15%), compared to atenolol (5% and 9%, respectively). Hence, the conclusion was drawn that losartan had beneficial effects beyond lowering blood pressure.

The LIFE study was an important study since it was one of the first studies to show the superiority of one class of antihypertensive agent (angiotensin receptor blocker, losartan) compared to another class (beta-blocker, atenolol). However, as expected, atenolol was associated with a reduction in heart rate (−7.7 bpm for atenolol vs. −1.1 bpm for losartan). This is a significant feature of this trial in interpreting the final results since the amplification of the aortic pulse toward the periphery is intrinsically dependent on heart rate due to the frequency characteristics of the brachial transfer function.[12] Hence, for a similar reduction in pulse pressure measured at the brachial artery, the pulse pressure at the aortic root would be relatively higher in those treated with a beta-blocker. Since the LIFE trial ran for over 4 years, those treated with atenolol would have had a relatively higher central aortic systolic pressure compared to those treated with losartan for a sufficiently long time to affect left ventricular remodeling. Thus, if central aortic pressure were measured in the LIFE study, some of the effect on regression of LVH could have been explained by the difference in central aortic pressure, even though the effect on brachial blood pressure was similar for both agents. The difference in central and peripheral systolic pressure due to heart rate was convincingly demonstrated in a later study (the Conduit Artery Functional Endpoint study) where central aortic pressure was estimated from the radial pulse calibrated to brachial systolic and diastolic pressure and comparisons were made between a calcium channel blocker (amlodipine) and a beta blocker (atenolol).[8]

The above studies provide evidence that central aortic pressure can give additional information compared to conventional brachial blood pressure on the effect of hypertension on end organ damage (LVH) when there are changes in other hemodynamic parameters such as heart rate. In addition, when pharmacological intervention for blood pressure lowering is guided by non-invasive measurement of central aortic pressure, the same reduction in brachial pressure can be achieved with reduced medication with no adverse effect on quality of life and LVH. A similar qualitative conclusion was reached in treatment of heart failure where titration of medication based on the central aortic waveform improved exercise capacity.[17] Interested readers are encouraged to read a more in-depth review of the current evidence on the utility of central aortic pressure in clinical practice.[18]

Pulse Wave Velocity

It has been over two decades since aortic stiffness, as assessed by pulse wave velocity, was first shown to be a marker of cardiovascular risk in patients with essential hypertension,[10] whereby the risk of being in a high cardiovascular mortality risk group was up to a staggering 7 times higher in those whose pulse wave velocity was in the upper quartile.[10] In the years since, increased pulse wave velocity has been firmly established as an independent risk factor for cardiovascular events such as stroke and coronary heart disease, as demonstrated in the Framingham study,[19] as well as cardiovascular and all-cause mortality in both general[20] and diseased populations such as those with hypertension.[21] The role of pulse wave velocity in the diagnosis and management of hypertension was further consolidated when increased pulse wave velocity was recognized as an influencing factor on the prognosis of hypertension by the 2007 Guidelines on the Management of Arterial Hypertension from the European Society of Hypertension (ESH) and European Society of Cardiology (ESC).[9] The most recent guidelines continues to recognize increased aortic stiffness as a factor influencing cardiovascular risk in patients with hypertension.[22] Furthermore, measurement of pulse wave velocity has been added as a recommendation for clinical evaluation of hypertension-mediated organ damage with a Class B recommendation and Level IIb evidence.[22]

The Framingham Heart Study was the first study to show that including pulse wave velocity in risk factor assessment in a general population was additive to standard risk factors such as systolic blood pressure.[19] In a cohort of 2232 participants, predicted cardiovascular risk was calculated based on age, sex, systolic blood pressure, use of antihypertensive medication, cholesterol, smoking, presence of diabetes mellitus, and aortic pulse wave velocity over a period of 8 years. The study showed that higher aortic pulse wave velocity was associated with a 48% increase in the risk of experiencing a first major cardiovascular event. Furthermore, inclusion of aortic pulse wave velocity in the risk assessment model resulted in significant improvement of risk reclassification and risk discrimination. A more recent meta-analysis of 16 studies, with a combined cohort of 17,635 participants, showed that addition of aortic pulse wave velocity in risk assessment improved the 5-year risk prediction of cardiovascular events by 5% in the whole cohort and 14% in the intermediate-risk group.[23] Together, these studies demonstrate that measurement of pulse wave velocity may be beneficial in risk stratification, particularly in individuals who are already at risk of cardiovascular events, such as those with hypertension.

The relationship between blood pressure and arterial stiffness is intrinsically inseparable. The mechanical design

of the arterial wall with its composite lamellae of elastin and collagen is such that an increase in pressure results in the recruitment of more collagen fibers, which is over 1000 times stiffer than elastin.[24] In other words, the artery stiffens with increasing blood pressure. As such, along with age, blood pressure is one of the main determinants of pulse wave velocity. However, this is not a unidirectional relationship. As mentioned earlier, increased arterial stiffness, in particular aortic stiffness, results in an increase in central aortic systolic pressure and a decrease in diastolic pressure, thereby widening pulse pressure. At the same time, elevated blood pressure increases pulsatile stress on the arterial wall, resulting in accelerated degradation of elastin fibers beyond the effects of normal aging[25] and further increasing arterial stiffness.[26] This bidirectional relationship between blood pressure and arterial stiffness raises the question of whether hypertension causes arterial stiffening, or whether arterial stiffening causes hypertension. Studies in both animal models[27] and humans[28] have shown that arterial stiffening can precede the development of hypertension. In the Baltimore Longitudinal Study of Aging, pulse wave velocity was an independent predictor of systolic blood pressure increase over a median follow-up of 4.3 years.[29] Furthermore, in individuals who were normotensive at baseline, pulse wave velocity predicted incident hypertension beyond median follow-up years.[29] In light of the above evidence, it can be seen that the value of pulse wave velocity measurement in the assessment of hypertension lies not only in the improved risk stratification of patients but also in the prediction of the development of hypertension in normotensive individuals.

Measurement of Central Aortic Pressure and Pulse Wave Velocity in Clinical Practice

Measurement of Central Aortic Pressure

In the past, central aortic pressure could only be measured invasively. Numerous commercial devices are now currently available for the non-invasive measurement of central aortic pressure.[18] One method implemented by several devices is the use of a generalized transfer function. The characteristics of the transmission of the pulse waveform from aorta to brachial artery are relatively constant between individuals in the adult population.[30] This permits a generalized transfer function, in essence a low pass filter, to be applied to a peripheral artery waveform to estimate the aortic waveform and thereby central aortic pressure.[31] Utilization of the generalized transfer function method requires the peripheral artery waveform to be calibrated and accuracy of the estimated central aortic pressure is dependent on the calibration method. Other methods for estimation of central aortic pressure have also been developed, such as identification of the late systolic peak in a peripheral arterial waveform.[32] Notwithstanding, all methods are reliant upon acquisition and analysis of a peripheral arterial waveform (pulse wave analysis) and on calibration. Discussion of issues surrounding calibration and subsequent accuracy of measured central aortic pressure is beyond the scope of this review. Commonly, the peripheral arterial waveform is obtained using applanation tonometry at the radial, brachial, or carotid artery and be calibrated to oscillometric brachial systolic and diastolic blood pressure (or mean and diastolic blood pressure). Brachial arterial waveform can also be obtained using a cuff over the arm, which can be integrated into oscillometric blood pressure measurement and is therefore less operator-dependent than tonometry. Studies have shown that central aortic pressure values of acceptable accuracy can be obtained with both tonometry-based[33] and cuff-based devices[34] when conventional brachial cuff pressure measurements are used to calibrate the peripheral waveform. One study[35] showed reduced accuracy with non-invasive brachial pulse waveform calibration compared to invasive pressure calibration. Figure 1 shows an example of a central aortic waveform derived from the cuff-measured brachial waveform using a generalized transfer function in a young and old individual, respectively.

Measurement of Pulse Wave Velocity

Measurement of pulse wave velocity requires the measurement of arterial waveforms from two arterial sites some distance apart. A fiducial point, most commonly the foot of the wave, is used to determine the time delay between the points on the two pulse waves, that is, transit time. Pulse wave velocity is then determined by dividing the arterial path length, measured as a linear distance between the arterial recording sites, by the transit time [Figure 2].

Although pulse wave velocity can be determined across any arterial segment, carotid-femoral pulse wave velocity, which can be measured non-invasively, is considered the gold standard in the assessment of aortic stiffness and is the measure recommended for use in the ESC/ESH Guidelines on the Management of Arterial Hypertension.[22] Determination of carotid-femoral pulse wave velocity involves obtaining arterial pressure waveforms from the carotid and femoral arteries. Carotid and femoral waveforms can be obtained by applanation tonometry, and most commercially available devices for carotid-femoral pulse wave velocity measurement are tonometry-based. Most tonometry-based devices require that the arterial waveforms be obtained sequentially, and an electrocardiogram (ECG) is additionally required. The transit time would then be determined with the R peak of the ECG as a common reference point. There are also devices available that are fully cuff-based, where both carotid and femoral pressure waveforms can be obtained with a cuff around the neck and thigh, respectively, or use a combination of both tonometry and cuff, whereby carotid waveform is obtained by tonometry and femoral waveform is obtained with a cuff around the thigh. Cuff-based devices are simpler to use and require less time than tonometry-based devices, as carotid and femoral waveforms can be obtained simultaneously without the need of an ECG. They also tend to be less dependent on operator experience, therefore, making them more suitable for use in a clinical setting. Other methods

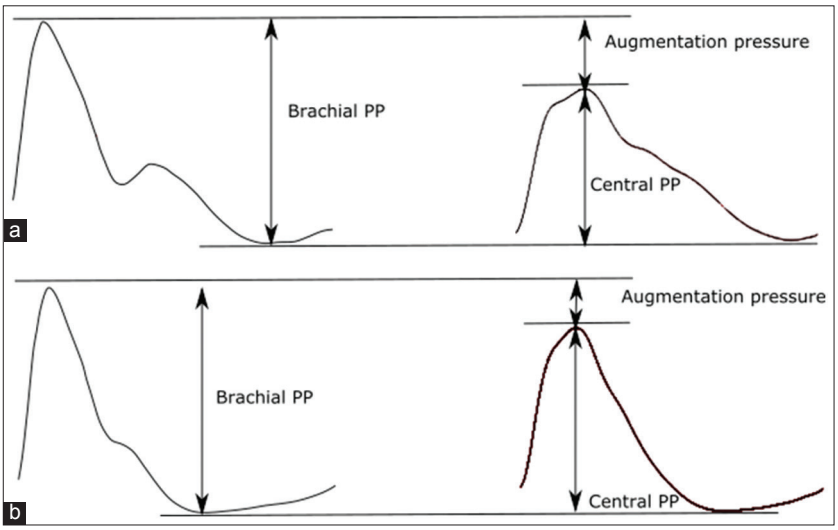

Figure 1: Examples of central aortic waveforms (right) derived from corresponding brachial waveforms (left) from (a) a young individual and (b) an older individual. Notice that in the older individual, the augmentation pressure and hence pressure amplification is reduced compared to the young individual. PP: Pulse pressure

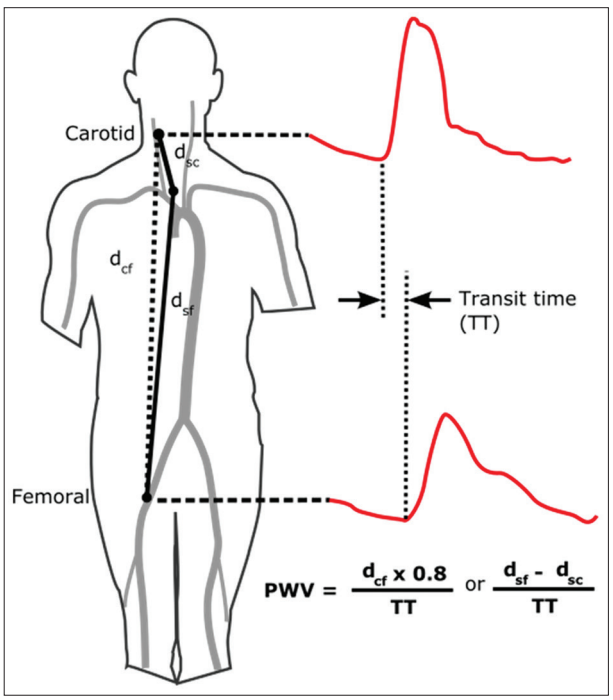

Figure 2: Schematic of carotid-femoral pulse wave velocity (PWV) determination. PWV is determined as arterial path length divided by the time delay between the foot of the pressure waves (transit time, TT), measured at the carotid and femoral artery, respectively. Arterial path length can be determined as direct linear distance from carotid to femoral recording sites (d_{cf}) multiplied by a factor of 0.8, or as the distance between sternal notch and femoral site (d_{sf}) minus the distance between carotid site and sternal notch (d_{sc})

of pulse wave velocity measurement, such as indirect estimation of pulse wave velocity based on pulse wave analysis using a single cuff around the arm,[36] and measurement over a different arterial segment, such as ankle-brachial pulse wave velocity,[37] are also available but beyond the scope of this review. A comprehensive review has recently been published on the measurement of arterial stiffness in humans[38] and interested readers are encouraged to refer to it.

An important aspect to pulse wave velocity measurement is the determination of arterial path length. For carotid-femoral pulse wave velocity, distance between the carotid and femoral recording sites can be determined by measuring distance over the body surface using a tape measure. It is currently recommended that the direct distance between the carotid and femoral recording sites be measured and multiplied by a factor of 0.8.[39] Another commonly used method is the subtraction method, whereby the distance between the carotid measurement site and the sternal notch is subtracted from the distance between the sternal notch and the femoral recording site, which is commonly on the inguinal fold for tonometry measurements or top edge of the thigh cuff for cuff-based measurements. The carotid-to-sternal-notch distance is subtracted to account for the pressure wave travelling in opposite directions from the aorta. Cuff-based devices may require an additional distance measurement from the inguinal fold to the top edge of the thigh cuff.

Impediments to the Use of Central Aortic Pressure and Pulse Wave Velocity in Clinical Practice

Despite the many years of research and established body of evidence on the value of central aortic pressure and pulse wave velocity, clinical uptake of their measurement remains scarce. One of the main reasons could be due to the limited number of randomized controlled trials with either central aortic pressure or pulse wave velocity as the treatment target or outcome

measure. While the body of evidence for the prognostic value of pulse wave velocity in hypertension is strong enough for it to be included in the guidelines, the benefit of using central aortic pressure over brachial blood pressure is still unclear.[22] To-date, there has only been one randomized trial that investigated the value of using central aortic pressure to guide hypertension treatment as compared with brachial blood pressure.[40] The results of this prospective, open-label, and blinded-endpoint trial showed that use of central aortic blood pressure resulted in a significant reduction of medication dosage to achieve the same blood pressure control, but there were no significant differences in left ventricular mass nor aortic stiffness when compared to treatment guided by brachial blood pressure. Recently, a double-blinded randomized controlled trial, the Guiding Hypertension Management Using Different Blood Pressure Monitoring Strategies (GYMNs study),[41] was set up to assess the optimal strategy for guiding hypertension management based on unattended office brachial blood pressure, home blood pressure, and central aortic blood pressure. The results of this trial are yet to be published, but the study will no doubt provide further insights as to whether central aortic blood pressure guided treatment will lead to better outcomes. Another reason for the lack of central aortic pressure measurements in clinical practice could be the lack of established reference values. At present, only Taiwan has published guidelines on the use of central aortic pressure in the management of hypertension, with a recommended cut-off value of 130/90 mmHg for the diagnosis of hypertension and treatment target.[42] A recent consensus statement on the clinical application of using central aortic pressure in the management of hypertension was also published from Taiwan.[43] On the other hand, the European guidelines state that measurement of central aortic pressure may be useful only in some circumstances, such as isolated systolic hypertension in the young with Class C recommendation and Level IIb evidence.[22] Due to the absence of pharmacological treatment to de-stiffen arteries beyond that of blood pressure control, there are currently no randomized controlled trials to-date with pulse wave velocity as a treatment target.

Practicalities of central aortic pressure and pulse wave velocity measurement may also pose a major barrier to the clinical uptake of these measurements. While central aortic pressure can now be readily determined with the use of an oscillometric cuff, measurement of pulse wave velocity still requires the use of applanation tonometry in most devices, which requires a certain level of operator expertise. Pulse wave velocity determination also requires straight distance measurement over the body surface, which can be difficult in some patients. As such, despite being included in the European guidelines as an important prognostic factor of hypertension, the same guidelines also stated that "routine use of (pulse wave velocity) measurement is not practical and is not recommended for routine practice."[22] This has led to the development of estimated pulse wave velocity based on age and mean arterial pressure,[44] which has been shown to provide similar risk prediction to measured pulse wave velocity.[45,46]

Conclusions

Both central aortic pressure and pulse wave velocity are valuable tools in the hemodynamic assessment of hypertension, especially in terms of providing additive value in assessing hypertension-related organ damage and in risk stratification. The body of evidence supporting their use in clinical practice continues to grow, but more randomized controlled trials may be needed, particularly for central aortic pressure, for sufficient improvement of the class of recommendation and level of evidence before widespread clinical uptake. In addition, more automated and operator-independent methods in the measurement of pulse wave velocity would be beneficial to ensure practicality of its use in a fast-paced clinical setting.

Declarations

JC is a part-scholarship recipient from and IT is a part-time employee of CardieX AtCor Medical, Australia.

References

1. Saklayen MG, Deshpande NV. Timeline of history of hypertension treatment. Front Cardiovasc Med 2016;3:3.
2. O'Rourke MF. Frederick Akbar Mahomed. Hypertension 1992;19:212-7.
3. Cameron JS, Hicks J. Frederick Akbar Mahomed and his role in the description of hypertension at Guy's Hospital. Kidney Int 1996;49:1488-506.
4. Morton AP, Lew EA, November WJ, Webster AC, Hutchinson JJ. Build and blood pressure study. Trans Soc Actuar 1959;11:987-97.
5. Kannel WB, Schwartz MJ, McNamara PM. Blood pressure and risk of coronary heart disease: The Framingham study. Dis Chest 1969;56:43-52.
6. Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, *et al.* Blood pressure lowering for prevention of cardiovascular disease and death: A systematic review and meta-analysis. Lancet 2016;387:957-67.
7. Dahlöf B, Pennert K, Hansson L. Reversal of left ventricular hypertrophy in hypertensive patients. Am J Hypertens 1992;5:95-110.
8. Williams B, Lacy PS, Thom SM, Cruickshank K, Stanton A, Collier D, *et al.* Differential impact of blood pressure-lowering drugs on central aortic pressure and clinical outcomes: Principal results of the conduit artery function evaluation (CAFE) study. Circulation 2006;113:1213-25.
9. Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, *et al.* 2007 guidelines for the management of arterial hypertension: The task force for the management of arterial hypertension of the European society of hypertension (ESH) and of the European society of cardiology (ESC). J Hypertens 2007;25:1105-87.
10. Blacher J, Asmar R, Djane S, London GM, Safar ME. Aortic pulse wave velocity as a marker of cardiovascular risk in hypertensive patients. Hypertension 1999;33:1111-7.
11. Kroeker EJ, Wood EH. Comparison of simultaneously recorded central and peripheral arterial pressure pulses during rest, exercise and tilted position in man. Circ Res 1955;3:623-32.

12. Avolio AP, Van Bortel LM, Boutouyrie P, Cockcroft JR, McEniery CM, Protogerou AD, *et al*. Role of pulse pressure amplification in arterial hypertension: Experts' opinion and review of the data. Hypertension 2009;54:375-83.
13. McEniery CM, Yasmin, Hall IR, Qasem A, Wilkinson IB, Cockcroft JR. Normal vascular aging: Differential effects on wave reflection and aortic pulse wave velocity the Anglo-Cardiff collaborative trial (ACCT). J Am Coll Cardiol 2005;46:1753-60.
14. Mitchell GF, Vita JA, Larson MG, Parise H, Keyes MJ, Warner E, *et al*. Cross-sectional relations of peripheral microvascular function, cardiovascular disease risk factors, and aortic stiffness: the Framingham Heart Study. Circulation 2005;112:3722-8.
15. Strauer BE. Structural and functional adaptation of the chronically overloaded heart in arterial hypertension. Am Heart J 1987;114:948-57.
16. Dahlöf B, Devereux RB, Kjeldsen SE, Julius S, Beevers G, de Faire U, *et al*. Cardiovascular morbidity and mortality in the losartan intervention for endpoint reduction in hypertension study (LIFE): A randomised trial against atenolol. Lancet 2002;359:995-1003.
17. Borlaug BA, Olson TP, Mohamed SA, Melenovsky V, Sorrell VL, Noonan K, *et al*. A randomized pilot study of aortic waveform guided therapy in chronic heart failure. J Am Heart Assoc 2014;3:1-10.
18. Cheng HM, Chuang SY, Wang TD, Kario K, Buranakitjaroen P, Chia YC, *et al*. Central blood pressure for the diagnosis of hypertension-is it a practical clinical tool in current practice? J Clin Hypertens 2020;22:391-406.
19. Mitchell GF, Hwang SJ, Vasan RS, Larson MG, Pencina MJ, Hamburg NM, *et al*. Arterial stiffness and cardiovascular events: The Framingham heart study. Circulation 2010;121:505-11.
20. Sutton-Tyrrell K, Najjar SS, Boudreau RM, Venkitachalam L, Kupelian V, Simonsick EM, *et al*. Elevated aortic pulse wave velocity, a marker of arterial stiffness, predicts cardiovascular events in well-functioning older adults. Circulation 2005;111:3384-90.
21. Laurent S, Boutouyrie P, Asmar R, Gautier I, Laloux B, Guize L, *et al*. Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. Hypertension 2001;37:1236-41.
22. Williams B, Mancia G, Spiering W, Rosei EA, Azizi M, Burnier M, *et al*. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J 2018;39:3021-104.
23. Ben-Shlomo Y, Spears M, Boustred C, May M, Anderson SG, Benjamin EJ, *et al*. Aortic pulse wave velocity improves cardiovascular event prediction: An individual participant meta-analysis of prospective observational data from 17,635 subjects. J Am Coll Cardiol 2014;63:636-46.
24. Shadwick RE. Mechanical design in arteries. J Exp Biol 1999;202:3305-13.
25. Yasmin, Wallace S, McEniery CM, Dakham Z, Pusalkar P, Maki-Petaja K, *et al*. Matrix metalloproteinase-9 (MMP-9), MMP-2, and serum elastase activity are associated with systolic hypertension and arterial stiffness. Arterioscler Thromb Vasc Biol 2005;25:372-8.
26. Smith ER, Tomlinson LA, Ford ML, McMahon LP, Rajkumar C, Holt SG. Elastin degradation is associated with progressive aortic stiffening and all-cause mortality in predialysis chronic kidney disease. Hypertension 2012;59:973-8.
27. Weisbrod RM, Shiang T, Al Sayah L, Fry JL, Bajpai S, Reinhart-King CA, *et al*. Arterial stiffening precedes systolic hypertension in diet-induced obesity. Hypertension 2013;62:1105-10.
28. Kaess BM, Rong J, Larson MG, Hamburg NM, Vita JA, Levy D, *et al*. Aortic stiffness, blood pressure progression, and incident hypertension. JAMA 2012;308:875.
29. Najjar SS, Scuteri A, Shetty V, Wright JG, Muller DC, Fleg JL, *et al*. Pulse wave velocity is an independent predictor of the longitudinal increase in systolic blood pressure and of incident hypertension in the baltimore longitudinal study of aging. J Am Coll Cardiol 2008;51:1377-83.
30. Karamanoglu M, O'Rourke MF, Avolio AP, Kelly RP. An analysis of the relationship between central aortic and peripheral upper limb pressure waves in man. Eur Heart J 1993;14:160-7.
31. Chen CH, Nevo E, Fetics B, Pak PH, Yin FC, Maughan WL, *et al*. Estimation of central aortic pressure waveform by mathematical transformation of radial tonometry pressure. Validation of generalized transfer function. Circulation 1997;95:1827-36.
32. Pauca AL, Kon ND, O'Rourke MF. The second peak of the radial artery pressure wave represents aortic systolic pressure in hypertensive and elderly patients. Br J Anaesth 2004;92:651-7.
33. Cheng HM, Lang D, Tufanaru C, Pearson A. Measurement accuracy of non-invasively obtained central blood pressure by applanation tonometry: A systematic review and meta-analysis. Int J Cardiol 2013;167:1867-76.
34. Gotzmann M, Hogeweg M, Seibert FS, Rohn BJ, Bergbauer M, Babel N, *et al*. Accuracy of fully automated oscillometric central aortic blood pressure measurement techniques. J Hypertens 2020;38:235-42.
35. Schultz MG, Picone DS, Armstrong MK, Black JA, Dwyer N, Roberts-Thomson P, *et al*. Validation study to determine the accuracy of central blood pressure measurement using the sphygmocor xcel cuff device. Hypertension 2020;76:244-50.
36. Hametner B, Wassertheurer S, Kropf J, Mayer C, Eber B, Weber T. Oscillometric estimation of aortic pulse wave velocity. Blood Press Monit 2013;18:173-6.
37. Tsuchikura S, Shoji T, Kimoto E, Shinohara K, Hatsuda S, Koyama H, *et al*. Brachial-ankle pulse wave velocity as an index of central arterial stiffness. J Atheroscler Thromb 2010;17:658-65.
38. Segers P, Rietzschel ER, Chirinos JA. How to measure arterial stiffness in humans. Arterioscler Thromb Vasc Biol 2020;40:1034-43.
39. Reference Values for Arterial Stiffness' Collaboration. Determinants of pulse wave velocity in healthy people and in the presence of cardiovascular risk factors: "Establishing normal and reference values". Eur Heart J 2010;31:2338-50.
40. Sharman JE, Marwick TH, Gilroy D, Otahal P, Abhayaratna WP, Stowasser M. Randomized trial of guiding hypertension management using central aortic blood pressure compared with best-practice care principal findings of the BP GUIDE study. Hypertension 2013;62:1138-45.
41. Cheng HM, Sung SH, Chen CH, Yu WC, Yang SM, Guo CY, *et al*. Guiding hypertension management using different blood pressure monitoring strategies (GYMNs study): Comparison of three different blood pressure measurement methods: Study protocol for a randomized controlled trial. Trials 2019;20:1-8.
42. Chiang CE, Wang TD, Ueng KC, Lin TH, Yeh HI, Chen CY, *et al*. 2015 Guidelines of the Taiwan society of cardiology and the taiwan hypertension society for the management of hypertension. J Chin Med Assoc 2015;78:1-47.
43. Cheng HM, Chuang SY, Sung SH, Wu CC, Wang JJ, Hsu PF, *et al*.

2019 consensus of the Taiwan hypertension society and Taiwan society of cardiology on the clinical application of central blood pressure in the management of hypertension. Acta Cardiol Sin 2019;35:234-43.
44. Greve SV, Laurent S, Olsen MH. Estimated pulse wave velocity calculated from age and mean arterial blood pressure. Pulse 2016;4:175-9.
45. Greve SV, Blicher MK, Kruger R, Sehestedt T, Gram-KampmannxE, Rasmussen S, *et al*. Estimated carotid-femoral pulse wave velocity has similar predictive value as measured carotid-femoral pulse wave velocity. J Hypertens 2016;34:1279-89.
46. Vlachopoulos C, Terentes-Printzios D, Laurent S, Nilsson PM, Protogerou AD, Aznaouridis K, *et al*. Association of estimated pulse wave velocity with survival: A secondary analysis of SPRINT. JAMA Netw Open 2019;2:e1912831.

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