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Consensus

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

Hao-Min Cheng,[1,2,3] Shao-Yuan Chuang,[4] Shih-Hsien Sung,[1,5] Chih-Cheng Wu,[6,7] Jiun-Jr Wang,[8] Pai-Feng Hsu,[1,9] Chia-Lun Chao,[10] Juey-Jen Hwang,[11,12] Tzung-Dau Wang[13] and Chen-Huan Chen[1,3]

The Taiwan Society of Cardiology (TSOC) and the Taiwan Hypertension Society (THS) have appointed a joint consensus group for the 2019 Consensus of the TSOC and THS on the Clinical Application of Central blood pressure (BP) in the Management of Hypertension with the aim of formulating a management consensus on the clinical application of central BP in the management of hypertension. This consensus document focuses on the clinical application of central BP in the care of patients with hypertension.

The major determinants of central BP are increased arterial stiffness and wave reflection, which are also the dominant hemodynamic manifestations of vascular aging. Central BP can be measured noninvasively using various techniques, including with convenient cuff-based oscillometric central BP monitors. Noninvasive central BP is better than conventional brachial BP to assess target organ damage and long-term cardiovascular outcomes. Based on the analysis of long-term events, a central BP threshold of 130/90 mmHg for defining hypertension has been proposed. Recent studies have suggested that a central BP strategy to confirm a diagnosis of hypertension may be more cost-effective than conventional strategies, and that guiding hypertension management with central BP may result in the use of fewer medications to achieve BP control. Although noninvasive measurements of brachial BP are inaccurate and central BP has been shown to carry superior prognostic value beyond brachial BP, the use of central BP should be justified in studies comparing central BP-guided therapeutic strategies with conventional care for cardiovascular events.

Key Words: Brachial BP • Central BP • Diagnosis • High BP • Hypertension • Management • Peripheral BP

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[1]Faculty of Medicine, National Yang-Ming University School of Medicine; [2]Center for Evidence-based Medicine, Department of Medical Education, Taipei Veterans General Hospital; [3]Institute of Public Health and Community Medicine Research Center, National Yang-Ming University, Taipei; [4]Institute of Population Health Science, National Health Research Institutes, Miaoli; [5]Department of Internal Medicine, Taipei Veterans General Hospital, Taipei; [6]Cardiovascular Center, National Taiwan University Hospital, Hsinchu Branch; [7]College of Medicine and Institute of Biomedical Engineering, National Tsing-Hua University, Hsinchu; [8]School of Medicine, Fu Jen Catholic University, Xinzhuang District, New Taipei City; [9]Healthcare and Management Center, Taipei Veterans General Hospital, Taipei; [10]Cardinal Tien Hospital An Kang District, New Taipei City; [11]Department of Internal Medicine, College of Medicine, National Taiwan University, Taipei; [12]National Taiwan University Hospital Yunlin Branch, Yunlin; [13]Cardiovascular Center and Division of Cardiology, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan.

Corresponding author: Dr. Chen-Huan Chen, Medical Building, National Yang-Ming University School of Medicine, No. 155, Li-Long St. Sec. 2, Shih-Pai, Taipei 11221, Taiwan. Tel: 866-2-2826-7202; Fax: 886-2- 2820-9477; E-mail: chchen3@ym.edu.tw

INTRODUCTION

With the increased availability of non-invasive central blood pressure (BP) measuring devices, central BP has gained increasing attention concerning its clinical application in the diagnosis of hypertension and its ability to guide BP management in patients with cardiovascular diseases. With the aim of reaching an agreement on the clinical application of central BP in the management of hypertension, the Taiwan Society of Cardiology (TSOC) and the Taiwan Hypertension Society (THS) appointed a joint consensus group for the "2019 Consensus of the TSOC and THS on the Clinical Application of Central BP in the Management of Hypertension". This consensus document focuses on the clinical application of central BP in the care of patients with hypertension.

Central BP refers to BP readings measured from the central aorta or common carotid arteries, with the major determinants being increased arterial stiffness and wave reflection.[1] BP measurements are usually obtained from the brachial arteries which are highly correlated with central BP, however individual discrepancies between central BP and peripheral BP may be substantial and highly variable and may be magnified during hemodynamic changes or after pharmacological interventions.[2] Moreover, brachial BP measured with conventional automatic BP monitoring (cuff BP) underestimates intravascular brachial systolic BP (SBP), overestimates diastolic BP (DBP), and substantially underestimates pulse pressure (PP), and therefore cannot serve as a direct substitute for their central counterpart.[3] Accumulating evidence has suggested that central BP may be more relevant than peripheral BP in predicting target organ damage and cardiovascular outcomes.[4]

Central BP can be measured noninvasively, including with convenient cuff-based central BP monitors. Hypertension can be defined by central BP based on the proposed central BP threshold of 130/90 mmHg. As suggested in recent studies, a central BP strategy to confirm the diagnosis of hypertension and guide hypertension management may be more cost-effective than conventional brachial BP strategies. Given the advantage of central BP over conventional cuff BP, the use of central BP is anticipated, however it should still be justified in studies comparing central BP-guided therapeutic strategies with classic guideline-guided strategies for preventing cardiovascular events. In this consensus document, details of the various aspects of the application of central BP measurements in clinical practice are provided and discussed accordingly.

DEFINITION OF CENTRAL BP

Consensus statement

- Central BP refers to BP readings measured from the central aorta or common carotid arteries.

Ejection of the stroke volume into the central aorta to maintain the circulation of blood flow requires that the pressure generated from contraction of the left ventricle can overcome the pulsatile and resistive loads of the entire arterial tree. Resistive load refers to total peripheral resistance from the terminal arterioles. Pulsatile load is complicated and is mainly determined by the diameter of the aortic root, stiffness of the large arteries, and wave reflections from arterial bifurcations and impedance mismatches along the arterial tree.[1] Thus, the arterial pressure waveform at the central aorta is determined by interactions between functions of the left ventricle, large arteries and arterioles, and structures of the aortic root, arterial bifurcations, and arterial narrowing.[5] BP measurements, including SBP and DBP, are simply readings from the peak and trough of the arterial pressure waveform. Mean BP (MBP) is derived from the area under the curve of the arterial pressure waveform, and PP is calculated as the difference between SBP and DBP. The pressure waveform at the common carotid arteries is similar to that in the central aorta because of the proximity of the two and low resistance in the cerebral circulation.[6] Therefore, BP readings derived from the common carotid arteries can be used as surrogates for readings from the central aorta.

DISCREPANCY BETWEEN PERIPHERAL AND CENTRAL BP

Consensus statements

- Conventional BP-measuring devices obtain readings from the brachial arteries that correlate with but differ from central BP readings.

- Individual discrepancies between central and peripheral BP may be substantial and highly variable and may be magnified during hemodynamic changes or after pharmacological interventions.

Currently, the diagnosis of hypertension is based on recordings from the brachial arteries, either with office, home, or ambulatory BP measurements. Brachial SBP and PP are almost always higher than the corresponding readings in the central aorta because of the phenomenon of PP amplification.[7-11] However, noninvasively measured brachial SBP and PP, either by the auscultatory method or automatic oscillometric sphygmomanometers, are usually lower than invasively measured intra-arterial readings.[12] Consequently, noninvasive brachial SBP may be highly correlated with central SBP.[13] Thus, it is reasonable to suggest that noninvasive brachial SBP could be used as an estimate of central SBP.

However, accumulating evidence suggests significant differences in central BP among individuals with similar brachial BP.[14,15] The degree of PP amplification varies within and between individuals,[16] and the variability depends on a number of factors including age, sex, height, heart rate, medications, and systemic vascular diseases.[14,17,18] In addition, noninvasive brachial SBP as a surrogate for central SBP has been shown to have a large random error.[15]

Individual discrepancies between central and peripheral BP may be magnified during hemodynamic changes or after pharmacological interventions.[19] Accurate monitoring and proper management of central BP are essential to avert organ damage in patients with hypertension. Although peripheral BP (brachial or radial) has been routinely used as a surrogate for central BP,[20] human studies conducted using invasive measurements of central and peripheral BP have shown comparable peripheral BP accompanied with distinctly different central BP, and discrepancies between peripheral and central BP can be significant and vary individually.[21]

Based on the major functionalities of the arterial system, aortic pressure can be separated into a reservoir pressure ($P_{reservoir}$) associated with arterial buffering mechanism, and an excess pressure (P_{excess}) associated with wave propagation. Recent evidence supports that $P_{reservoir}$ is largely invariant, whereas P_{excess} varies from central to peripheral due to impedance mismatch potentially attributed to atherosclerosis, vasoconstriction, and vascular shunting.[21] This impedance mismatch may be exacerbated during drug interventions, and studies have shown that some antihypertensive drugs affect central BP more than peripheral BP.[22]

DISADVANTAGES OF CONVENTIONAL CUFF BRACHIAL BP

Consensus statements

- Cuff brachial BP underestimates intravascular brachial SBP, overestimates DBP and substantially underestimate PP.
- Cuff brachial BP measurements cannot serve as a direct substitute for their central counterpart.
- Central BP may be more relevant than peripheral BP in predicting target organ damage and cardiovascular outcomes.

Brachial BP is usually measured using a device with a pneumatic cuff to externally collapse and release the brachial artery in a controlled manner. As the cuff pressure drops below the brachial SBP, blood flow will begin to spurt through the artery to expand with each pulse. Maximal oscillation occurs when the cuff pressure is close to the MBP.[23] The blood flow will be unimpeded once the cuff pressure falls below the brachial DBP. Brachial SBP and DBP can therefore be defined by either auscultation over the artery or cuff pressure oscillations. Although brachial cuff pressure is now the principal method used to diagnose hypertension, evidence shows that cuff measurements underestimate intra-arterial brachial SBP and overestimate intra-arterial brachial DBP.[23] In addition, there is large individual variability between the brachial cuff pressure and intra-artery brachial pressure.[24] Picone et al. presented a meta-analysis of 74 studies with 3073 participants, in which brachial cuff-measured BP was shown to underestimate intra-arterial brachial SBP by 5.7 mmHg, and overestimate intra-arterial brachial DBP by 5.5 mmHg, resulting in a -12 mmHg underestimation of brachial PP.[25]

The relationships and discrepancies between central and peripheral BP depend on the characteristics of the arteries.[26] Although the arterial pressure wave travels away from the heart towards the periphery, the MBP

and DBP, but not SBP and PP, remain steady.[26] Usually, SBP increases, and therefore PP is amplified along with propagation of the pressure wave.[3] Given that brachial cuff SBP always underestimates intra-arterial brachial SBP, brachial cuff SBP may be an approximation for central SBP.[3] However, individual differences vary to a large extent, which may compromise the usefulness of brachial cuff SBP as a surrogate for central SBP in an individual. Picone et al. reported that values of brachial cuff SBP were lower than those of central SBP by > 5, 10, and 15 mmHg in 67%, 40%, and 22% of their subjects, respectively.[3] In contrast, brachial cuff DBP was significantly higher than central DBP, and therefore cuff PP was significantly lower than its central counterpart.[3]

Central BP reflects the hemodynamic load on the heart and large arteries better than brachial BP, particularly in individuals with prominent PP amplification. Kollias et al. demonstrated that central SBP was more closely associated with left ventricular mass index, carotid intima-media thickness, and pulse-wave velocity compared with brachial SBP.[27] In addition, longitudinal studies further support that regression of left ventricular mass index and carotid intima-media thickness are more related to changes in central BP rather than brachial BP.[28,29] Because the aorta is the major conduit of blood flow to the vital organs, central BP has also been shown to outperform brachial BP in the prediction of microalbuminuria and cognitive aging in community-based populations.[30,31]

With regards to the relationship between central BP and cardiovascular outcomes, Wang et al. reported that central SBP and PP were more predictive of cardiovascular mortality in a Taiwanese cohort.[4] In addition, a meta-analysis of 11 studies with 5648 subjects showed that central SBP and PP were associated with cardiovascular events, as well as brachial measures.[32] Recently, the ASCOT study also suggested that the clinical benefits of different antihypertensive agents may be more associated with a reduction in central rather than brachial BP,[2] which encourages the application of central BP for clinical practice.[33]

CENTRAL BP CAN BE OBTAINED NONINVASIVELY AND USED FOR THE DIAGNOSIS OF HYPERTENSION

Consensus statements

- Central BP can be obtained non-invasively with either tonometry-based, cuff-based techniques, or even image-based techniques.
- A central SBP cut-off value of 130 mmHg can be used to diagnose hypertension.
- The diagnosis of hypertension using central BP may be more cost-effective than that using conventional cuff brachial BP.
- Measurement of central BP with an SBP cut-off value of 130 mmHg is recommended when a diagnosis of hypertension is clinically suspected but cannot be established using current conventional BP criteria (COR: IIb; LOE: B).
- Validation standards for central BP monitoring have been proposed in response to a wide variety of new devices, which can be classified into type I and type II central BP monitoring.

Non-invasive techniques to estimate central BP have been developed to resolve the significant disagreements between central and peripheral BP among individuals.[34] For the diagnosis of hypertension, such disagreements between central and noninvasive brachial BP may be clinically relevant when central BP is also used as a diagnostic criterion.[15,33,35] Central SBP overlaps despite there being no overlap in brachial SBP when central SBP is used to classify BP.[36] A large portion of subjects with high-normal brachial SBP have comparable central SBP to those with stage 1 hypertension.[36] Overlapping has also been noted in subjects with normal brachial BP, in whom their central BPs were in the same category as those with stage 1 hypertension. If central BP is a better target for therapy, the misclassification by brachial BP may lead to over- or undertreatment of central BP and may be clinically relevant.[37]

Currently, tonometry-based[38-40] or cuff-based techniques are used to obtain non-invasive central BP.[41-43] Carotid pressure waveform, acquired non-invasively with arterial tonometry, can serve as a surrogate for central aortic pressure waveform.[10,38,39] A radial pressure waveform can also be acquired and mathematically transformed into a central aortic pressure waveform.[44] Interestingly, a central SBP estimate can also be measured by identifying the late systolic shoulder of the acquired radial pressure waveform.[10,41,45-48] To obtain pressure waveforms, image-based techniques have also been proposed with ultrasound[49] or magnetic resonance imaging[50] of the carotid or aortic diameter/area distension waveforms.

The convenient measurement of central BP may facilitate the application of the central BP concept into daily clinical practice. As such, cuff-based techniques,[41,42] which utilize static cuff pressure to obtain oscillometric signals as the surrogate for intra-arterial pressure waveforms to obtain central BP, have been developed. Central BP can be derived by implementing a generalized transfer function,[51] prediction equations,[41] or even a mathematical low path filter.[52] Cuff-based non-invasive central BP measurements obtained using a more user-friendly procedure may have the potential to be a useful routine parameter in the busy clinical environment. It is worth noting that an accurate BP measurement for calibrating pressure waveforms is essential for any central BP measuring techniques.[19] Therefore, the panel of this consensus referred to the procedural details mandatory for accurate BP measurements in the "Correct methods for office blood pressure measurement" in "the 2015 Guidelines of the TSOC and the THS for the Management of Hypertension".

To diagnose hypertension with central BP, a diagnostic threshold for central BP based on an outcome-driven approach was derived from the Kinmen cohort,[53] and then this threshold was validated in the independent Cardiovascular Disease Risk Factors Two-Township Study cohort[54] to examine its discriminatory ability for long-term cardiovascular outcomes.[33] Using this proposed threshold, central SBP/DBP 130/90 mmHg seemed to be reliable and valid for defining hypertension based on the consistent results in the Derivation and Validation Cohorts and comparable prognostic performance across different age and sex subgroups. In this outcome-driven study, diagnostic thresholds of central BP for optimal BP, prehypertension, and hypertension were also provided (Table 1).

Furthermore, the diagnostic performance of central BP may outperform brachial BP monitoring,[55] and the cost-effectiveness of central BP monitoring has also been shown to be superior to conventional brachial BP monitoring based on lifetime costs and quality-adjusted life-year analyses using a cohort Markov model.[56] In addition, Sharman et al. suggested that guiding hypertension management with central BP to achieve BP control may result in the use of fewer medications without adverse effects.[37] It has also been observed that differences in DBP and MBP between central and peripheral arteries are minimal,[19] and that the major discrepancies occur in SBP and PP. As such, with reference to the conventional definition of hypertension as a brachial SBP of 140 mmHg,[57,58] central SBP with a cutoff value of 130 mmHg has been proposed.[33] Measuring central SBP is recommended when a diagnosis of hypertension is clinically suspected but cannot be established using the current conventional BP criteria (COR: IIb; LOE: B) in the 2015 Taiwan Society of Cardiology/Taiwan Hypertension Society hypertension guidelines.[59]

In response to the increasing number of noninvasive central BP monitoring devices, a validation standard has been proposed by the Artery Society task force.[60] In this consensus statement, efforts have been made to reach agreement relating to methods for assessing and reporting the accuracy of central BP devices, and to provide recommendations regarding appropriate protocols to assess and report the evaluation of accuracy (validation) of central BP devices. Device manufacturers are encouraged to report the purported measurement function of their central BP device. The most important concept in this document is the proposal for the classification of a wide variety of devices, among which a type I device can provide an estimate of central BP relative to measured brachial BP, and the pressure difference between central and peripheral sites is relatively accurate; and a type II device can estimate intra-arterial central BP, and the absolute central BP value is relatively accurate despite inaccuracy at the peripheral site.[60]

PHENOTYPES OF HYPERTENSION BASED ON THE DISCREPANCY BETWEEN CENTRAL AND BRACHIAL BP

Consensus statement

- Adults with isolated central hypertension or isolated

Table 1. Outcome-driven diagnostic thresholds for central BP measurement*

	Central SBP, mmHg		Central DBP, mmHg
Optimal BP	< 110	and	< 80
Prehypertension	110-129	and/or	80-89
Hypertension	≥ 130	and/or	≥ 90

Threshold values were obtained by rounding the point estimates to an integer value ending in 0 or 5.
DBP, diastolic blood pressure; SBP, systolic blood pressure.

brachial hypertension may have an increased risk of coronary heart disease compared to those without central or brachial hypertension.

The phenotypes of hypertension can be defined based on the discrepancy between central and brachial BP.[61,62] Based on the Hypertension Guideline of European Society of Hypertension/European Society of Cardiology for brachial hypertension (brachial SBP ≥ 140 mmHg or brachial DBP ≥ 90 mmHg or using antihypertensive medicine) and central hypertension criteria[33] (≥ 130 mmHg for central SBP or ≥ 90 mmHg for central DBP or using antihypertensive medicine), subgroups of isolated central and isolated brachial hypertension among adults in a national representative cohort have been identified. The prevalence of isolated central hypertension may not vary with age or sex. Adults with isolated central hypertension may have a significantly higher estimated 10-year risk of coronary heart disease than those without central or brachial hypertension.[63] In the Northern Shanghai study[64] which enrolled an elderly Chinese population, subjects with isolated central hypertension may have had a higher left ventricular mass index, carotid-formal pulse wave velocity, and urinary albumin-creatinine ratio than those without central or brachial hypertension.[64] When brachial hypertension is defined based on the 2017 ACC/ AHA BP thresholds (130/80 mmHg), a considerable number of subjects with isolated brachial hypertension may be observed. Subjects with isolated brachial hypertension may demonstrate little evidence of vascular aging but may have an increased risk of coronary heart disease similar to those with isolated central hypertension, when compared to subjects without brachial or central hypertension.[65]

USING CENTRAL BP TO MANAGE HYPERTENSION

Consensus statement

- Different classes of antihypertensive drugs may exert different effects on lowering central BP.

Lowering of central BP using antihypertensive medications

Many studies have demonstrated differential responses of central BP versus brachial BP to various antihypertensive agents, and that these differences are highly variable among individuals. Antihypertensive drugs including angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and dihydropyridine calcium blockers, as well as nitrates, may have a more beneficial effect on central BP than beta-blockers.[22]

Different classes of antihypertensive drugs may exert different effects on pulse pressure amplification.[5,37,66,67] Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, dihydropyridine calcium blockers, and nitrates may have a more beneficial effect on PP amplification than diuretics and beta-blockers. The observed detrimental effect of beta-blockers (mainly atenolol) on cardiovascular outcomes[68] can be explained by the unfavorable effect on PP amplification.[22,2] In the Café substudy of the ASCOT trial, the combination of an angiotensin-converting enzyme inhibitor (perindopril) with a calcium-channel blocker (amlodipine) lowered central BP more than the combination of a beta-blocker (atenolol) and a thiazide diuretic, despite a similar effect on brachial BP.[2] In the J-core study,[69] the combination of olmesartan with azelnidipine lowered central BP more than the combination of olmesartan with hydrochlorothiazide.[69]

Treatment of hypertension to central BP target

Although the central BP threshold of 130/90 mmHg for the diagnosis of hypertension has been proposed,[33] the treatment targets in patients with elevated central BP have not been defined. Previous studies have shown that guiding hypertension management with central BP may result in the use of fewer medications to achieve BP control without adverse effects.[37]

In subjects with uncomplicated hypertension with a low to median risk, it is reasonable to lower the central BP to < 130/90 mmHg. However, outcome-driven central BP-guided treatment target studies should be conducted for other specific compelling disease status.

GAP IN THE KNOWLEDGE AND CONCLUSIONS

Consensus statements

- Efforts should be made to reduce the calibration errors of central BP measurements resulting from the inaccurate non-invasive brachial BP used to calibrate the peripheral waveforms.

- More evidence is required to demonstrate the usefulness of central BP monitoring for the management of hypertension in routine clinical practice.

In a previous systematic review,[19] Cheng et al. showed that current central BP estimation methods are theoretically suitable. Nonetheless, the major source of errors for these central BP measurement techniques was inaccurate measurements of non-invasive BP used to calibrate the peripheral waveforms. In the era of "precision medicine," clinical decisions should be based on more accurate BP measurements. Therefore, the measurement accuracy of both noninvasive brachial and central BP can still be improved. Future studies to reduce these calibration errors[70] should be conducted by improving the accuracy in the measurement of non-invasive brachial BP.[25,71]

Even though central BP has been shown to carry superior prognostic value beyond brachial BP in some studies,[42,44,46] it has been argued that the lack of a consistently higher predictive value of central BP compared with brachial BP may reflect a true pathophysiological issue or potential bias by an inadequate method used for central BP measurements.[72,73] Further studies comparing central BP-guided therapeutic strategies with classic guideline-guided strategies for preventing cardiovascular events are required.[74]

Moreover, most outcome studies have been conducted in the elderly, in whom brachial and central pressures are similar. No outcome studies have been conducted in younger patients with a much greater difference between brachial and central pressures. Clinical trials investigating whether treatments preferentially reduce central versus brachial BP and whether the difference between central and peripheral BP is related to better outcomes are needed. In addition, future prospective studies are required to investigate whether central BP-guided strategies are better than conventional brachial BP strategies in hypertension screening in the community or in clinical practice.

CONCLUSIONS

Central BP can be measured noninvasively using various techniques, including convenient cuff-based oscillometric central BP monitors. Noninvasive central BP is likely to be better than conventional brachial BP to assess target organ damage and long-term cardiovascular outcomes. More evidence is required to support the use of central BP in diagnosing hypertension and monitoring its management in routine clinical practice.

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DECLARATION OF CONFLICT OF INTEREST

All the authors declare no conflict of interest.

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