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COMMENTARY

The second systolic radial blood pressure peak predicts cardiovascular risk only in subjects below 50 years of age

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INTRODUCTION

It is now well known that the pressure waveform is distorted as it travels distally from the aorta to the upper limb[1] (Figure 1). As a consequence, the characteristics of the contour, as well as, the amplitude (pulse pressure, PP) of the pressure waveform change substantially between the central (aortic/carotid) and peripheral (brachial/radial) arterial sites. The pathophysiology of this phenomenon—named as PP amplification due to the gradual widening of the PP as the wave travels distally—is not fully elucidated. It is attributed mainly (1) to the presence of stiffness and diameter gradient across the arterial tree and (2) to the spatial variation in the timing of the incident (forward traveling) and reflected (backward traveling) pressure waves.[1] It is however unambiguous that arterial aging (normal or premature due to cardiovascular (CV) risk factors) is the major modulator of this phenomenon.[1]

Current data suggest that the indices (for example, amplitude or reflection points) derived from the analysis of the central pressure waveform are potentially better predictors of CV risk and of effective antihypertensive drug treatment[1,2] than those derived from the analysis of the peripheral pressure waveform, including systolic blood pressure (SBP) and diastolic blood pressure, which are classically used in clinical practice. This hypothesis launched a new era in hypertension research that aims at the noninvasive assessment of central hemodynamics, although it is clear that this approach has methodological limitations.[3] An alternative approach would be to analyze the peripheral pressure waveform, beyond peak SBP and end diastolic blood pressure, to obtain more information related to the central hemodynamics.

In this line of action, in this study Matsumoto *et al.*[4] analyzed the radial pressure waveform, by means of applanation tonometry and a commercially available device, in a population undergoing screening examination. CV risk was assessed from the Framingham equation. They provided evidence regarding (1) the value and limitations of the second peak of the radial pressure wave (SBP2) as predictor of CV risk, and (2) the fact that SBP2 has different physiology from SBP. Before commenting on the findings and limitations of the study,[4] several issues related to the physiology of SBP2 and the related methodology will be shortly addressed.

CONSIDERATIONS ON THE PERIPHERAL PRESSURE WAVEFORM

Early invasive studies in the fifties[1] showed that the pressure waveform at the level of the aorta has an early peak (S1), attributed to the forward traveling wave and a late higher systolic peak (S2), due to the augmentation of the systolic phase by the reflected pressure wave (Figure 1). Conversely, at the level of the peripheral artery there is an early high peak (S1), representing the forward traveling wave, and a shorter second peak (S2 or SBP2), due to the 'delayed' arrival of the reflected wave. Although these are the typical patterns of pressure waveforms, several variations do exist.[1]

The most commonly applied method for recording the peripheral pressure wave is that of applanation tonometry.[3] This is a relatively simple and reproducible method that records directly the pressure signal by means of pressure–voltage association. Echo-tracking can be also used for the recording of brachial diameter variation with time.[3] This technique is more time consuming and requires higher operator skills; it classically applied at the level of carotid artery.[3] The common drawback of both methods is the need of pressure calibration to transform the voltage or diameter waves in pressure waveforms.[1,3] Moreover, when the radial signal is calibrated by the brachial pressure an additional error is introduced[2,3] due to the presence of PP amplification between the radial and the brachial artery, leading to underestimation of peak SBP as well of SBP2. Recently a new oscillometric method was applied to assess the pressure waveform at the brachial artery.[5] This method is extremely applicable but introduces artificial pressure wave reflections and modifies the systemic circulation due to the occlusion of the blood flow at the level of the brachial artery. Whether it is appropriate for research or clinical applications is questionable.[5]

From physiology's point of view, SBP2 represents the arrival of the reflected wave. Therefore, it has been used for the quantification of the reflected wave at the periphery by means of peripheral augmentation index (AI)[6,7] (Figure 1). It has been repeatedly shown that peripheral and central AI are very well associated, even after pharmaceutical[7] or exercise[6] modulation, implying that peripheral AI might be clinically useful for

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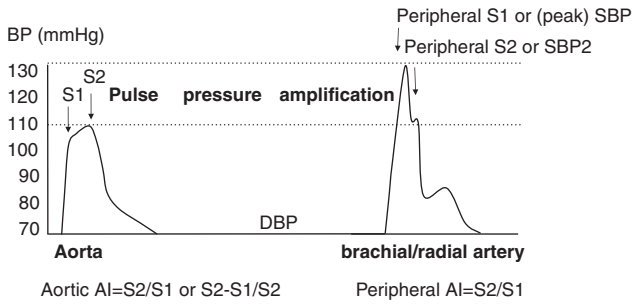

Figure 1 Typical patterns of peripheral and central pressure waveforms. AI, augmentation index; SBP, systolic blood pressure; DBP, diastolic blood pressure; S1, first systolic peak; S2, second systolic peak.

CV risk prediction to the extend that central AI is.

It has been also proposed that the SBP2 of the radial curve represents aortic SBP[8] (Figure 1) and thus could serve as its surrogate marker. This 'unexpected' observation has been reproduced in noninvasive and invasive studies,[9] which verified that, in general, the SBP2 of the radial waveform is a good estimate of the central SBP. However, at lower levels of BP radial SBP2 tended to underestimate central SBP.[9] It seems reasonable to advocate that, to the extent that peripheral SBP2 is mainly modulated by wave reflections without reflecting the effect of other hemodynamic parameters (for example, aortic characteristic impedance and left ventricular function) on the pressure waveform, significant deviations between SBP2 and central SBP are expected under various CV conditions.

CONSIDERATIONS ON THE RESULTS

The major finding of the study[4] was that SBP2 had overall a similar, and not additive to SBP, predictive value of CV risk. Most importantly, Matsumoto *et al.*[4] showed that SBP2 lost the predictive value in subjects older than 49 years of age. This observation might be strongly associated with the mechanics of age-related PP increase, and especially central PP. PP is known to be a better predictor of CV events after the age of 50 years.[1] During the past decades, the role of arterial stiffening was highlighted in the age-induced PP increase.[1] This concept includes the increase of the forward as well as of the backward reflected pressure wave. It was recently quantified and suggested[10] that the age-related increase of the backward reflected waves, rather than age-induced aortic stiffening *per se*, is the most important modulator of PP. The Anglo-Cardiff Collaborative study[11] showed that there is an age-dependency regarding the relative contribution of the incident and the reflected wave on central PP. Although backward reflections seem to be important determinants of the age-related PP increase from early on, the contribution of the incident wave is more pronounced after the age of 60 years. Interestingly, data from the same study[12] have shown that although the age-related increase of wave reflections, assessed as AI, forms a plateau after the age of 60 years, aortic stiffening sharply increases after that age. These data combined provide evidence why SBP2, an index of wave reflections, cannot predict CV risk above the age of 50 years.

This study[4] also showed that there is positive linear association between heart rate and SBP but a negative association between heart rate and SBP2. Although the former might be mediated by the effect of heart rate on cardiac output or larger artery stiffness, the latter is in line with the well-established association between heart rate and wave reflections, at least as assessed by AI.[1] It has also shown that the distribution of SBP2 level (quintiles) within the quintiles of SBP was highly variable. Taken together, these two findings suggest that SBP and SBP2 are defined by partly different hemodynamic parameters. These data were not adjusted for confounding factors; however, only 10% of the population was treated with blood pressure lowering drugs and thus it is not expected that drugs confounded these results.

Besides the previously described general methodological limitations, the application of these results are limited by the cross-sectional design of the study as well as from the fact that CV risk was calculated by means of Framingham equation, which (1) includes SBP in the algorithm, but not SBP2 and (2) may have various predictive ability in different age groups. Most importantly, SBP2 may be difficult to identify in several occasions (for example, older subjects) with obvious implications regarding its ability to predict CV risk.

In conclusion, the physiological relevance of peripheral SBP2 and central SBP has to be examined further in a wider range of patterns of pressure waveforms to be validated as surrogate of central SBP and an index of CV risk.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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