Editorial Commentary

Pulse Wave Analysis
What Do the Numbers Mean?

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See related article, pp 1108–1116

Applanation tonometry, a simple noninvasive technique for recording a high-fidelity waveform from an accessible pulse, has facilitated pulse wave analysis in large population studies. Most interest has focused on estimating an aortic or “central” waveform by the application of a filter or generalized transfer function applied to a radial waveform.1 Systolic pressure and pulse pressure differ between central and peripheral arteries as a result of peripheral amplification. By contrast, there is little regional variation in mean and diastolic pressures within large arteries and conduit arteries. A synthesized aortic waveform can, thus, be calibrated on the assumption of equality of mean and diastolic pressures at central and peripheral sites and used to estimate central systolic and pulse pressures. The main limitation of this approach, at least for the estimation of central systolic blood pressure, is the accuracy of the peripheral blood pressure measurements used to calibrate the waveform.2 Most studies and a recent meta-analysis suggest that central pressures provide a better prediction of cardiovascular risk than peripheral pressures,3 a finding intuitively rationalized in terms of the load on the left ventricle and coronary and carotid arteries.

In addition to central blood pressure, a variety of indices can be obtained relating to inflection points or shoulders in the arterial waveform. Central augmentation pressure (AP) is the height above the first systolic shoulder of the aortic waveform and central augmentation index (AI; cAI) the ratio of AP to central pulse pressure (Figure). AP is thought to relate to pressure wave reflection from the periphery of the circulation and cAI to be an index of pressure wave reflection. However, this interpretation has been challenged, and it has been suggested recently that cAI is determined mainly by the Windkessel or reservoir function of the aorta.4 Experimentally, AP and cAI can be changed independent of aortic stiffness by nitrovasodilatation, which selectively dilates muscular arteries from which reflections may arise.5 These findings are more in line with reflection as the predominant determinant of AP and cAI. Irrespective of the determinants of cAI, it appears to be an independent predictor of cardiovascular events.3 Why this should be so is less obvious than for central systolic pressure. Suggestions (not mutually exclusive) are that it is a marker of dysfunction of the arterial wall and that its prognostic impact relates to loading of the left ventricle.

Peripheral AI (pAI) is the ratio of the height of the late systolic shoulder in the peripheral (usually radial) pulse to the peripheral pulse pressure (Figure). Largely ignored in favor of cAI, there is now renewed interest in pAI. This is because it is recognized that cAI and pAI are closely related.6 It is possible that this is in part a consequence of the transfer function used to generate the aortic pulse from the radial pulse. In this regard it should be noted that, although the use of the transfer function to estimate central systolic blood pressure is well established, its use for estimation of central augmentation pressure is less well validated. Secondly, it is now appreciated that the late systolic shoulder of the radial waveform corresponds with central systolic blood pressure.7 It follows, therefore, that pAI is the ratio of central: peripheral pulse pressure, and, thus (even if its determinants are complex), it has a simple interpretation in terms of pulsatile load.

Although it is clear that much remains to be elucidated with regard to the determinants of APs and indices, their interrelationship, relationship with central/peripheral blood pressure, and, above all, why they predict risk, can we use these measures for risk stratification and/or as targets for therapy? In this issue of Hypertension, Chirinos et al8 have used individual data from a number of large population studies to provide normative population means for central (using a slightly different definition than the conventional one, see Figure) and radial AI adjusted for age, body height, and heart rate, which are important determinants of AI. This allows for a standardized comparison between values obtained in an individual and the population mean for subjects of the same age and characteristics as the individual. The deviation of AI from the mean can then be used as an index of risk for the individual. How much this will contribute to risk stratification for an individual and how AI compares with other biophysical measures of arterial wall structure/function remain to be clearly defined. It should also be noted that this approach effectively measures relative rather than absolute risk and, therefore, differs from the current approach to risk estimation. Perhaps more importantly than risk stratification, normative values potentially allow a targeted strategy for subjects confirmed to be at risk. Thus, for subjects in whom levels of peripheral blood pressure are at what are currently considered optimal levels but in whom pAI is elevated (indicative of raised central relative to peripheral pulse pressure), a therapy with a selective action to lower central pulse pressure might be beneficial.
Figure. Peripheral (radial) and aortic arterial pressure waveforms. Diastolic blood pressure (DBP) and mean arterial blood pressure (area under the waveforms) are equal. Peripheral systolic blood pressure (pSBP) exceeds central (aortic) systolic blood pressure (cSBP). cSBP corresponds with the late systolic shoulder of the peripheral pressure waveform, so peripheral augmentation index (pAI), the ratio of the late systolic shoulder: peripheral pulse pressure (pPP) equals the ratio of central pulse pressure (cPP):pPP. Central augmentation pressure (AP) is the height above the early systolic shoulder and central augmentation index (cAI) the ratio of AP to cPP. Chirinos et al define cAI as the ratio of the second peak to the first peak, which equals cPP/p1 when AP is positive (negative values can be seen in young subjects).

Of at least equal interest to the normative equations for AI is the relation between AI and risk factors and the comparison of AI between subjects of differing ethnicity investigated by Chirinos et al. Al was seen to relate very weakly to risk factors other than blood pressure. A weak positive relation to smoking and a weak or nonsignificant relation to low-density lipoprotein cholesterol, and an intriguing negative relation to diabetes mellitus was observed in most groups. These findings suggest that the prognostic value of AI is probably not driven by it being a marker of damage to the arterial wall by risk factors but because of the adverse hemodynamic consequences of a raised AI. With regard to ethnicity, values of AI, after adjustment for age, heart rate, mean arterial pressure, and body size, were markedly higher in black Africans and Andean Hispanics compared with white British subjects, whereas North American Indians demonstrated lower values than white British subjects. These results need to be interpreted with some caution, because they may have been influenced by the sampling frame of the various studies, and the comparison did not include a contrast between subjects of the same ethnicity in differing environments. The latter has shown that environment may be a more important determinant of vascular function than ancestral genetics, with the vascular phenotype ultimately reflecting a complex gene-environment interaction. Nonetheless, the finding of a higher AI in ethnic groups known to have higher rates of left ventricular hypertrophy, which cannot be accounted for by resting or ambulatory brachial blood pressure, is intriguing. It suggests that regulation of arterial tone and/or arterial remodeling may be a major factor influencing left ventricular mass through an action to increase central relative to peripheral blood pressure.

Chirinos et al are to be congratulated for bringing together these data that enhance our understanding of the epidemiology of pulse wave measures. Future collaborations relating to the prediction of outcomes will further add to the use of AI as a clinical tool, be it for risk stratification or as a target in clinical trials. Meanwhile, clarifying the hemodynamic determinants and consequences of a raised AI will improve our understanding of ventricular-vascular coupling and help identify, prevent, and reverse target organ damage in hypertension.

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