From 24-Hour Blood Pressure Measurements to Arterial Stiffness
A Valid Short Cut?

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The articles by Li et al and Dolan et al, in this issue of Hypertension and focused on the development of a new approach to estimate arterial stiffness, highlight the role of arterial mechanical properties in the determination of cardiovascular risk.

In the past, arterial stiffening and increases in systolic blood pressure (SBP) and pulse pressure (PP) have been considered a part of normal aging, and no treatment for these alterations has been proposed. The pathophysiology, structural bases, and determinants of arterial stiffness have been extensively studied these last years.3-5 Although arterial stiffening is a common situation, it has now been confirmed that aortic stiffness is an independent predictor for total and cardiovascular mortality, coronary morbidity—mortality, and fatal stroke in patients with essential hypertension, diabetes mellitus, or end-stage renal failure, and in the general population in the elderly.6,7 It is therefore important to identify subjects who are at higher risk for developing arterial stiffness with aging and determine the environmental and genetic factors that can accelerate arterial stiffening.

In recent years, several devices have been developed for the evaluation and measurement of arterial stiffness. Arterial stiffness can be quantified by the measurement of several parameters such as cross-sectional arterial distensibility and compliance, pulse wave velocity (PWV), analysis of pulse wave contours (mainly augmentation index and reflection waves), measurements of elastic modulus, stress-strain relationships, etc. During the past 5 years, among these approaches, PWV and augmentation index (AI) have become the mainstays for the evaluation of arterial stiffness in clinical and epidemiological studies.8 PWV depends mainly on the mechanical properties of large arteries, whereas AI also depends on mechanical properties of small peripheral arteries, through wave reflection process along the arterial tree. The QKD index (corresponding to the time between the onset of the ECG QRS complex [Q] and the Korotkoff [K] sound at diastolic pressure [D] heard over the brachial artery during blood pressure measurement) is based on the same principle as PWV and was the first approach to estimate arterial stiffness during 24-hour ambulatory blood pressure measurements.9

Several recent epidemiological and clinical studies have demonstrated that measuring arterial stiffness provided a higher predictive value than BP measurement in the evaluation of the cardiovascular risk. Moreover, one recent study showed that in end stage renal disease patients, the reduction in morbidity and mortality with antihypertensive therapy10 was only observed in patients whose pulse wave velocity decreased independently of age and blood pressure evolution. However, large controlled studies are needed to establish the relationship between arterial stiffness regression and prevention of cardiovascular events. The recent experience with 24-hour BP measurements underscores the importance for having a similar strategy for the evaluation of the impact of arterial stiffness under ambulatory conditions.

In the present issue of Hypertension, the articles by Li et al and Dolan et al propose a new stiffness index defined as 1 – the regression slope of diastolic blood pressure (DBP) over SBP derived from 24-hour ambulatory BP measurements and its predictive value in cardiovascular mortality.

The main conclusions of the article from Li et al was that ambulatory arterial stiffness index (AASI) was closely correlated with PWV and that AASI correlated more closely with central and peripheral augmentation index than the 24-hour pulse pressure. This latter observation was consistent even after adjustment for major determinants of arterial stiffness and wave reflections. The presence of a positive relationship between AASI and age and mean arterial pressure was an expected result since they represent the 2 main determinants of large artery stiffness. The higher AASI observed in women underscores the importance of wave reflections in the AASI determination. The study by Dolan et al showed that in a prospective follow-up of 11 291 hypertensive patients, AASI was correlated with cardiovascular mortality. In adjusted analyses, AASI was a better predictor of fatal strokes, whereas 24-hour PP was a better predictor of cardiac events. Both AASI and PP were able to predict cardiovascular mortality in hypertensive subjects, whereas AASI seems to be a better predictor than PP in normotensive subjects.

An important issue is to determine whether this is really a new index for measuring arterial stiffness. The definition given by the authors indicates that it represents changes in DBP as a function of SBP over a 24-hour period. One interesting aspect is that this index is calculated in each
subject based on large-scale variations of SBP during a 24-hour period (more than 70 mm Hg in the cases shown in Figure 1 of the article by Dolan et al). The authors show that the lower the DBP variations for given SBP changes, the higher the stiffness index, and they define normal values of this index according to age. The fact that determining this index is based on large variations of SBP confers a dynamic component as opposed to the usual static measurements.

The results that show different values of AASI in subjects having the same PP indicate that AASI may represent an advantage for a better estimation of stiffness than PP. However, a crucial point is whether this index really measures large artery stiffness asPWV does, or whether it is largely influenced by peripheral resistance levels. The answer to this question has the same limitations as PP, because both AASI and PP are measured using SBP and DBP (ie, hemodynamic parameters depending on cardiac function, arterial geometry, and arterial stiffness). The statistical evidence provided in the present articles cannot give a definitive answer to the question on the dependency of the AASI index to large artery stiffness.

One could suggest that AASI may be a reliable indicator of the relationship between the pulsatile and the steady components of BP over 24 hours. The links between AASI and arterial stiffness should be further studied following acute or chronic changes of arteriolar vasomotricity using pharmacological agents. The fact that AASI is better correlated than PP with the augmentation index is in favor of the hypothesis that AASI is highly dependent on the mechanical properties of small arteries. In favor of this hypothesis is also the result observed in the study by Dolan showing that this index better predicted fatal strokes whereas 24-hour PP better predicted cardiac events. Previous epidemiological studies have also shown that cardiac events were better correlated to casual and ambulatory pulse pressure, whereas strokes were better correlated with mean arterial pressure, a rough indicator of small artery resistance.

Finally, the following point may be of some clinical interest concerning this index: in subjects aged <40 years, AASI was correlated with central and peripheral augmentation index, whereas 24-hour PP was not. Actually, in younger subjects, high SBP and PP at the brachial artery may not reflect high arterial stiffness since they overestimate central aortic pressure values (amplification of the pressure waves) and are often related to sympathetic overactivity (high cardiac output) in younger subjects. The demonstration that AASI is associated with arterial parameters even in younger subjects makes AASI an interesting index for the evaluation of arterial alterations even in younger subjects. For strokes, the higher predictive value of AASI as compared with PP seems to be more pronounced in dichotomized analyses using the upper 95th percentile. However, these results should be analyzed with some caution considering the relatively small number of patients in these groups.

In conclusion, the novelty of these studies is to show that the AASI may be complementary to PP in the evaluation of cardiovascular risk and could be a more sensitive predictor of stroke, especially in low risk patients (young, normotensive patients). One of the interesting aspects of this method is that it is easy to measure since it is based on SBP and DBP values throughout the 24-hour period. However, we still believe that the use of this index should not slow down the further development of methods that directly measure arterial stiffness and those that analyze pressure waveform contours.

References
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