Arterial Stiffness in Arterial Hypertension

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Introduction

In recent years, there has been great emphasis on the role of arterial stiffness in the development of cardiovascular (CV) diseases. Arterial stiffness and wave reflections are now well accepted as the most important determinants of increasing systolic and pulse pressure in our aging community, and, therefore, causes of CV complications and events, including stroke and myocardial infarction.

Pathophysiologic Aspects

A generally accepted mechanistic view is that an increase in arterial stiffness causes a premature return of reflected waves in late systole, increasing central pulse pressure, and, thus, systolic blood pressure. Indeed, the arterial pressure waveform is a composite of the forward pressure wave created by ventricular contraction, and a reflected wave. Waves are reflected from the periphery, mainly at branch points or sites of impedance mismatch. In elastic vessels, because pulse-wave velocity (PWV) is low, the reflected wave tends to arrive back at the aortic root during diastole. In the case of stiff arteries, PWV rises, and the reflected wave arrives back at the central arteries earlier, adding to the forward wave, and augmenting the systolic pressure. This phenomenon can be quantified through the augmentation index—defined as the difference between the second and first systolic peaks, expressed as a percentage of the pulse pressure. Apart from a high PWV, changes in reflection sites can also influence the augmentation index.

Any rise in systolic blood pressure increases the load on the left ventricle, increasing myocardial oxygen demand. In addition, arterial stiffness is associated with left ventricular hypertrophy, a known risk factor for coronary events in normotensive and hypertensive patients. The increase in central pulse pressure (PP) and the decrease in diastolic blood pressure may directly cause subendocardial ischemia. The measurement of aortic stiffness, which integrates the alterations of the arterial wall, may also reflect parallel lesions present at the site of the coronary and cerebral arteries.

Arterial stiffness and wave reflections contribute to the "amplification phenomenon," which explains why brachial PP should not be confounded with central PP (common carotid or aorta). Brachial PP overestimates central PP in young subjects, and may underestimate central PP in elderly subjects with hypertension and/or diabetes.

Measurements of Arterial Stiffness and Wave Reflection

Carotid-femoral PWV is the "gold standard" for arterial stiffness. Carotid-femoral PWV is a direct measure, has the largest amount of epidemiologic evidence for its predictive value for CV events, and requires little technical expertise. The measurement of PWV is generally accepted as the most simple, noninvasive, robust, and reproducible method with which to determine arterial stiffness. Carotid-femoral PWV, measured along the aortic and aorto-iliac pathway, is the most clinically relevant, because the aorta and its first branches are what the left ventricle "sees," and are thus responsible for most of the pathophysiologic effects of arterial stiffness. Carotid-femoral PWV has been used in epidemiologic studies demonstrating the predictive value of aortic stiffness for CV events.

PWV is usually measured using the foot-to-foot velocity method from various waveforms. These are usually obtained, transcutaneously, at the right common carotid artery and the right femoral artery (ie, "carotid-femoral" PWV), and the time delay (Δt, or transit time) measured between the feet of the two waveforms. A variety of different waveforms can be used, including pressure, distension, and Doppler. The distance (D) covered by the waves is usually assimilated to the surface distance between the two recording sites. PWV is calculated as PWV = D (meters) /Δt (seconds).

Local arterial stiffness (carotid, brachial, femoral) benefits from a certain amount of epidemiologic evidence for its predictive value for CV events, requires a higher level of technical expertise, and is indicated for mechanistic analyses in pathophysiology, pharmacology, and therapeutics.

Carotid pulse pressure and augmentation index are only indirect, surrogate measures of arterial stiffness. However, they provide additional information concerning wave reflections. They have demonstrated their predictive value in patients with end-stage renal disease (ESRD) and require some technical expertise.

Epidemiologic Evidences

A major reason for measuring arterial stiffness and wave reflections "routinely" in clinical practice comes from the recent demonstration that arterial stiffness has an independent predictive value for CV events. A large amount of evidence indicates that carotid-femoral PWV is an intermediate end point for CV events, either fatal or nonfatal. Aortic PWV has a better predictive value than classic CV risk factors entering various types of risk scores. Carotid augmentation index and pulse pressure have shown an independent predictive value for all-cause mortality in ESRD patients, but not yet in patients at lower risk or in the general population.

The value of arterial stiffness as surrogate end point for CV events has not yet been unequivocally demonstrated. A major issue is indeed to determine the impact of arterial stiffness attenuation on survival, and particularly to demonstrate whether a reduction in PWV could predict a reduction in CV events, independent of the normalization of classic CV risk factors. A direct answer to the issue of the predictive value of aortic stiffness as surrogate end point for CV events has been afforded in ESRD patients, showing that the insensitivity of PWV to reduced BP is an independent predictor of mortality.

Further Research

Although a large number of publications reported the changes in arterial stiffness and wave reflections after various interventions, either nonpharmacologic or pharmacologic, several issues remain to be addressed.

The impact of aortic stiffness attenuation on CV mortality, coronary events, and stroke yet remains to be established in other populations, particularly those with lower but still some CV risk—that is, those with hypertension, dyslipidemia, diabetes, and moderate chronic kidney disease.

To allow a better understanding of the predictive value of indices of arterial stiffness for an individual patient, normal values applicable to individual populations are required. This requires both a cross-sectional and a longitudinal approach to remove the potential influence of birth cohort effects and provide greater evidence of predictive values and causality. Differences between population normative data should be explored as they may help explain why cardiovascular risk varies between countries and what may be driving arterial stiffening.

Finally, it is also important to demonstrate whether a therapeutic strategy aiming at normalizing arterial stiffness and wave reflection proves to be more effective than usual care in preventing CV events.