Advance in Vascular Phenotype Assessment in Children and Adolescents

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Cardiovascular damage occurring in adults finds its roots in risk factors operating early in life. Among the factors influencing cardiovascular risk, blood pressure values represent an important measurable marker of the level of potential cardiovascular risk in children and adolescents. Indeed, there is growing evidence that mild blood pressure elevations are much more common than was thought in the past in a pediatric population. Furthermore, hypertension in childhood has gained ground in cardiovascular medicine thanks to the progress made in several areas of pathophysiological and clinical research.1

It is not uncommon for high blood pressure in the young to be accompanied by evidence of early organ damage, left ventricular hypertrophy, and increased carotid intima-media thickness. Likewise, functional changes in the vascular tree that are both the cause, as well as the consequence, of early vascular alterations can also be detected.2 Evidence of both early blood pressure elevation and alterations in vascular function have been described in children and adolescents under different conditions that predispose an individual to increased cardiovascular risk.3 Vascular phenotypes of large and small vessels provide a novel viewpoint for studying when target organ damage begins, and because it can be clinically relevant, it represents a field of growing interest. The introduction of various methodologies that assess vascular function under noninvasive conditions has shown endothelial dysfunction and arterial stiffness to be the most relevant vascular phenotypes based on longitudinal studies in adults.4,5

The measurement of pulse wave velocity is generally accepted as the simplest, noninvasive, robust, and reproducible method with which to determine arterial stiffness. Carotid-femoral pulse wave velocity is a direct measurement, and it corresponds well with the widely accepted propagative model of the arterial system. Measured along the aortic and aorto-iliac pathway, it provides the most clinically relevant data, because the aorta and its first branches are what the left ventricle “sees” and are, thus, responsible for most of the pathophysiological effects of arterial stiffness. The pulse wave velocity is calculated as the ratio between the distance covered by the wave and the transit time. Although these findings are of great interest, what these measures indicate about vascular structure and function in young children is not entirely clear, especially in the context of childhood growth and development.

To date few studies have attempted to provide normal ranges of pulse wave velocity for populations that include children,6,7 and they have been hampered by the small numbers of pediatric subjects. The report in this issue by Reusz et al8 provides reference values for pulse wave velocity in 1008 healthy children and teenagers. According to the data presented, the main factors independently related to pulse wave velocity are age, height, and mean arterial pressure. Older and taller youths with higher mean arterial pressure are those with the higher pulse wave velocity. Sex was also a determinant of pulse wave velocity. In fact, the pulse wave velocity of boys and girls was similar in the first 2 age quartiles but not in older quartiles. Thresholds for elevated pulse wave velocity in children are based on the concept that pulse wave velocity changes with age and body size, making it impossible to use a single level to define abnormal pulse wave velocity as is done in adults. Therefore, the reference values were presented for sex, age, and height. This approach avoids potential bias when the study is performed in subjects with extreme growth patterns where only age and sex are used as variables.

Other than the clinical use of providing values, the information also constitutes a suitable tool for longitudinal clinical studies assessing subgroups of children who are at long-term risk of cardiovascular disease. It is worth remembering that the cardiovascular status in children and adolescents is carried over into adult life.

Despite the importance of having reference values, there are several limitations when attempting to create recommendations in the use of pulse wave velocity in children and adolescents. One is the relationship between the dimensions and the elastic properties of the vascular tree and their changes in such periods of rapid growth, such as adolescence. Because this can be minimized by the simultaneous consideration of age, sex, and height, the most important limitation is that the values are purely statistically based, and, like blood pressure values, there are no prospective studies with sufficiently long follow-up to directly link childhood values with the presence of organ damage in other territories or with the occurrence of cardiovascular disease.

Parameters for estimating vascular abnormalities in the large vessels other than pulse wave velocity have also been introduced into pediatrics. The augmentation index, a quantitative measure of the contribution of wave reflection to the
central pressure waveform, and other aortic-derived parameters can provide additional information regarding vascular phenotype. Efforts addressed at collecting reference values in these parameters from the pulse wave analysis can provide a suitable tool for forwarding the assessment of risk of cardiovascular disease.

A new understanding of early vascular phenotype has the potential for shifting the focus from traditional blood pressure values to evaluation of the target organ damage represented both by properties of the arterial vessel wall itself, as well as cardiac and renal involvement. Certainly, more studies in young individuals, especially longitudinal investigations, are needed to better assess the role of pulse wave velocity measurement and other parameters of vascular alterations in children and adolescents. The clinical use of pulse wave velocity depends on the use of normal ranges as reference values. The present information represents an important starting point for the future development of stronger normative data.

**Disclosures**

None.

**References**

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*Hypertension*. 2010;56:185-186; originally published online June 21, 2010;
doi: 10.1161/HYPERTENSIONAHA.110.154617

*Hypertension* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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World Wide Web at:
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