Arterial Stiffness, Fatness, and Physical Fitness
Ready for Intervention in Childhood and Across the Life Course?

J. Kennedy Cruickshank, Mohammadreza Rezailashkajani, Guillaume Goudot

Arterial distensibility and its converse stiffness have come of age as physiological concepts and now as a target for intervention. The central hypothesis sustained so far is that an individual’s “arterial stiffness” measured as aortic pulse wave velocity (PWV) is a convenient, integrated index of vascular pathology over a person’s life course, more precise and reliable than other risk factors individually. For example, blood pressure (BP), whether casual or 24 hour, is more sensitive to stimuli and, therefore, more variable. Arterial distensibility is in part dependent on BP, yet its prognostic power is because of its “independence” from BP, including pulse pressure. It appears to indicate the general burden of atherosclerotic disease and subclinical damage from multiple risk factors over time: the “wear and tear” of constant distension and recoil (part of “aging”), effects of smoking, lipid metabolism, (hyper)glycemia, ethnicity, how family history expresses itself, etc.

European hypertension guidelines now include PWV as a recommended but optional measure. The relationship of arterial distensibility with cardiac function and structure, known as aorto-ventricular coupling, is tantalizing because, as a bioengineering feedback loop, cause and effect are still unclear. Many other key questions remain, most critically related to the natural history of arterial stiffness but also fundamental ones of basic structural biology in the vessel wall.

A clue to the natural history of arterial stiffness is published in this issue of Hypertension, an Australian study of 9- to 10-year-old, generally prepubescent schoolchildren. The study shows a clear relationship among degree of body fat, physical fitness, and arterial stiffness, measured by carotid-femoral PWV. The link of PWV with fitness was not independent of body fat. Why should this article be of interest, being only cross-sectional, whereby association may well not imply cause? The answer is its insight into primary prevention and underlying mechanisms. The study’s strengths include its community base, large number of healthy children properly sampled, gold-standard “DXA” assessment of body composition, and an accepted method for PWV measurement. Its weaknesses include PWV measured sequentially rather than simultaneously at carotid and femoral sites over only 8 cardiac cycles. Another is the use of a 20-m shuttle run to assess cardiorespiratory fitness, which can be characterized by a variety of methods that the authors understandably could not apply but do not discuss or compare. Similarly, the pedometer is insensitive for assessing physical activity, especially in children, who may remove it. Perhaps as a result, only 20% of the variance of the PWV measured was related to any of their variables. However, these weaknesses would tend to bias the results toward the null so that any association with PWV was remarkable.

Opportunities
If the hypothesis(es) listed above are not refuted and they stand the test of time and of effective intervention, the interplay of fatness and physical fitness on regional and central arterial performances offers tremendous opportunities. First and most widely applicable is a role for arterial stiffness in public health education, rather more immediate than what BP can offer. Promoting to children and adolescents how their blood vessels and heart work and respond to exercise might just encourage practical uptake of physical activity but also scientific interest in their own human biology. Some relatively simple concepts can be grasped by teachers and potentially at least secondary or high school children: how blood vessel expansion after each heart beat becomes limited over time (“stiffening”) and that the vessels can then no longer act as effectively to “smooth” the circulation of blood while the heart rests, which can lead to disease. It may be no coincidence that the lay public use restriction is effective. Other dietary factors, such as moderate alcohol intake and types of fat, including oddities such as α-linoleic acid, fish oil, garlic powder, and dark chocolate, all apparently lower arterial stiffness (see Reference3). Whether and how these alter arterial pathology, per se, are unclear.

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602
Third, these data provide momentum for the definitive test of the use of arterial stiffness as a target: full-scale randomized trials of pharmacological interventions on the background of these lifestyle maneuvers. Such trials are long overdue, but their time surely has arrived.

Why Stiffness Rather Than Other Vascular Measures (Intima-Medial Thickness, Flow-Mediated Dilatation, or Central Pressure)?

Noninvasive vascular measures available in youth are the same as those in adults, including carotid intima-medial thickness, forearm flow-mediated dilatation (FMD), and central pressures. Intima-medial thickness and flow-mediated dilatation both demand highly trained observers and, more troublesome, the change in intima-medial thickness values from 7 to 18 years of age seems to be minimal. A disadvantage of flow-mediated dilatation is that forearm vessels are not subject to atheroma, and the ischemic time hurts many people. However, flow-mediated dilatation values are markedly reduced in obese, diabetic, and hypercholesterolemic children, and there is little doubt that improved endothelial function promptly improves vessel distensibility in arteries with little disease (probably via endothelial NO synthase). Finally, "central" BP, derived from the radial or carotid tonometric waveform, varies as brachial BP does, even if interventions may differentially affect these values. The use of central BP in children is not established yet, but the technique has its enthusiasts.

We would argue that for a brief, one-time estimate of general arterial health and as a more complete index of arterial integrity, measurement of arterial stiffness via PWV is the most useful. It has greater simplicity; less general variability and, hence, good repeatability; is a more complete index of arterial integrity; and is much less uncomfortable for the participant. One issue before its widespread acceptance is that several techniques for different arterial paths exist, confusing to those happy with BP measurement alone. Which technique should be used? Most devices measuring PWV over the carotid-femoral path use Doppler (flow wave) and tonometric (pressure wave) methods at each site, R-wave gated or not. Length measures are arbitrary and may be prone to error (eg, suprasternal notch to the probe site on the neck or groin). Tonometry requires a surface vessel, whereas Doppler ultrasound can penetrate short distances through adipose or other tissue. We prefer Doppler methods for insonating the central descending aorta (from the arch at the left subclavian junction to just proximal to the bifurcation around the umbilicus), which minimizes diameter tapering of vessels and reflection artifacts that result. However, these devices, although relatively simple, are not as quick to use as tonometry or commercially available, even if they are cheaper and among the oldest in use.

Finally, there are more sophisticated techniques, eg, for aortic impedance, which require blood flow measures.

For children, carotid-femoral tonometry, despite its anatomic drawbacks, is probably the quickest, as used by Sakuragi et al via the well-known SphygmoCor. Other recent methods include the so-called ankle-brachial PWV by the Collin-Omron device (in fact cardiac-radial and cardiac-to-posterior tibial or dorsalis pedis, which the software can provide). A novel Hungarian-origin device, the Arteriograph, using just upper-arm oscillometry and the supraprosternal notch-to-pubis distance, has been validated. Note that only the Doppler methods and the Collin-Omron device allow femoral-to-dorsalis pedis PWV measurement over a muscular artery pathway, which may be of particular interest in growing children.

Pharmacological Interventions

Many antihypertensive, lipid-lowering, and anti–tumor necrosis factor drugs reduce PWV, as do discontinued “advanced glycation end-product” breakers in diabetes mellitus and hormone replacement therapy. Importantly, as studied to date, statins reduce PWV but not central pressure.

Conclusion

Changes of arterial stiffness with physical fitness, perhaps mediated through body fat, start early in childhood. In principle, because of less variability, PWV has apparently greater precision than any BP measure. As an index of general arterial status, effective interventions on PWV offer greater power, and, thus, a much smaller sample size in which to test efficacy on cardiovascular outcomes. Trials should, therefore, cost much less. The key question is whether PWV reduction results in reduced cardiovascular events and mortality, a hypothesis that needs testing in randomized trials as soon as possible.

Disclosures

There are no conflicts of interest to disclose: J.K.C.’s unit continues to test out and use various devices, bought, loaned, or donated, for measuring pulse wave velocity, including those mentioned in the text.

References


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