



Invited commentary

Early arterial abnormalities in young adulthood

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The conclusion of the paper by Koivistinen and coworkers on young adults, published on *Atherosclerosis* [1] is that pulse wave velocity (PWV), a vascular marker related to the elastic properties of the arterial wall reflects a different aspect of subclinical damage than brachial flow mediated dilation (FMD, an estimate of a functional disturbance of vasodilatory capacity of the vessel) or carotid intima media thickness (CIMT, a marker of early atherosclerotic plaques).

This statement is plausible and is not contradicted by the finding of a significant correlation between PWV and CIMT in older adults, in the age range of 46–76 years. The lack of consistent correlation between PWV and brachial FMD, in this study is not surprising in view of the problems of standardization of the methods, in general and in younger age in particular [2], of the method evaluating vasodilatory capacity of the arterial wall, which in general precludes its adoption in large-scale surveys. Furthermore, the response of the brachial artery to reactive hyperemia, with increasing age and/or in patients with severe coronary artery disease is so blunted that it can be unsuitable to use the technique in older patients with CVD. However, the B-mode ultrasonographic measurements of the brachial artery intima-media thickness has been shown to reflect the extent of coronary artery stenosis in patients with advanced atherosclerosis [3]. In the study of Koivistinen FMD was not measured in the older group of subjects.

On the other hand, measurements of PWV and CIMT have been used with success in epidemiological surveys and clinic trial and are widely accepted methods for the detection of preclinical arterial

damage, even in childhood and adolescence [2,4]. What is the difference between these non invasive vascular methods? Pulse wave velocity is one of the methods used to evaluate arterial stiffness [5] in humans. Other methods are based on the measurement of arterial diameter change and distensibility or arterial pulse waveform analysis [2]. Increasing arterial stiffness corresponds to increasing PWV and central arterial stiffness can indirectly be assessed non-invasively by pulse wave analysis [5]. The PWV is an established independent predictor of all-cause and cardiovascular mortality in both populations with and without pathological conditions [6].

Very few data are available to explore the elastic properties of the arterial wall and pathology data with non-invasive methods. However, it is thought that extracellular matrix accumulation and diffuse thickening lead to increase in arterial stiffness [7]. The proportion of collagen and elastin in the extracellular matrix is affected along this process (with a relative reduction in elastin content). A consistent and strong relation between arterial stiffness and high blood pressure has been demonstrated [8] and disturbance in the elastic properties most likely is diffuse from its beginning and would precede and enhance the development of atherosclerotic plaques. CIMT identifies, already in late childhood and adolescence, atherosclerosis-prone arterial sites [4]. Carotid thickenings are strongly related to several cardiovascular risk factors and preferentially develop in proximity of arterial bifurcations (such as carotid bifurcation) [9], and are focal (plaques) in most instances. CIMT predicts CVD, however, a close association between CIMT progression and the risk of future vascular events remains to be proven.

In the years, with the progression of arterial damage, focal arterial lesions (plaques) develop in the areas of diffuse thickening. At the same time, a more and more extensive part of the surface area,

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on the luminal side of the arteries, becomes covered with plaques and the arterial disease tends to be diffuse. In the adulthood, by the age of 50 years, arteries present a picture of complex damage, including diffuse intima-media thickening (reflected in abnormalities in the elastic properties) and focal lesions (atherosclerotic plaques) prone to thrombosis. It would thus be explained why in early adulthood PWV, a functional estimate of early diffuse abnormality of extracellular matrix of the arterial media, is not correlated with foam cell infiltration and focal thickening, better described by CIMT. In older age, with diffuse thickening leading to atheroma lesions, and atheroma diffusely involving the arterial wall, patients at high risk of cardiovascular events would present abnormalities of both estimates of arterial stiffness (such as PWV) and pre-clinical atherosclerotic plaques (as detected by measurement of IMT).

In a clinical set-up, PWV might be useful to detect and monitor early arterial damage (of diffuse type) in young hypertensive patients. B-mode ultrasound and measurement of CIMT might be accurate for early detection and monitoring of atherosclerotic plaques in young hypercholesterolemia patients and other subjects at high CV risk. In the case of older patients, PWV and measurement of CIMT do not provide the same type of information on arterial damage, nevertheless they are both effective in identifying individuals at high risk of cardiovascular events, including acute coronary syndromes, stroke and sudden death.

Both the above discussed non-invasive methods of vascular diagnosis are enough standardized and of demonstrated consistency of measurements [2,10] to be transferred from research to clinical set-ups [8,11].

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