Defining vascular aging: From bench to bedside

Stephane Laurent
Department of Pharmacology, Georges Pompidou Hospital, Paris Descartes University

The growing interest for the clinical measurement of arterial aging through the non-invasive assessment of arterial stiffness is associated with accumulating evidence that arterial stiffness has independent predictive value for cardiovascular events. In this review, we will address several issues. (1) The basic mechanisms of arterial ageing of large arteries have been intensively investigated during the last decades, and involve structural and functional changes of the “lamellar unit” or “musculo-elastic complex” under cumulative mechanical stress and disorders of molecular functions. Recently, the role of vascular smooth muscle cells has been emphasized, not only through connections with the extra-cellular matrix, modulating specific signaling pathways, but also through cell contraction and stiffness. The effects of cellular senescence and the role of sirtuin on cell stiffness are underlined. Arterial stiffness is now well accepted as an integrator of all damages done to the arterial wall, either well identified cardiovascular risk factors (high blood pressure, diabetes, …) or poorly identified ones (oxidative stress, inflammation, …). (2) The hemodynamics consequences of arterial ageing have been studied in healthy populations. In young healthy subjects, the mismatch of impedance between elastic proximal arteries and stiffer medium size muscular arteries can generate partial wave reflections, far from the small resistance arteries. Partial reflections limit the transmission of pulsatile energy to the periphery and protect the microcirculation. In older subjects, aortic stiffness increases, the stiffness gradient is attenuated, and less wave reflections are generated. The pulsatile pressure is not sufficiently dampened and is transmitted, damaging the microcirculation. (3) The concept of early vascular aging(EVA) is elaborating on the core idea that it is possible to early identify subjects with signs of an unsuccessful vascular aging that would lead them into cardiovascular disease and irrecoverable residual risk despite primary or secondary prevention measures undertaken later in time. Aortic stiffness, measured as regional pulse wave velocity, is generally accepted as one of the most precise and robust measurement of EVA. Essential hypertension is a good example of EVA, since arterial stiffness is increased at a given age in response to a higher blood pressure. However, other diseases associated with chronic low-grade inflammation are associated with elevated arterial stiffness despite normal blood pressure. Current epidemiological studies show that a high percentage of young subjects have abnormally high PWV, thus present with EVA. (4) International guidelines for routine clinical practice have included the measurement of regional stiffness for stratifying cardiovascular risk and determining primary or secondary prevention. (5) Novel apparatus have been developed for measuring arterial stiffness at the regional or local level. Regional stiffness is most often determined through pulse wave velocity between two arterial sites. Methods using a single-site cuff-based pulse wave velocity measurement are promising. Local determination of arterial stiffness, obtained either with the well-established high-resolution echotracking systems or more recently with magnetic resonance imaging, is rather indicated for pathophysiological and pharmacological studies.