Clinical application of non-invasive assessment of vascular damage: current status and future perspectives

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While risk scores are invaluable for adapted preventive strategies in clinical decision making, they are not flawless and their head-to-head comparison opens many questions. Moreover, a significant gap exists between predicted and actual event rates, leading to under- and over-prediction, thus raising the issue of calibration. Additional tools to further stratify the risk of patients at an individual level are biomarkers. A surrogate endpoint is a biomarker that is intended as a substitute for a clinical endpoint. In order to be considered as a surrogate endpoint of cardiovascular events, a biomarker should satisfy several criteria, such as **proof of concept**, **prospective validation**, **incremental value**, **clinical utility**, **clinical outcomes**, **cost-effectiveness**, **ease of use**, **methodological consensus**, and **reference values**.

We scrutinized the role of peripheral (i.e. not related to coronary circulation) noninvasive vascular biomarkers for primary and secondary cardiovascular disease prevention. Most of the biomarkers examined fit within the concept of early vascular aging. The addition of a vascular biomarker adds modestly, yet significantly beyond classical risk factors and may be useful in patients classified as having intermediate CV risk and in whom there is a therapeutic dilemma. On the basis of stringent criteria, vascular biomarkers can be classified in three groups:

- Biomarkers that fulfill most of the criteria and, therefore, are close to being considered a clinical surrogate endpoint are carotid ultrasonography, ankle-brachial index and carotid-femoral pulse wave velocity;
- Biomarkers that fulfill some, but not (yet) all of the criteria are brachial ankle pulse wave velocity and central haemodynamics/wave reflections;
- Biomarkers that do no not at present fulfill essential criteria are flow-mediated dilation and endothelial peripheral arterial tonometry.

Nevertheless, it is still unclear whether a specific vascular biomarker is overly superior. Indirect evidence can be deducted from large studies and meta-analyses, but a prospective study in which all vascular biomarkers are measured is still lacking. In selected cases, the combined assessment of more than one biomarker may be required. Instead of a “one size fits all” approach, a tailored choice of the best vascular biomarkers for each patient, dictated by clinical setting and comorbidities may be preferable, although research is still needed to identify the ideal vascular biomarker for the various clinical conditions. Importantly, the promise of vascular biomarker-driven therapeutic decisions should be validated through randomized clinical trials data.