Pulse Wave Velocity Ratio

The New "Gold Standard" for Measuring Arterial Stiffness

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Large arteries play an important role in converting flow oscillations—resulting from intermittent ventricular ejection—into continuous blood flow, along the arterial tree. These arteries can accommodate ≈50% of the stroke volume by distending their walls, with ≈10% of the energy produced by the heart being diverted to this distension and stored in the walls,[1] and this ability is the result of a high elastin content in their arterial wall. However, the composition of the arterial wall changes from central to peripheral arteries, with a dominant collagen content in the peripheral arteries. Arteries become stiffer with increasing age and in different diseases (hypertension, chronic kidney disease [CKD], diabetes mellitus, or atherosclerosis), but this increase is more important in larger arteries than in the peripheral ones. In the peripheral arteries, there is even described a decrease in the stiffness of arterial wall, interpreted as an adaptation to an increased central aortic stiffness.[2] This reversal of the normal arterial stiffness gradient, named stiffness mismatch, enhance the transmission of pulsatile energy into the periphery and microcirculation and, theoretically, increase the risk for damage to microvascular beds in highly perfused organs.

The carotid-femoral pulse wave velocity (cf-PWV) is used at this moment as the "gold standard" for measuring aortic stiffness[3] and has the most evidence linking it to cardiovascular outcomes. Its ability to independently predict cardiovascular events was ascertained by the newest European Society of Cardiology/European Society of Hypertension Guidelines, which recommend its use as a potential additional measurement, if available and technically possible, for the assessment of asymptomatic organ damage[4] in hypertensive patients. However, being based only on observational studies, this recommendation is not shared by all investigators.[4] A recent meta-analysis that included 17 635 patients from 16 studies, showed that cf-PWV may enable a superior identification of high-risk populations that could benefit from more aggressive cardiovascular disease risk factor management.[5] Importantly, its predictive power was stronger in younger patients and was not modified by the presence of hypertension, diabetes mellitus, or CKD, by sex or smoking status. In non-CKD patients arterial stiffness is linked to a greater extent with arterial wall thickening than with modifications of the intrinsic elastic properties of the arterial wall. In CKD patients, the latter seems predominant during the arterial modeling process, secondary to fibroelastic intimal thickening, calcification of elastic lamellae, increased extracellular matrix, and more collagen content.[1] These are most probably associated with the uremic milieu that predisposes the vascular bed to more significant injuries. CKD patients have an increased risk of cardiovascular mortality and morbidity as compared with the general population, and the increased arterial stiffness is one of the most important contributors to these undesirable events. There is data now showing that the aortic stiffness (as measured by the cf-PWV) is a strong and independent predictor for cardiovascular mortality in end-stage renal disease, in contrast to a lack of prediction for measures derived from peripheral muscular arteries (carotid-radial pulse wave velocity).[6]

In this issue of the Journal, Fortier et al[7] make use for the first time of the stiffness mismatch phenomenon as a prognostic marker of arterial stiffness. On the basis of their previous work,[8] they hypothesized that the ratio of cf and carotid-radial pulse wave velocity (the PWV ratio) could be a better prognostic predictor of mortality than cf-PWV. The fact that the PWV ratio is independently associated with the outcome is not surprising. Of interest is that this parameter proves to be a more powerful indicator of mortality that the cf-PWV, the current "gold standard" for risk assessment associated with arterial stiffness.

All new biomarkers should be properly validated in different prognostic models. Taken alone, these potential biomarkers could improve the accuracy of the diagnostic, but when entered into already established risk prediction models (such as Framingham), they frequently fail to show a significant benefit. In the current report, the authors show in a high-risk population that the discriminative power of the PWV ratio for mortality is better than that cf-PWV.[7] But is this information adding more value above and beyond that of traditional risk factors or it reclassifies more exactly the patients at risk? Are these results similarly reliable to PWV measurements and generalizable to other, lower-risk populations? Is the amelioration of this parameter associated with a reduced incidence of adverse events? Currently, the cf-PWV was shown to possess the ability to answer positively to all these questions, and for the new PWV ratio to be implemented into clinical practice it should be tested against this established risk factor in more complex risk prediction models.

The study by Fortier et al[7] included 310 end-stage renal disease patients that were followed for a median of 29 months. Although the authors adjust for important confounders in their analysis—such as age, sex, diabetes mellitus, cardiovascular

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comorbidities, dialysis modality, or different biochemical parameters, other specific characteristics of end-stage renal disease should have been taken into consideration. Overhydration is intimately linked with arterial stiffness in end-stage renal disease.[9] In addition, a recent study showed that only patients randomized to a strict volume control using bioimpedance had a significant reduction in the cf-PWV values,[10] reinforcing the causal relationship between these 2 parameters. As mentioned in the article, other important limitations are the lack of serial PWV measurements and that of a cardiovascular outcome, as these might have improved our understanding of the physiopathological aspects of the arterial remodeling process.

In conclusion, Fortier et al[7] propose for the first time a new parameter for estimating arterial stiffness' risk. There is a great heterogeneity in the biomechanical properties of large arteries and this study highlights the importance of the interaction between elastic and muscular arteries opening a new area for future research in the field of cardiovascular risk assessment.

Disclosures

None.

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