The usefulness of several new markers, which can be classified as biochemical markers, proteomic markers and physiological markers, has been proposed for assessment of cardiovascular risk. To date, however, none of these has surpassed, in terms of the usefulness, the conventional risk factors used for cardiovascular risk assessment. Risk stratification based on conventional risk factors is generally accepted as the standard initial step for overall cardiovascular risk assessment. Therefore, new markers may not be particularly useful for overall cardiovascular risk assessment, but may be of value in particular subsets of subjects (ie, low-, intermediate- or high-risk subjects) and for specific objectives (eg, screening for latent cardiovascular disease and/or prediction of the prognosis, including the risk of new onset of cardiovascular disease). Therefore, in the application of the new risk markers, the characteristics of the subjects and the specific objectives should be considered.

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Considering the report by Helfand et al.,1 the following criteria are proposed for the clinical application of the new markers: its application should (1) be general, valid, reproducible and simple; (2) have acceptable reference values; (3) have a significance independent of the conventional risk factors; (4) allow reclassification of a substantial portion of the study subjects as low- or high-risk; (5) after reclassification (as in (4)), allow the subjects to be managed differently than they would have otherwise been. For example, the Framingham risk score (FRS), calculated based on the conventional cardiovascular risk factors, is offered as the most thoroughly validated prospective risk assessment tool for coronary heart disease (CHD), and any new marker should provide additive predictive value and serve to improve upon the result of the previous assessment.

The Women’s Health study demonstrated a moderate improvement in the prediction of CHD risk by the addition of an 18-biomarker panel to the conventional risk factors in postmenopausal women.2 On the contrary, Helfand et al conducted a meta-analysis in which they could not confirm the usefulness of 9 additive risk factors (ie, 5 biochemical markers, periodontal disease, ankle–brachial index, coronary calcium score as assessed by electron-beam computed tomography, and the carotid intima–media thickness) for further CHD risk stratification in the subjects assessed as having intermediate risk based on conventional risk factors.3

Recently, vascular function tests, such as flow-mediated vasodilatation of the brachial artery (FMD), pulse wave velocity (PWV), and components of the arterial pressure waveform have been focused on as new tools for the management and risk evaluation of cardiovascular disease.4 FMD is a marker not only of early-stage atherosclerotic vascular damage, but is also related to abnormal endothelial nitric oxide (NO) bioavailability. The impaired NO bioavailability contributes to the initiation/progression of atherosclerosis.5 PWV is a marker related to arteriosclerosis (ie, increased structural arterial stiffness). Furthermore, increased arterial stiffness, reflected by an increased PWV, exerts unfavorable effects on the cardiovascular system (eg, by causing impaired coronary blood supply, increased cardiac afterload, microvascular damage, etc).6 Thus, they are markers not only of vascular damage, but also of cardiovascular risk.

Recent prospective studies have demonstrated that the addition of FMD and of PWV to the FRS assessment may improve the risk assessment for cardiovascular events, as compared with FRS alone in the general population (ie, low-to intermediate-risk subjects).5,6 On the other hand, in subjects with CHD (ie, high-risk subjects), prospective studies conducted on relatively small numbers of study subjects have demonstrated that FMD and PWV can predict future cardiovascular events;6,7 however, no prospective studies have been conducted on large numbers of study subjects.

In this issue of the Journal, Park et al examined the interrelationship between FRS and vascular function tests (FMD and PWV), and demonstrated that neither FMD nor PWV improved the predictive power of FRS assessment for CHD diagnosed by coronary angiography in subjects who were scheduled to undergo coronary angiography.8 Thus, neither FMD nor PWV may provide significant additive value to the FRS in the screening for latent CHD. Then, the next logical step would be to clarify whether FMD or PWV might improve the prognostic accuracy in subjects with CHD as compared to assessment by FRS alone or FRS plus other biochemical markers such as troponin-T, natriuretic peptides, copeptin, mid-regional pro-adrenomedullin, and/or proteomic markers.9

### References


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