<S3-2>

Evaluating Cardiovascular Risk: From Global Risk Scoring to Biomarkers and Subclinical Atherosclerosis

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Cardiovascular risk assessment is the foundation of preventive cardiology and involves the consideration of initial evaluation by global risk scoring followed by consideration of biomarkers and subclinical disease modalities to further refine risk assessment, especially when the treatment decision is not clear from global risk assessment.

More than 25 years ago, the Framingham Heart Study developed the first risk scores for prediction of coronary heart disease events, that have since been followed by risk scores developed in other parts of the world, including the European SCORE algorithms for cardiovascular mortality as well as most recently the ACC/AHA Pooled Cohort Risk algorithms for atherosclerotic cardiovascular disease (ASCVD). Risk scores should always be evaluated on the basis of applicability to the general population it is being utilized for, scope of the endpoint being predicted (e.g., hard coronary heart disease versus total cardiovascular disease), and the time frame of the prediction (e.g., 10-year versus lifetime). In addition, most risk scores are developed for primary prevention populations without cardiovascular disease, but some are developed for specific diseases such as diabetes or in those with pre-existing cardiovascular disease.

While most prevention guidelines recommend beginning with a global risk score for initial cardiovascular risk assessment, they recognize the role of certain additional factors including novel biomarkers and measures of subclinical atherosclerosis to further refine risk assessment. An important criterion for guidelines to consider these measures is whether they provide incremental predictive value and adequate net reclassification improvement (NRI) over global risk scoring. The ACC/AHA Guidelines for Cardiovascular Risk Assessment recommend the consideration of premature family history of ASCVD, hs-C-reactive protein, ankle brachial index measures, and coronary calcium scoring to further inform the treatment decision if uncertain based on global risk assessment, while noting coronary calcium screening is likely to be the most useful of these tests. Other guidelines also consider certain psychosocial measures such as social support as well as assessment of carotid plaques from carotid ultrasound. The appropriateness of any of these assessments, however, should be dictated on the basis of whether the results obtained would affect how the patient is being managed.

Finally, given the limitations of current risk assessment methods that focus on exposure to risk factors of other measures at a given point in time or the prediction of longer term risk (e.g., 10 years), of current recent interest is the role that Mendelian randomization studies may play in most accurately predicting risk based on them estimating "lifetime exposure". And to address the need to identify who is at greatest risk of acute near-term events, ongoing investigations are evaluating how novel mixtures of biomarkers from complementary pathologies might be better able to identify who is at the greatest short-term risk of an acute cardiovascular event.