

Preface



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Guest Editor

Physicians are constantly asked by patients about their risk for atherosclerotic cardiovascular disease and its thrombotic manifestations—myocardial infarction, stroke, and angina. The past 50 years have produced an enormous array of laboratory and imaging methodologies, plus algorithms on how to use these methodologies, to predict cardiovascular risk over a 10-year period. The Framingham Study, which started shortly after World War II and comprised an original cohort of individuals plus another cohort of offspring, has been an important laboratory for testing the predictive power of many risk factors. The Framingham scoring algorithm, which calculates 10-year coronary heart disease risk using age, gender, hypertension, smoking status, and LDL and HDL cholesterol levels has become the standard against which new methodologies are tested to see if they improve cardiovascular risk prediction.

Numerous laboratory measures of ischemic cardiovascular disease are emerging as the understanding of vascular biology progresses.

- Inflammation is now recognized as a major component of clinical atherosclerosis. Many markers of systemic inflammation have been tested, with ultrasensitive C reactive protein (usCRP) being advocated as the most sensitive, stable, and least costly.
- Oxidative processes, such as oxidation of LDL particles or effects on endothelium-dependent vasodilation, may be important in atherogenesis. Measures of oxidized LDL and isoprostanes have become potential laboratory measures of this oxidative process and thus could potentially be used as clinical cardiovascular risk factors.

- Lipoprotein-associated phospholipase A2 (Lp-PLA2) hydrolyzes oxidized phospholipids in LDL, producing products that can stimulate the inflammatory cascade, and is thus being studied and promoted as a risk factor for atherosclerotic disease.
- Homocysteine as a risk factor for atherosclerotic cardiovascular disease was suggested by increased vascular events in those with homozygous homocysteinuria, and was subsequently found to predict increased risk for coronary heart disease in those with elevated values within the normal population distribution. But levels considered high risk and goals for treatment have varied. Several recent clinical trials of lowering homocysteine have not proven effective in lowering ischemic cardiovascular events, thus illustrating the difficulties in establishing an emerging risk factor in clinical practice.
- Thrombosis and fibrinolysis are important pathophysiologic components of clinical atherothrombotic events—myocardial infarction, angina, and stroke. Their importance in clinical events has led to their measurement as potential risk factors for clinical manifestations of atherosclerosis.
- Insulin resistance has become one of the latest measures of cardiovascular risk. Risk for coronary heart disease is increased in those having decreased insulin sensitivity, a state variably called prediabetes, insulin resistance, or metabolic syndrome, and increasing global obesity has made this risk increasingly important from the public health point of view. What, if any, measures of insulin sensitivity can be used as reliable predictors of cardiovascular risk?
- Urinary microalbuminuria has proven to be a strong risk predictor for ischemic cardiovascular clinical events, but may be a marker of vascular target-organ damage as opposed to a risk factor causing clinical disease.

All of these emerging risk markers or factors predictive of clinical ischemic cardiovascular events are discussed in this first volume of *Atherosclerotic Cardiovascular Disease: Emerging Laboratory Risk Factors*.

Lipids risk factors have traditionally been the most important clinical laboratory measurements in predicting risk, starting originally with total serum cholesterol. Ultracentrifugation separated lipoproteins by density, and the development of the Friedewald equation, which calculated an accurate value for LDL cholesterol from the rapid, enzymatic determination of triglycerides, HDL, and VLDL cholesterols, allowed the now-routine lipid profile to become the standard for assessing individual lipoprotein risk for ischemic cardiovascular disease in the United States. Results from this technique have had tremendous success in predicting individual and population risk, and still remain the mainstay of lipid measures in clinical trials and practice.

As techniques to further characterize and subdivide lipoproteins have been developed, such as vertical ultracentrifugation, gel electrophoresis,

nuclear magnetic resonance spectroscopy, and antibody techniques to measure apolipoproteins, their ability to potentially improve risk prediction for atherosclerotic events has been growing. The second volume in this series discusses the following lipoprotein measures:

- Standard lipid profile
- Apolipoproteins
- Postprandial lipoproteins
- Polyacrylamide gradient gel electrophoresis
- Vertical ultracentrifugation
- Nuclear magnetic resonance spectroscopy

The enormous clinical expenditure on clinical lipid determinations has generated competitive marketing strategies for use of all of these in physicians' offices. Physicians ordering such tests often have difficulty with interpretation. The incremental predictive value of each new measure must be adequately demonstrated. Therapeutic goals for those at low and at high risk must be determined. The second issue in this series explores these methodologies from the methodologic point of view and from the epidemiologic evidence for their predictive advantage to the standard lipid profile in clinical practice.

The authors in this series are experts in their fields, some more expert in methodologies, some in their clinical application, some expert in both. All have tackled methodologic and clinical issues. I am deeply grateful for the enthusiasm, promptness, thoroughness, and exceptional writing skills displayed in preparing this series. It has been a pleasure and highly informative for me, as I hope the series will be for the reader.

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