Cholesterol, Lipoproteins, High-sensitivity C-reactive Protein, and Other Risk Factors for Atherosclerosis

Joseph Rudolf, MD, Kent B. Lewandrowski, MD*

KEYWORDS

• Laboratory medicine • Cardiac markers • Biomarkers • Atherosclerosis
• Lipoprotein • Cholesterol biomarker • High-sensitivity CRP • Apolipoprotein E

KEY POINTS

- Intensive study has led to a deeper understanding of the pathogenesis of coronary disease and risk stratification in recent decades.
- Traditional risk factor assessment has focused on parameters derived from the Framingham Heart Study (age, hypertension, cholesterol, family history, and cigarette smoking).
- New emerging risk factors, both biological and genetic, are reshaping the understanding of heart disease and the approach to risk stratification.

INTRODUCTION

Coronary heart disease (CHD) is a common and costly epidemic in the Western world. According to statistics compiled by the American Heart Association there is a 7% prevalence of coronary artery disease (CAD) in adults 20 years of age and older.[1] In 2008, 1 in every 6 deaths in the United States was attributable to CHD, resulting in approximately 400,000 deaths nationwide.[1] The direct cost of care for patients with cardiovascular disease and stroke is estimated to exceed US$170 billion per year.[1]

Significant progress has been made in the understanding of the pathogenesis of CHD and its treatment since the identification of the first cardiovascular risk factors in the Framingham Heart Study. Although there are proven laboratory tests for the assessment of cardiovascular risk and effective means of modifying cardiovascular risk factors, understanding of the pathophysiology of CHD is still incomplete. The American Heart Association laid out ambitious goals for the year 2020, "to improve

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Division of Laboratory Medicine, Department of Pathology, Massachusetts General Hospital, Harvard Medical School, 55 Fruit Street, Boston, MA 02114-2696, USA
* Corresponding author.
E-mail address: klewandrowski@partners.org

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the cardiovascular health of all Americans by 20%, while reducing deaths from cardiovascular diseases and stroke by 20%."[2] Reaching this goal will require more aggressive efforts to expand conventional risk assessment and treatment to the general population, along with the implementation of a new generation of laboratory tests focusing on novel biomarkers of cardiovascular risk and genetic screening.

PATHOGENESIS OF ATHEROSCLEROSIS

The pathogenic manifestation of atherosclerotic disease involves the development of raised intimal lesions in affected arteries filled with a lipid core, known as atheromas. Atheromas cause morbidity and mortality via multiple mechanisms, including obstruction of luminal blood flow, rupture of atheromatous plaques leading to thrombosis, and the facilitation of aneurysmal formation predisposing patients to vessel rupture.[3]

To date, many risk factors for cardiovascular disease have been identified, including both constitutional and modifiable risk factors (**Box 1**). Of the constitutional risk factors, family history is the single most important risk factor, implicating a strong role for a genetic contribution to cardiovascular risk. Other important nonmodifiable risk factors have been implicated in the form of both age and gender, whereby cardiovascular risk increases with age and premenopausal women have a markedly decreased risk compared with men. Modifiable risk factors include serum lipid levels, hypertension, cigarette smoking, and diabetes mellitus.[3]

At the cellular level, the development of atherosclerosis is described by the response to injury hypothesis. This hypothesis states that atherosclerosis results from the "chronic inflammatory and healing response of the arterial wall to endothelial damage and lesion progression occurs through the interaction of modified lipoproteins, monocyte-derived macrophages, and T lymphocytes with normal cellular constituents of the arterial wall."[4] Inflammation plays a role at all stages of atherosclerosis. Endothelial damage resulting from the deposition of lipoproteins in vessel walls triggers the release of inflammatory mediators. These inflammatory mediators attract monocytes, which engulf deposited lipoproteins leading to the transformation of

Box 1
CHD risk factors

CHD risk factors
Age
Men greater than or equal to 45 years of age or women greater than or equal to 55 years of age
Family history of premature CHD
Current cigarette smoking
Hypertension
Low high-density lipoprotein
High low-density lipoprotein
CHD risk equivalents
Other atherosclerotic disease (peripheral arterial disease, abdominal aortic aneurysm, carotid artery disease)
Diabetes
Multiple CHD risk factors and 10-year Framingham Risk Score greater than 20%