

# Identifying the Vulnerable Patient with Rupture-Prone Plaque

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**Atherosclerotic cardiovascular disease is the leading cause of morbidity and mortality in the United States, and the obesity epidemic combined with aging of the population seems destined to increase the burden of this disease. Traditional cardiovascular risk assessment accounts for <50% of the variability in risk in the United States. Therefore, better and more effective identification of persons at high cardiovascular risk is needed. Our understanding of atherosclerosis has shifted from a focal disease whose hallmark is symptoms caused by a severe stenosis to a systemic disease characterized by endothelial dysfunction (ED) and plaque inflammation, with the potential for rupture and thrombosis mainly in those with subcritical stenosis. Under the new paradigm, clinicians require updated strategies to better assess the quality of arterial plaque. Effective tools for primary and secondary prevention of heart attack and stroke include intensive lifestyle modification, blood pressure reduction, and lipid-modifying therapies. These interventions are now understood to decrease plaque inflammation and thereby promote plaque stability. Lipoprotein-associated phospholipase A<sub>2</sub> (Lp-PLA<sub>2</sub>) appears to be a specific marker of plaque inflammation that may play a direct role in the formation of rupture-prone plaque. In contrast, traditional risk factors, lipid measurement, and most vascular imaging modalities do not directly assess the acute ischemic potential in the arterial wall. Measuring Lp-PLA<sub>2</sub> levels in human serum or plasma is noninvasive and relatively inexpensive. Lp-PLA<sub>2</sub> may provide additional clinically relevant information that shows which patients have a high level of atherosclerotic disease activity as manifested by vascular inflammation, ED, and increased risk for progression toward rupture-prone plaque. © 2008 Elsevier Inc. All rights reserved. (Am J Cardiol 2008;101[suppl]:3F-10F)**

Cardiovascular disease (CVD), consisting of cardiac death and stroke, continues to be the leading cause of death in the United States, surpassing all cancers, stroke, accidents, and diabetes mellitus (Figure 1),<sup>1</sup> despite significant advances in treating CVD over the past 20 years. Cardiovascular health complications, subsequent disease manifestations, and decreases in functionality and quality of life as a result of cardiovascular events continue to place immense economic and emotional burdens on much of the population. An estimated 80 million US adults (1 in 3) have >1 types of CVD.<sup>1</sup> Of these, 15.8 million individuals in the United States were diagnosed with coronary artery disease (CAD), resulting in >400,000 deaths annually.<sup>1</sup> As the US population ages, the prevalence of CVD will place an intolerable burden on the quality of life and the nation's economy without significantly more intensive application of already-proven primary and secondary prevention therapies.

It is widely understood by healthcare providers and the general public that the incidence of heart disease is ex-

remely high for men. Indeed, the lifetime risk for myocardial infarction (MI) in men is 42%. Far less recognized, however, is the toll of CVD on women. Heart disease is the number 1 killer of women, far surpassing breast cancer, lung cancer, stroke, and other cancers (Figure 2).<sup>2</sup> Data show that 1 in 4 women will die of heart disease, regardless of race or ethnicity. Heart disease strikes women at younger ages than men, and the risk increases in middle age. Additionally, approximately 66% of women who have heart attacks never fully recover.<sup>2</sup>

Overall, the American Heart Association estimates that 50 million individuals in the United States are diagnosed with cardiometabolic syndrome, and an additional 8 million are undiagnosed.<sup>1</sup> Khot et al<sup>3</sup> report that there are 4 established conventional risk factors in CAD: hypertension, smoking, hypercholesterolemia, and diabetes. Yet, approximately 62.4% of individuals already diagnosed with CAD present with only 0 to 1 of these major modifiable risk factors. Fully 19% present with absolutely no risk factors (Figure 3) and another 43% have only 1 risk factor.<sup>3</sup> Therefore, Framingham risk scoring may incorrectly identify many persons who develop CAD as being at low risk for developing CAD. The Adult Treatment Panel III national cholesterol guidelines acknowledge this by explaining that the major cardiovascular risk factors "account for only about half of the variability in coronary heart disease risk in the US population."<sup>4</sup>

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*Statement of author disclosure:* Please see the Author Disclosures section at the end of this article.

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