

Review of the Evidence for the Clinical Utility of Lipoprotein-Associated Phospholipase A₂ as a Cardiovascular Risk Marker

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A substantial body of peer-reviewed studies has been published validating the role of inflammation in atherogenesis and supporting lipoprotein-associated phospholipase A₂ (Lp-PLA₂) as a cardiovascular risk marker independent of and additive to traditional risk factors. As with elevated high-sensitivity C-reactive protein, an elevated Lp-PLA₂ level approximately doubles the risk for primary and secondary cardiovascular events. Interestingly, when both inflammatory markers are increased together, they provide an even greater predictive capability to help identify very-high-risk individuals who would benefit most from aggressive lipid-lowering therapy. High levels of Lp-PLA₂ are present in inflamed, rupture-prone plaques, and it appears that Lp-PLA₂ is released from these plaques into the circulation. Over 25 prospective epidemiologic studies have demonstrated the association of elevated Lp-PLA₂ levels with future coronary events and stroke—11 of 12 prospective studies have shown a statistically significant association between elevated Lp-PLA₂ and primary coronary or cardiovascular events, 12 of 13 have shown a statistically significant association with recurrent coronary or cardiovascular events, and 6 studies have shown a positive association with stroke. Lp-PLA₂ should be viewed today as an important cardiovascular risk marker whose utility is as an adjunct to the major risk factors to adjust absolute risk status and thereby modify low-density lipoprotein cholesterol goals. The low biologic fluctuation and high vascular specificity of Lp-PLA₂ makes it possible to use a single measurement in clinical decision making, and it also permits clinicians to follow the Lp-PLA₂ marker serially. Ultimately, Lp-PLA₂ may also be classified as a risk factor, but this should not detract from its utility today as a risk marker. © 2008 Elsevier Inc. All rights reserved. (Am J Cardiol 2008;101[suppl]:41F–50F)

The goal of this article is to review the rapidly converging evidence for lipoprotein-associated phospholipase A₂ (Lp-PLA₂), a vascular inflammatory enzyme, as a clinically useful marker to improve identification of individuals whose level of risk is greater than clinically apparent for cardiovascular disease (CVD) events who may benefit from more intensive risk-reducing interventions. CVD risk assessment forms the basis for directing risk-reducing therapies in clinical practice, given the efficacy and safety of current pharmacologic agents targeting lipids, blood pressure, and blood glucose on a background of therapeutic lifestyle modification.

Lipid-lowering therapies, specifically statins, are effective in the primary and secondary prevention of myocardial

infarction (MI) and stroke. The availability of generic statins provides a cost-effective opportunity for CVD risk reduction and presents the challenge of identifying appropriate individuals in the general population who would most benefit from these agents. Accounting for established risk factors may explain only half of all coronary artery disease (CAD) events that occur.¹ This shortcoming has fueled intense interest in identifying new biomarkers that may add to the predictive power of traditional risk factors.

The guiding principle of the Adult Treatment Panel III (ATP III) guidelines is that the estimation of absolute 10-year CAD risk is used to stratify individuals to optimal low-density lipoprotein (LDL) cholesterol goals because intensity of treatment should be matched to absolute risk.² ATP III also recognized that coronary heart disease (CHD) risk is not fully revealed by traditional risk factor assessment, noting that “when major risk factors are present, they account for only half of the *variability* in CHD risk in the US population”¹ and proposed that emerging risk factors “be taken into consideration according to clinical judgment as optional modifiers of therapy but they should be used only as an adjunct to adjust the estimate of absolute risk status obtained with the major risk factors.”

Within the past decade, evidence has accumulated that inflammation plays a critical role in the initiation and pro-

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