

Lipoprotein-Associated Phospholipase A₂ and Risk of Stroke

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Stroke is the second-leading cause of death worldwide and is a disabling disease of both older and younger adults. Stroke is also among the most highly preventable disorders because there are well-defined risk factors and preventatives. The establishment of new risk markers or factors for stroke risk assessment provides a new avenue for stroke prevention. Lipoprotein-associated phospholipase A₂ (Lp-PLA₂) is an enzyme that hydrolyzes oxidized phospholipids, releasing lysophosphatidylcholine, which has proinflammatory properties thought to be involved in the development of atherosclerosis and plaque rupture. In 2005, the Lp-PLA₂ blood test was approved by the US Food and Drug Administration (FDA) for assessing the risk of ischemic stroke and coronary artery disease. In epidemiologic studies, low-density lipoprotein cholesterol and other lipid factors have not been shown to be consistent predictors of stroke risk. Lp-PLA₂ measures, on the other hand, have shown a consistent association with stroke risk, conferring about a 2-fold increase in stroke occurrence. This relation has been studied in both first and recurrent stroke and is reviewed in this article. Importantly, a recent study has now shown that Lp-PLA₂ may increase the area under the curve beyond that of traditional cardiovascular risk factors and C-reactive protein. Therefore, Lp-PLA₂ determination may provide a pivotal opportunity to appropriately classify previously misclassified persons who are actually at high risk of stroke and in need of aggressive stroke intervention. © 2008 Elsevier Inc. All rights reserved. (Am J Cardiol 2008;101[suppl]:34F–40F)

The global burden of stroke is immense. Stroke is the second-leading cause of death throughout the world. Of the 5.7 million annual stroke deaths worldwide, 87% occur in low- and middle-income countries. There are about 16 million first-ever strokes annually. Globally, there are >50 million stroke and transient ischemic attack (TIA) survivors, and >1 in 5 survivors will have another stroke within 5 years.¹

In the United States, stroke is the third-leading cause of death, after heart disease and cancer. Stroke accounts for 6% of all deaths in the United States, with as many as 150,000 deaths per year.^{2,3} There are about 780,000 new strokes annually, of which 600,000 are first attacks and 180,000 are recurrent strokes. There are approximately 5–6 million stroke survivors in the United States. Stroke is the leading cause of adult disability, with 15%–30% of stroke victims experiencing permanent disability and 20% requiring institutional care at 3 months after onset.³ Not surprisingly, stroke is very costly, with recent estimates suggesting that the total direct and indirect costs are \$62.7 billion.³

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A number of populations are at risk for stroke. It should no longer be considered a disease confined to the elderly because about a third of stroke victims are <65 years of age.⁴ Blacks have twice the risk of stroke compared with whites.³ Hispanics are also at higher risk. Women are at higher risk of stroke mortality because, on average, they live longer than men. In adults, we have seen an exponential increase in stroke at age 55, with about a doubling of stroke risk for every 5- to 10-year period thereafter.³ However, anyone is at risk for stroke if they have vascular risk factors, a history of other vascular diseases, such as myocardial infarction (MI) or peripheral vascular disease, or if there is a family history of stroke. Interestingly, stroke kills more than twice as many US women every year than breast cancer, and more women than men die of stroke.⁵ Black women are also at an increased risk of stroke. Finally, it is estimated that 30% of strokes in women occur in those <65 years of age.⁴

Modifiable stroke risk factors include medical and lifestyle factors.⁶ Lifestyle factors, such as smoking, heavy alcohol consumption, poor diet, and physical inactivity or lack of exercise, are also believed to elevate the risk of stroke. The important modifiable medical risk factors are hypertension, MI, atrial fibrillation, diabetes mellitus, blood lipids, and asymptomatic carotid stenosis. A history of TIA also elevates risk. The risk of stroke is 24%–29% 5 years after a TIA, which is comparable to the 25%–40% risk of having a second stroke after an initial stroke has occurred.^{7–10}