

# Abstract

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## Enhanced expression of Lp-PLA2 and lysophosphatidylcholine in symptomatic carotid atherosclerotic plaques.

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**BACKGROUND AND PURPOSE:** Circulating lipoprotein-associated phospholipase A(2) (Lp-PLA(2)) has emerged as a novel biomarker for cardiovascular diseases. However, the correlation between the plaque expression of Lp-PLA(2) and plaque oxidative stress, inflammation, and stability as well as the clinical presentation remains poorly defined, especially for cerebrovascular disease. Therefore, this study was performed to test the hypothesis that Lp-PLA(2) expression is higher in symptomatic than in asymptomatic carotid plaques of patients undergoing carotid endarterectomy.

**METHODS:** The expression of Lp-PLA(2) in 167 carotid artery plaques was determined by immunoblotting and immunostaining. Plaque oxidative stress, inflammation, and stability were quantified by NAD(P)H oxidase p67phox and MMP-2 immunoblotting, oxidized LDL (oxLDL) immunoreactivity, macrophage and Sirius red collagen staining. Lysophosphatidylcholine 16:0 (lysoPC) concentration was measured in 55 plaques using liquid chromatography tandem mass spectrometry.

**RESULTS:** Lp-PLA(2) expression was significantly higher in plaques of symptomatic patients than asymptomatic patients (1.66+/-0.19 versus 1.14+/-0.10, P<0.05) and localized mainly to shoulder and necrotic lipid core areas in colocalization with oxLDL and macrophage content. Similarly, Lp-PLA(2) expression was related to collagen content, which was lower in plaques from symptomatic patients than in plaques from asymptomatic patients (9.1+/-2.2 versus 18.5+/-1.7% of staining/field, P<0.001). LysoPC plaque concentration was significantly higher in plaques of symptomatic than asymptomatic patients (437.0+/-57.91 versus 228.84+/-37.00 mmol/L, P<0.05).

**CONCLUSIONS:** Symptomatic carotid artery plaques are characterized by increased levels of Lp-PLA(2) and its product lysoPC in correlation with markers of tissue oxidative stress, inflammation, and instability. These findings strongly support a role for Lp-PLA2 in the pathophysiology and clinical presentation of cerebrovascular disease.

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