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Endothelial LOX-1 plays a critical role in inflammatory thrombosis

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Aim: LOX-1 is implicated in the progression of arteriosclerosis and inflammatory diseases. In this study, we explored whether LOX-1 is involved in inflammation-related thrombosis.

Methods: To analyze thrombosis, tail-bleeding time assay was performed using male C57BL/6J (WT) and LOX-1 deficient mice (LOX-1KO). Platelet counts and thrombin-antithrombin complex (TAT) were also measured. To analyze which tissue is responsible in LOX-1-supported thrombosis, tamoxifen-inducible endothelial cell-specific LOX-1KO mice (EC-LOX-1KO) were generated and employed. LOX-1 expression in tissues was analyzed by qRT-PCR. Soluble LOX-1 (sLOX-1) in mouse plasma was measured by ELISA.

Results: In normal condition, tail-bleeding time did not show significant difference between WT and LOX-1KO. Under inflammatory condition, in WT, the bleeding time was shortened in LPS injection (5 mg/kg, i.p.) group compared to the control saline group. Consequently, platelet count was decreased, and TAT level was increased in this condition. LOX-1 expression level increased in any tissues examined and plasma sLOX-1 level increased after LPS injection. On the other hand, in LOX-1KO, above LPS-dependent changes were significantly suppressed. Furthermore, EC-LOX-1KO showed similar results to LOX-1KO, suggesting that endothelial LOX-1 plays a crucial role in thrombosis under inflammatory conditions.

Conclusions: Endothelial LOX-1 promotes inflammation-related thrombosis, which suggests prothrombotic role of endothelial LOX-1 in atheromatous inflammatory lesion.