**CARBAMYLATION VERSUS OXIDATION OF LDL: COMPETITION, MECHANISMS AND ROLE IN CARDIOVASCULAR DISEASE**

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Background and Objective: Both oxidized LDL (oxLDL) and carbamylated LDL (cLDL) are considered important for initiating atherosclerosis in patients with end-stage kidney disease (ESKD) through vascular endothelial cell dysfunction or injury. The two LDL modifications are not mutually exclusive and likely coexist on the same LDL particle. However their effects on each other, their relationship related to pro-atherosclerotic effects on cells, and associations with cardiovascular disease (CVD) in ESKD patients have not been investigated.

Methods: We analyzed the competition between LDL carbamylation and oxidation, tested biological effects of LDL isoform that carries both modifications, carbamylated-oxidized LDL (coxLDL), toward the endothelial cells, assessed its ability to cause foam cell development, and determined the roles of scavenger receptors in this process. Blood plasma cLDL and oxLDL were measured by ELISAs in patients with ESKD.

Results: Our data suggest that there is a competition between carbamylation and oxidation of LDL, and that oxidation is a much stronger inhibitor of carbamylation than vice versa. coxLDL is highly cytotoxic to endothelial cells, strongly induces their proliferation and formation of foam cells from macrophages using predominantly CD36 scavenger receptor. oxLDL was associated with CVD among women, with thick cIMT in the full sample, and with high CAC in women and non-smokers; cLDL was associated with CVD among men younger than 62, especially smokers.

Conclusions: These data illustrate coexistence of the two modifications, and that cLDL and oxLDL independently, and potentially, by forming coxLDL may constitute mechanisms underlying elevated CVD risk among patients with ESKD.