Weiming Yu, Tiziana Parasassi, Liana R Kuriashkina, and Enrico Gratton.

Oxidation-mediated proteolysis - a mechanism for initial vascular damage revealed by a multiphoton microscope.

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Biophys J. 2000; 78(1 Pt 2), 2618- Pos.

Abstract

It is commonly believed that oxidation is involved in the initial damage process of the inner wall of the artery that leads to atherosclerosis. However, it is still unclear what biochemical mechanisms are involved in the initiation process. We have performed a series of microscopy and spectroscopy studies using a two-photon fluorescence microscope examining the autofluorescence of viable rat aortas maintained under near physiological conditions. We found there was structural damage in the elastin/collagen fiber network within the aorta extracellular matrix after oxidative stress for as short as 30 min using oxidized lower-density-lipoprotein (oxLDL). In our study, we did not perform any sample manipulation, such as fixing, coloring or labeling, as had been typically done in previous studies that physically and chemically altered the sample. This approach allowed us performing sensitive studies and monitoring subtle changes resulting from oxidative stress. Based on our results and reports of previous related studies, we proposed and demonstrated a molecular mechanism in which a protease was involved and the structural damage of the vascular wall was the result of the degradation of elastin/collagen. For the first time, we have linked the oxidative damage from the naturally circulating lipoproteins (oxLDL) to the proteolytic degradation of vascular matrix fibers. Our findings possess wide interests for biochemists, biophysicists, physicians and pharmacologists since this topic connects the vascular pathology of aging to atherosclerosis. This work was supported by NIH grant PHS 5 P41-RR03155.