

# Serum glycomarkers of endoplasmic reticulum stress and lysosomal-endosomal functional disturbances in cardiovascular diseases

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Ischemia and hypertension cause stress of intracellular organelles leading to a disruption of their functions. The hallmark of the endoplasmic reticulum stress is alteration of protein homeostasis. This organelle triggers unfolded protein response to restore cellular homeostasis, in particular through activation of endoplasmic reticulum-associated degradation (ERAD) of misglycosylated and /or misfolded proteins. ERAD is one of the main intracellular sources of free oligosaccharides (FOS), unbound structural analogues of glycans of glycoconjugates. The lysosomal-endosomal degradation of glycoconjugates is a different source of their appearance. FOS structures and their alterations may reflect functional status of these organelles. Free oligosaccharides in plasma obtained from patients with cardiovascular diseases, before and after standard treatment, were investigated to evaluate this idea. After plasma deproteinization and FOS purification the oligosaccharides were labeled with anthranilic acid, separated into the neutral and charged fractions with ion-exchange chromatography. FOS were analysed using high-performance liquid chromatography (HPLC). HPLC profiles of FOS revealed a changing pattern of heterogeneity, depending on the severity of the disease. Three main enlarged glycan species in the neutral fraction and one peak in the charged fraction distinguished the FOS of the patients from those of the healthy volunteers. After treatment, the spectrum changes were observed in neutral fractions. The depth of these changes had individual features but a full profile recovery was not observed. There was no impact of the treatment on the charged fraction. That might indicate a stress prolongation of endosomal-lysosomal system in spite of the therapy. The study of free oligosaccharides of blood plasma is a new field of Glycobiology allowing a non-invasive evaluation of an organism state at the level of the cell organelle functional status in norm and different diseases.