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ABSTRACT N. CO25

LABORATORIO E FATTORI PREDITTIVI

THROMBOINFLAMMATION AND ROS ACCUMULATION IN INDIVIDUALS WITH HIGH LIPOPROTEIN(A) LEVELS.

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Background:
Lp(a) is considered one of the strongest genetically determined and independent risk factors for cardiovascular disease (CVD) through mechanisms involving increased atherogenesis, inflammation, and thrombosis. Elevated Lp(a) levels are associated with increased cardiovascular risk even in individuals with low LDL cholesterol. Despite growing evidence, therapeutic strategies targeting Lp(a) are limited, with no effective treatments currently available, particularly for primary prevention. Platelets are key mediators of thrombosis and vascular inflammation, and emerging evidence suggests that elevated Lp(a) levels may influence platelet reactivity. However, the physiological effect of Lp(a) on platelets activity remains unclear. To gain deeper insight into this interaction, proteomic analysis may represent a powerful approach: by profiling the platelet proteome in individuals with high Lp(a), it could be possible to identify signaling alterations contributing to the increased cardiovascular risk. Proteomic analysis could also help to elucidate mechanisms linking Lp(a) to prothrombotic states and potentially reveal novel biomarkers or therapeutic targets for individuals at high cardiovascular risk.
Objectives:
To investigate the platelet proteomic profile of patients with elevated Lp(a) levels, with the aim to evaluate how Lp(a) modulates molecular pathways involved in platelet production and turnover, inflammation, oxidative stress, and in regulation of thrombotic processes.
Methods:
In a cross-sectional study, we enrolled donors referring to the Blood Transfusion Service of Pescara Hospital with levels of Lp(a) above (n=20) or below (n=20) 50 mg/dL patients with higher (n=20) and lower (n=20) levels of Lp(a). Blood and urine sampling was performed. A proteomic analysis was performed on pooled samples of platelet pellets from 5 patients with the highest and lowest Lp(a) levels, Pool A and Pool B respectively, selected from a population of blood donors and stratified according to Lp(a) levels (cut-off: 50 mg/dL). For validation, circulating and platelet MRP-8/14 protein levels were analysed by ELISA assay and Western blotting analysis, and urinary 8-iso-$PGF_{2\alpha}$ excretion levels were measured.
Results:
Proteomic and bioinformatic analysis showed an activation of pathways related to "Inflammation of organ" and "accumulation of ROS" in patients with elevated Lp(a) levels. As a validation, circulating and platelet MRP-8/14, involved in both the pathways, was higher in patients with elevated Lp(a) levels (p=0.064, p= 0.041) than in patients with low Lp(a), thus confirming proteomics. The urinary excretion rate of the F2-isoprostane 8-iso-$PGF_{2\alpha}$ (p=0.039), in vivo marker of lipid peroxidation, was higher in subjects with elevated Lp(a) levels.
Conclusions:
Our findings suggest that individuals with elevated Lp(a) levels exhibit increased thromboinflammatory activity and pro-oxidative state, as reflected by proteomic analysis of inflammatory and ROS pathways and higher levels of 8-iso $PGF_{2\alpha}$, but also higher circulating and platelet-derived levels of MRP-8/14. These results support the hypothesis that Lp(a) contributes to a pro-oxidative and pro-inflammatory milieu, potentially through modulation of platelet activation and function. These findings highlight the need for further investigation into Lp(a)-mediated platelet activation and suggest MRP-8/14 as a potential biomarker and therapeutic target in patients with elevated Lp(a).

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