Lipoprotein(a) levels across histological severity in metabolic dysfunction–associated steatotic liver disease

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Background: Metabolic dysfunction–associated steatotic liver disease (MASLD) encompasses a spectrum ranging from simple steatosis to metabolic dysfunction–associated steatohepatitis (MASH) and cirrhosis. Lipoprotein(a) [Lp(a)] is a well-established atherogenic risk factor, but its relationship with MASLD and its histological severity has been poorly investigated. The aim of this study was to describe plasma Lp(a) levels across different histological stages and features of MASLD.

Methods: Eighty-eight patients enrolled in the PLINIO study (ClinicalTrials.gov Identifier: NCT04036357) who underwent liver biopsy were included. Plasma Lp(a) levels were measured using a specific ELISA kit. Patients were stratified according to histological diagnosis into simple steatosis (MASLD-SS), MASH, and cirrhosis. In a subgroup of 29 patients, immunohistochemical analysis was performed to assess hepatic Lp(a) expression on liver biopsy samples.

Results: Plasma Lp(a) levels increased progressively with histological severity (MASLD-SS: 22.1 [20.2–26.6] mg/dL; MASH: 28.7 [24.2–32.8] mg/dL; cirrhosis: 31.1 [29.4–33.1] mg/dL; p=0.001). Plasma Lp(a) correlated positively with fibrosis stage (rS=0.401, p<0.001), inflammation grade (rS=0.214, p=0.045), hepatocellular ballooning (rS=0.383, p<0.001), and NAFLD Activity Score (rS=0.410, p<0.001). In multivariable regression analysis including demographic and clinical variables, plasma Lp(a) was independently associated with LDL cholesterol (β=0.003, p=0.012) after adjustment for age, sex, ALT, and diabetes. At immunohistochemical analysis, no overall correlation was found between hepatic and plasma Lp(a) or histological features. However, after excluding cirrhotic patients, hepatic and plasma Lp(a) levels correlated significantly (rS=0.436, p=0.033). Among patients with MASH, hepatic Lp(a) expression was higher in those with more severe ballooning (p=0.043).

Conclusions: In this histologically characterized MASLD cohort, Lp(a) levels increased with disease severity and correlated with fibrosis and activity parameters. These findings suggest a potential role for Lp(a) in MASLD progression and warrant further studies to clarify its contribution to liver disease pathogenesis and cardiovascular risk in this population.

Age-Related Enhancement of COX-1–Mediated Thromboxane Production in Patients with Atrial Fibrillation

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Background: Enhanced platelet activation contributes to the increased cardiovascular risk of elderly patients with atrial fibrillation. The biological mechanisms underlying this phenomenon are not fully clarified. This study investigated whether age-related increases in serum thromboxane B_2 (TxB_2) are associated with platelet cyclooxygenase-1 (Cox-1) upregulation in older individuals.

Methods: Serum levels of Cox-1 and TxB_2 were assessed in patients with atrial fibrillation enrolled between 2022 and 2023. A subset of participants underwent in vitro analyses to evaluate the inhibitory effect of aspirin on platelet TxB_2 generation and to quantify platelet Cox-1 expression across different age groups (<65 vs. ≥65 years). The relationship between Cox-1 expression and aspirin-mediated inhibition of TxB_2 was also explored. Associations were analyzed using Spearman correlation, and mediation analysis was performed to assess indirect effects.

Results: The study included 134 patients. Age showed a positive correlation with both Cox-1 expression (R = 0.42, p <0.01) and TxB_2 levels (R = 0.44, p <0.01). Additionally, Cox-1 expression was positively associated with TxB_2 concentrations (R = 0.50, p <0.01). Mediation analysis demonstrated that Cox-1 partially mediated the relationship between age and TxB_2 levels (β = 5.23, 95% CI: 2.33–8.63). In vitro experiments revealed a reduced sensitivity to aspirin in older patients, as reflected by higher IC_{50} values for inhibition of platelet TxB_2 production (96.78 µM in ≥65 years vs. 48.92 µM in <65 years). This reduced response was accompanied by increased platelet Cox-1 expression in the elderly group. Moreover, higher Cox-1 levels were inversely correlated with aspirin-induced inhibition of platelet TxB_2 (R = –0.64, p <0.01).

Conclusions: Advancing age is associated with increased thromboxane production, driven in part by platelet Cox-1 upregulation. This alteration is accompanied by a reduced capacity of aspirin to suppress Cox-1 activity, potentially contributing to the heightened thrombotic risk observed in elderly patients.