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ABSTRACT N. CO42

ALTERAZIONI DELLE PIASTRINE E CONDIZIONI GENETICHE

OXIDATIVE STRESS MAY CONTRIBUTE TO ENHANCED THROMBOPOIESIS THROUGH MIR-150: IMPLICATIONS FOR ASPIRIN RESPONSE.

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Background and Aims: Variability in platelet cyclooxygenase-1 (COX-1) turnover affects individual responses to aspirin (ASA). Due to ASA's short half-life, increased platelet (PLT) production can limit its antiplatelet effect over 24 hours. We previously showed that poor ASA responders have enhanced megakaryopoiesis (MK) and proPLT formation, restoring COX-1 activity more rapidly. Type 2 diabetes mellitus (T2DM) is characterized by elevated oxidative stress, which may alter PLT microRNA (miRNA) profiles, increasing PLT reactivity and resistance to ASA. We evaluated CCL5 (a chemokine promoting MKs) and miR-150 (regulator of MK-erythroid progenitors) in patients with shortened ASA effect (10–24h) and faster PLT COX-1 recovery. We aimed to assess lipid peroxidation (via urinary 8-iso-$PGF_2\alpha$), circulating CCL5, and their association with miR-150.

Methods: We enrolled 100 high cardiovascular (CV) risk T2DM patients on chronic low-dose ASA (100 mg/day). Blood samples were collected at 10h (T10) and 24h (T24) following a witnessed ASA administration. Patients were stratified into tertiles based on serum thromboxane B_2 (TXB_2) slope, comparing 1st and 3rd tertiles. Urine and fasting blood were analyzed for PLT-associated miR-150 (index of MK activity), CCL5 (marker of PLT activation), and urinary 8-iso-$PGF_2\alpha$ (oxidative stress biomarker).

Results: Patients with accelerated COX-1 recovery had higher urinary 8-iso-$PGF_2\alpha$ ($p=0.019$) and circulating CCL5 ($p=0.017$), which were correlated ($rho=0.273$, $p=0.032$). CCL5 correlated with thrombopoietin ($\rho=0.399$, $p=0.022$) and PLT count ($\rho=0.286$, $p=0.002$), both elevated in the 3rd tertile ($p=0.023$ and $p=0.047$). Circulating miR-150-5p was upregulated ($p=0.058$) and correlated with 8-iso-$PGF_2\alpha$ ($rho=0.274$, $p=0.063$). No significant difference was found in PLT miR-150-5p levels; however, these levels correlated with CCL5 ($rho=0.262$, $p=0.042$). TargetScan identified prostaglandin F receptor as a miR-150-5p target.

Conclusions: In high CV risk T2DM patients, reduced ASA response is linked to faster PLT COX-1 recovery. Increased oxidative stress (8-iso-$PGF_2\alpha$), CCL5, and miR-150-5p levels may contribute to enhanced thrombopoiesis. Their correlations suggest oxidative stress drives MK activation and PLT production. These biomarkers may help identify ASA hyporesponsiveness and guide improved antiplatelet strategies in high-risk patients.

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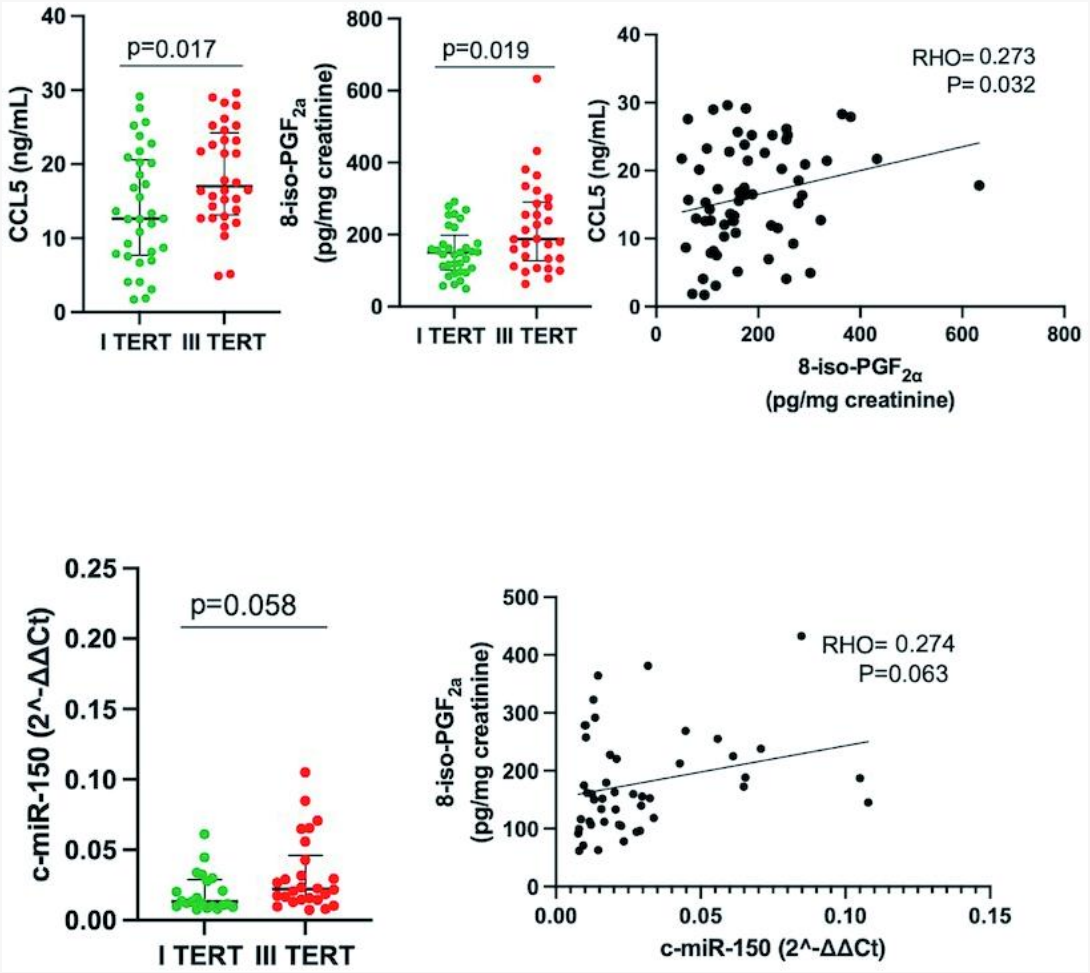
p=0.017
CCL5 (ng/mL)
I TERT
III TERT
p=0.019
8-iso-PGF2a (pg/mg creatinine)
RHO= 0.273
P= 0.032
8-iso-PGF2α (pg/mg creatinine)
p=0.058
c-miR-150 (2^-ΔΔCt)
RHO= 0.274
P=0.063