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ABSTRACT N. CO43

ALTERAZIONI DELLE PIASTRINE E CONDIZIONI GENETICHE

EARLY PLATELET DYSFUNCTION IN SEPSIS: AN ICU PILOT STUDY.

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Background and Aim
Platelets play a key role in hemostasis and immune response during infection. In sepsis, platelets interact with endothelial cells and leukocytes, contributing to inflammation and microvascular thrombosis. Thrombocytopenia is a known marker of poor prognosis, whereas platelet dysfunction during sepsis has barely been investigated. This study aims at exploring early platelet function changes in septic patients and their corrrelation to sepsis severity markers, such as procalcitonin and SOFA score.

Methods
Ten adult patients with sepsis or septic shock admitted to the ICU of "Fondazione Policlinico Universitario A. Gemelli" and seven healthy controls were enrolled. Blood samples were collected at admission (T0), after 48 hours (T1) and 7 days (T2). We performed the following tests 1) light transmission aggregometry (LTA) on samples with platelet counts ≥150 × 10^3/µL2) flow cytometry measurement of platelet P-selectin and PAC-1 expression 3) flow cytometry measurement of platelet–leukocyte aggregates; 4) thromboelastography (TEG) platelet mapping to measure maximal platelet aggregation induced by ADP and arachidonic acid in whole blood 5) ELISA measurement of plasma soluble P-selectin and CD40L levels. Platelet activation markers were correlated with procalcitonin levels and SOFA scores. Healthy controls were sampled only at T0.

Results
A marked impairment of platelet function was observed in all septic patients already at the time of admission (T0), even in the absence of thrombocytopenia. LTA showed significantly reduced aggregation in response to 2 µM ADP and 5 µM epinephrine at all time points (**Fig. 1 A,B**). Flow cytometry showed a severe and persistent reduction of PAC-1 expression upon ADP- and TRAP-induced stimulation in all patients (**Fig. 1D-F**). The severe impairment of PAC-1 expression was evident at T0 and was present also in patients with normal platelet counts (**Fig 1D,F**) . On the contrary, in our cohort thrombocytopenia developed later, peaking at T1 (48 hours). Thromboelastography platelet mapping also demonstrated a significant reduction of maximal aggregation induced by ADP and by arachidonic acid in sepsis patients. Interestingly, a significant association between ADP-induced platelet aggregation and SOFA score was found (**Fig. 1C**), In addition to the above functional defects, circulating soluble platelet activation markers (CD40L and P-selectin) and platelet-leukocytes aggregates were reduced, suggesting a global impairment in platelet activation pathways. These changes correlated with clinical severity: patients with more pronounced platelet dysfunction showed higher SOFA scores and elevated procalcitonin levels at T0.

Conclusions
We show that in sepsis patients platelet dysfunction occurs very early, precedes thrombocytopenia and correlates with sepsis severity markers. *Ex vivo* platelet hyporeactivity likely reflects *in vivo* platelet exhaustion in sepsis patients as a consequence of direct activation of platelets by microorganisms and/or cytokines released by immune cells. Early detection of platelet dysfunction may help guide early interventions to prevent hemostatic imbalance and organ failure in septic patients.

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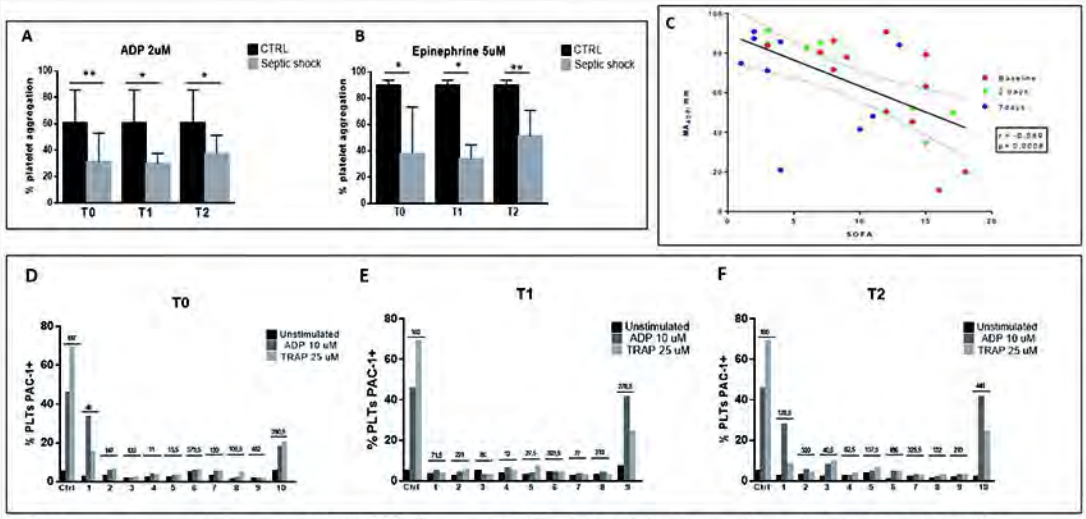

A) Platelet aggregation measured by LTA after stimulation with ADP (2 µM) at time points T0, T1, and T2. Statistical analysis was performed using Student's t-test and Mann–Whitney test. Significant differences were observed at T0 (**p = 0.0095), T1 (*p = 0.0238), and T2 (*p = 0.0140). **B)** Platelet aggregation measured by LTA after stimulation with EPI (5 µM) at time points T0, T1, and T2. Statistical analysis was performed using Student's t-test and Mann–Whitney test. Significant differences were observed at T0 (*p = 0.0303), T1 (*p = 0.0238), and T2 (**p = 0.0022). **C)** Correlation between MAADP and SOFA score at the three time points. **D–F)** Flow cytometry measurement of PAC-1 expression in platelets after stimulation with ADP (10 µM) and thrombin receptor-activating peptide (TRAP, 25 µM) at T0, T1, and T2. The numbers above the graphs indicate platelet count × 10^3.