

Piastrine: Alterazioni qualitative o quantitative

IMPACT OF HEPATOCELLULAR CARCINOMA ON CIRCULATING RETICULATED PLATELETS IN PATIENTS WITH AND WITHOUT LIVER CIRRHOSIS

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Background and Aims. Reticulated platelets (RePLTs) are bigger and more reactive platelets with an increased RNA content. In liver cirrhosis, increased platelet turnover leads to the release of these “emergency platelets'', which would counteract bleeding events. However, their role in hepatocellular carcinoma (HCC) remains unclear. The aim of this study is to evaluate RePLT levels and platelet activation in HCC patients with and without cirrhosis.

Methods. Sixty subjects were prospectively enrolled into four groups: healthy controls (CTRL), cirrhosis without HCC (cirrhosis+ HCC-), HCC on a healthy liver (cirrhosis- HCC+), and HCC on cirrhosis (cirrhosis+ HCC+). Exclusion criteria were advanced liver disease (Child-Pugh B/C), portal vein thrombosis and antiplatelet therapy. RePLTs were defined through CD41 and SYTO-13 positivity in the morphological gate set between the 3 µm and 10 µm beads population diameter using flow cytometry and their activation was evaluated by phosphatidylserine and P-selectin exposure across different reticulation strata (low/high/very-high). Multivariable linear regression assessed the independent association between HCC and RePLTs. Repeated-measures ANOVA tested the effect of reticulation and group interaction.

Results. Sixty subjects were included: CTRL (n = 28), cirrhosis+ HCC- (n = 16), cirrhosis- HCC+ (n = 5), and cirrhosis+ HCC+ (n = 11). RePLTs were lower in HCC (median: 4.02% in CTRL, 3.76% in cirrhosis+ HCC-, 1.98% in cirrhosis- HCC+, and 1.55% in cirrhosis+ HCC+; p = 0.004). In a multivariable linear regression, HCC was independently associated with reduced RePLTs (coefficient -2.51%; 95% CI -4.55 to -0.46; p = 0.018). Both phosphatidylserine and P-selectin increased significantly with increasing reticulation ($p < 0.001$ for both). The increase across reticulation strata differed by group for both markers ($p < 0.001$ for both), showing blunted activation in HCC groups. Specifically, in the three reticulation strata, phosphatidylserine increased from 1.07%, 8.29% and 46.0% in CTRL and 0.57%, 11.5% and 68.6% in cirrhosis+ HCC–, with smaller increases in cirrhosis– HCC+ (2.54%, 2.83% and 7.27%) and cirrhosis+ HCC+ (4.74%, 7.54% and 20%). Similarly, P-selectin increased from 3.02%, 29.6% to 93.7% in CTRL and 3.63%, 45.6% to 96.6% in cirrhosis+ HCC–, versus more limited increases in cirrhosis– HCC+ (1.29%, 2.38% to 15.6%) and cirrhosis+ HCC+ (1.59%, 5.01% to 35.3%).

Conclusions. HCC is independently associated with decreased levels of circulating RePLTs. HCC patients exhibited reduced platelet activation as reticulation increases, as demonstrated by significant reticulation-by-group interactions for both phosphatidylserine and P-selectin. Further studies are needed to elucidate the underlying mechanisms and clinical relevance.