



TERAPIE ANTICOAGULANTI E GESTIONE DELLE
COMPLICANZE

MAPPING HEMOSTATIC BIOMARKER EXPRESSION ACROSS CANCER TYPES AND STAGES WITHIN THE HYPERCAN COHORT

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Background and Aims. Systemic hypercoagulability is a recognized hallmark of malignancy. Growing evidence suggests that markers of hemostatic activation may serve as surrogates for tumor aggressiveness and prognosis, other than thrombosis; however, a comprehensive characterization of this "hemostatic signature" within an inflammatory milieu across large prospective cohorts remains limited. This study aims to evaluate tumor-specific procoagulant profiles within a large, prospective, multicenter cohort of patients diagnosed with common solid malignancies.

Methods. We analyzed 4,292 patients from the HYPERCAN study (NCT02622815) with newly diagnosed non-small cell lung (NSCLC), gastric (GC), colorectal (CRC), and breast cancer (BC). Plasma samples were collected at diagnosis to assess thrombin generation (TG_{CAT}), D-dimer, fibrinogen, and prothrombin fragment 1+2 (F1+2). All participants provided informed consent, and data were analyzed using SPSS 21.0.

Results. Metastatic disease was predominant in the NSCLC (67%), GC (53%), and CRC (47%) cohorts, whereas 75% of the BC cohort consisted of high-risk surgically resected patients. Fibrinogen levels were significantly elevated in me-

tastatic cases compared with resected cases across all tumor types ($p < 0.001$), with the highest concentrations observed in metastatic NSCLC. Notably, CRC exhibited a stage-dependent, stepwise increase in fibrinogen (348 to 444 mg/dL; $p < 0.05$). While FVIII was consistently higher in metastatic groups (except GC), D-dimer peaks were most pronounced in metastatic GC and NSCLC ($p < 0.002$). Although F1+2 effectively differentiated metastatic from localized disease in NSCLC, GC, and BC ($p < 0.05$), it showed no discriminatory power in CRC. Finally, the highest TG-Peak and ETP values were found in BC and NSCLC; in the latter, TG values positively correlated with disease burden, significantly distinguishing metastatic from resected patients ($p < 0.003$).

Conclusions. These data demonstrate that cancer-associated hypercoagulability is a heterogeneous, tumor-specific hallmark rather than a uniform systemic event. While fibrinogen and D-dimer remain robust indicators of metastatic progression—particularly in NSCLC and GC—the sensitivity of markers like F1+2 and TG varies by histotype. These findings underscore the necessity of tailored hemostatic profiling to better understand biological heterogeneity and improve risk stratification across diverse malignancies.