

HYPERCOAGULATION AND BIOMARKERS

DIFFERENTIAL EXPRESSION OF HEMOSTATIC BIOMARKERS ACROSS CANCER TYPE AND DISEASE STAGE: A PROSPECTIVE ANALYSIS OF 4,292 PATIENTS FROM THE HYPERCAN STUDY

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Background. Cancer-associated hypercoagulability is a well-recognized phenomenon, yet the relationship between systemic hemostatic activation, specific tumor types, and disease burden remains insufficiently characterized.

Aim. To investigate whether baseline hemostatic biomarkers correlate with cancer type and stage, and to identify specific procoagulant profiles typical of non-small cell lung cancer (NSCLC), gastric cancer (GC), colorectal cancer (CRC), or breast cancer (BC).

Methods. This prospective analysis included 4,292 patients (median age 61; F 2813/M 1445) from the HYPERCAN cohort (NCT02622815) with newly diagnosed NSCLC, GC, CRC, and BC. Pre-chemotherapy plasma samples were analyzed for Thrombin Generation (TG), measured via Calibrated Automated Thrombogram (CAT) at 5 pM TF (Peak and ETP), and for D-dimer, Fibrinogen, Factor VIII (FVIII), and Prothrombin fragment 1+2 (F1+2).

Results. The NSCLC, CRC, and GC cohorts included predominantly metastatic cancer patients (67%, 47%, and 53%, respectively), whereas the BC cohort included primarily high-risk resected breast cancer patients (75%). Distinct biomarker profiles emerged across malignancies and stages. NSCLC exhibited the most aggressive procoagulant profile.

Metastatic NSCLC patients had the highest median fibrinogen (508 mg/dL) and significantly elevated TG (Peak and ETP) compared with resected cohorts ($p < 0.003$). Across almost all cohorts, fibrinogen and FVIII levels were significantly higher in metastatic vs. resected cases ($p < 0.001$). Notably, CRC showed a significant stepwise increase in fibrinogen across all burden stages ($p < 0.05$). D-dimer levels were highest in metastatic GC and NSCLC ($p < 0.002$), whereas the lowest values were observed in resected BC cohort. F1+2 significantly differentiated metastatic from resected disease in NSCLC, GC, and BC ($p < 0.05$), but failed to distinguish between resected and locally advanced stages and showed no significant difference in the CRC cohort. The highest TG-Peak and ETP values were observed in the NSCLC and BC cohorts.

Conclusions. These findings show that although systemic hypercoagulability is a hallmark of metastatic progression, hemostatic activation is highly tumor-specific. NSCLC exhibits a unique, potent procoagulant signature marked by elevated fibrinogen, D-dimer, and thrombin generation. These results suggest that hemostatic biomarkers may serve as specific indicators of tumor type and burden, potentially guiding individualized risk stratification and clinical management.