

LABORATORIO E FATTORI PREDITTIVI

INFLAMMATION AND FIBRINOLYSIS BIOMARKERS AS PREDICTORS OF CANCER RISK IN HEALTHY SUBJECTS: RESULTS FROM THE HYPERCAN STUDY.

C. Ticozzi¹, S. Bolognini^{1,2}, P. Gomez-Rosas^{1,3}, L. Russo^{1,2}, Cj. Tartari^{1,2}, F. Schieppati^{1,2}, G. Sampietro⁴, L. Barcella¹, M. Marchetti^{1,2}, A. Falanga^{1,2}.

¹Immunohematology and Transfusion Medicine, Hospital Papa Giovanni XXIII, Bergamo; ²School of Medicine and Surgery, University of Milano-Bicocca, Milan; ³Maastricht University Medical Center, Cardiovascular Research Institute Maastricht, Maastricht, The Netherlands; ⁴Unit of Epidemiology and Statistics, ATS Bergamo.

Background and aims: The association between inflammation, coagulation, and tumor progression is well established. Furthermore, there is evidence suggesting that chronic inflammation, coupled with endothelial disruption, may increase the risk of cancer development. The aim of this study is to assess whether the presence of an inflammatory state can be a predictor of cancer diagnosis in a cohort of healthy individuals enrolled in the HYPERCAN study (ClinicalTrials.gov ID#NCT02622815).

Methods: From 2012 to 2022, 10,294 healthy blood donors from Bergamo province were enrolled in the HYPERCAN study and followed up for cancer occurrence. To evaluate the persistence of the inflammatory status, blood samples were collected at enrolment (T0) and after 6-18 months (T1), along with clinical data, hematological parameters and a lifestyle questionnaire. Plasma C-reactive protein (CRP), measured by the apDia BV ELISA kit, was the biomarker of inflammation, whereas tissue plasminogen activator (tPA), assessed with the Hyphen Biomed ELISA kit, was the index of fibrinolysis and endothelial involvement. All statistical analyses were performed using SPSS 21.0.

Results: For this exploratory analysis, from the overall blood donor population enrolled, we studied 160 individuals who developed cancer during follow-up, i.e. cancer cases [73%

males, median age 53 years, range (40-64)], who were randomly selected and matched with 178 control subjects who remained cancer-free during follow-up [69% males, median age 48 years, range (37-62)]. The most frequently diagnosed cancers were prostate in males (26%), and breast cancer in females (18%).

At T0, cancer cases showed significantly higher median levels of both CRP [0.3 ug/mL (5th-95th: 0-3.6), vs 0.2 ug/mL (0-2.6), p=0.005] and tPA [5.4 ng/mL (5th-95th: 0.5-15.0), vs 0.95 ng/mL (0.3-14.5), p=0.001], as compared to the control group.

At T1, plasma levels of CRP [0.7 ug/mL (5th-95th: 0.12-3.8), vs 0.2 ug/mL (0-2.75), p=0.001] remained significantly higher in cancer cases, while tPA did not. Additionally, linear regression analysis established an association between CRP and tPA levels (B=0.537, p=0.035).

Linear multivariate analysis corrected for age and gender showed that having high levels of tPA at enrolment and being older were factors significantly associated with cancer occurrence (p<0.05).

Conclusions: Our study shows that increased levels of CRP and tPA are significantly associated with a subsequent cancer diagnosis, particularly for CRP this correlation is confirmed at two different time points. Inflammatory and fibrinolytic parameters may serve as valuable biomarkers for predicting the risk of developing cancer.

Email: chiaraticozzi97@gmail.com