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ABSTRACT N. CS04

TROMBOEMBOLISMO VENOSO

ASSOCIATION BETWEEN ELEVATED PLASMA LEVELS OF TISSUE PLASMINOGEN ACTIVATOR (TPA) AND OCCULT CANCER RISK: A NESTED CASE-COHORT ANALYSIS IN 10,294 HEALTHY SUBJECTS.

S. Bolognini[1|2], C. Ticozzi[1], P. Gomez-Rosas[1|3], L. Russo[1|2], Cj. Tartari[1|2], F. Schieppati[1|2], G. Sampietro[4], L. Barcella[1], M. Marchetti[1|2], A. Falanga[1|2].

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

BACKGROUND AND AIMS

Tissue plasminogen activator (tPA), an enzyme involved in the fibrinolytic system, has been associated with cancer progression, but limited prospective data are available. Therefore, its role in predicting cancer risk is yet undefined. This study aimed to investigate whether circulating tPA levels predict cancer occurrence in a large cohort of healthy subjects, i.e. blood donors enrolled in the prospective HYPERCAN study (ClinicalTrials.gov ID#NCT02622815).

METHODS

A total of 10,294 blood donors (72% males; mean age 48 years) were enrolled between 2012 and 2022 and followed up every 6 months for cancer incidence, with a follow-up of at least 5 years. Malignancies were identified through clinical records, and tPA levels were measured from baseline blood samples using a commercial ELISA kit. A nested case-cohort design was applied, comparing cancer cases to controls from the same cohort. Statistical analysis was performed with SPSS 21.0. All participants provided written informed consent.

RESULTS

Over a median follow-up of 9 years (range 5–11), 300 cancer cases were identified, with 35 early diagnoses (within 6 months) excluded. The final analysis included 980 participants (59% male, mean age 51): 265 cancer cases and 715 controls. Most cases (91%) occurred within 5 years from enrollment. Prostate and breast cancers were the most common in men and women, respectively, followed by gastrointestinal (GI) cancers. Compared to controls, cancer cases were significantly older and more likely to be active smokers and have hypertriglyceridemia ($p<0.05$). Median tPA levels in the cohort were 4.4 ng/mL (IQR 1.4–7.9), significantly higher in men (6.7 ng/mL) than in women (3.4 ng/mL, $p<0.05$). Multivariable Cox regression analysis adjusted for age, glucose levels, smoking habits, and alcohol intake showed that elevated tPA (HR 1.04 [1.01–1.07], $p=0.003$) and cholesterol (HR 1.01 [1.00–1.10], $p=0.010$) levels independently predicted cancer risk. In particular, tPA levels above 7.85 ng/mL were linked to a higher overall cancer risk (HR 1.78 [1.39–2.29], $p<0.001$) and GI cancer risk (HR 3.29 [1.70–6.38], $p<0.001$). Gender-specific analyses using recalculated tPA cut-offs (>8.8 ng/mL in men, >5.66 ng/mL in women) showed that tPA levels also predicted breast cancer risk (HR 2.21 [1.09–4.47], $p=0.017$) in women, while no association was found with prostate cancer in men.

CONCLUSIONS

This prospective study demonstrates that elevated tPA levels are associated with increased cancer risk, particularly gastrointestinal tumors, and breast cancer in women. These findings support the potential role of tPA as a predictive biomarker and its integration into future cancer screening strategies in the general population.

Email: *sbolognini@asst-pg23.it*