

INFLAMMATION

PREDICTIVE VALUE OF INFLAMMATORY AND ENDOTHELIAL BIOMARKERS FOR CANCER RISK IN HEALTHY INDIVIDUALS: EVIDENCE FROM THE HYPERCAN STUDY

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Introduction. Chronic inflammation and endothelial dysfunction are critical drivers of the tumor microenvironment, fostering a favourable environment for cellular transformation and progression. By disrupting vascular integrity and promoting sustained oxidative stress, these processes create a biological landscape that facilitates both the initiation and spread of malignancy.

Aim. This exploratory study aimed to investigate whether inflammatory and endothelial activation biomarkers are suitable for predicting cancer occurrence in a cohort of healthy individuals enrolled in the HYPERCAN project.

Materials and Methods. Between 2012 and 2022, 10,294 healthy blood donors from Bergamo province were enrolled and followed up for cancer occurrence. Blood samples were collected at enrolment (T0) and after 6-18 months (T1), together with clinical data, hematological parameters, and lifestyle information. A nested case study identified an exploratory subcohort of 201 individuals. High-sensitivity C-reactive protein (hsCRP) was measured as an inflammatory biomarker, while thrombomodulin (TM) and von Willebrand factor antigen (vWF-Ag) were assessed as markers of endothelial activation. Statistical analyses were performed using R software (version 4.2.2).

Results. The subcohort included 201 subjects (131 males and 70 females), median age 47 years (range 35-64). Sixty-seven subjects developed cancer (47 males and 20 females; median age 52 years), most commonly prostate cancer in males (20%) and breast cancer in females (12%), while 134 individuals remained cancer-free (median age 46 years). At baseline (T0), cancer cases showed higher hsCRP (0.34 vs 0.00 µg/mL, $p < 0.001$) and TM levels (4.30 vs 3.46 ng/mL, $p < 0.01$) compared with controls. These differences persisted at follow-up (T1), with higher hsCRP (0.6 vs 0.01 µg/mL, $p < 0.001$) and TM (4.32 vs 3.07 ng/mL, $p < 0.01$). No significant differences in vWF-Ag were observed. Linear regression showed a positive association between hsCRP and TM ($B = 0.180$, $p = 0.013$). Multivariate analysis adjusted for age and sex confirmed that hsCRP, TM and older age were independently associated with cancer occurrence ($p < 0.05$).

Conclusions. Elevated CRP and TM levels are strongly associated with subsequent cancer diagnosis in healthy individuals. Persistent inflammation combined with endothelial activation may represent an early indicator of increased cancer risk, supporting potential use of these biomarkers for identifying high-risk subjects.