



Prevalence of factor V Leiden and prothrombin G20210A in patients with gastric cancer

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Supported by a Research Grant from the University of Siena (PAR)

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Received: 2006-01-12 Accepted: 2006-02-18

Key words: Gastric cancer; Genetic polymorphism; Factor V Leiden; Prothrombin G20210A

Battistelli S, Stefanoni M, Genovese A, Vittoria A, Cappelli R, Roviello F. Prevalence of factor V Leiden and prothrombin G20210A in patients with gastric cancer. *World J Gastroenterol* 2006; 12(26): 4179-4180

<http://www.wjgnet.com/1007-9327/12/4179.asp>

Abstract

AIM: To analyze the prevalence of the two commonest thrombophilic mutations, factor V Leiden and prothrombin G20210A, in patients with gastric cancer.

METHODS: One hundred and twenty-one patients with primary gastric carcinoma and 130 healthy subjects, comparable for age and sex, were investigated. Factor V Leiden was detected by using polymerase chain reaction and restriction enzyme digestion, and prothrombin G20210A gene mutation by allele-specific PCR.

RESULTS: Among the 121 cancer patients, factor V Leiden was found in 4 cases (GA genotype: 3.3%) and prothrombin G20210A in 10 cases (GA genotype: 8.3%). Of the 130 control subjects, factor V Leiden was detected in 6 cases (GA genotype: 4.6%) and prothrombin G20210A in 8 cases (GA genotype: 6.1%). No double heterozygous carriers of both mutations were found in either group. The prevalence of both factor V Leiden and prothrombin G20210A variant was not statistically different between the cancer patients and the healthy subjects.

CONCLUSION: Our study suggests that, in gastric cancer, the risk factors of thrombophilic cancer state are on acquired rather than on a genetic basis and that prothrombin G20210A does not seem to be a cofactor in gastric cancer pathogenesis.

INTRODUCTION

The pathogenesis of haemostatic disorders in cancer is complex and mainly on acquired basis. To date, little conclusive information is available in literature about the association of cancer hypercoagulability and inherited thrombophilia. The most common genetic defect in Caucasian population is factor V Leiden, a glutamine to arginine switch at amino-acid 506, due to G to A transition at nucleotide 1691 of coagulation factor V. This point mutation makes factor Va resistant to the proteolytic action of activated protein C so that activated factor V persists, rather than being inactivated. Another genetic defect is prothrombin G20210A polymorphism, a G to A transition at nucleotide 20210 in the 3'-untranslated region of the prothrombin gene, associated with elevated levels of prothrombin, which contributes to thrombotic risk by promoting enhanced thrombin generation.

Recently, Miller *et al*^[1] found an increased incidence of neoplasia of the digestive tract in men with persistent activation of the coagulation pathway. In addition, there is some evidence that prothrombin G20210A gene mutation may be involved in cancer development and/or progression. The prevalence of factor V Leiden and prothrombin G20210A gene polymorphism was analyzed in a cohort of 175 patients with gastrointestinal carcinoma and a significantly increased prevalence of prothrombin gene mutation in the patient group as compared to normal controls was detected^[2]. On the contrary, Paspatis *et al*^[3] demonstrated that the prevalence of both factor V Leiden and prothrombin G20210A in 74 colorectal cancer patients was found to be similar to that of 192 colonoscopically selected control subjects. To the best of our knowledge, no data regarding the prevalence of factor V Leiden and prothrombin G20210A in the subset of patients with gastric cancer are available in the literature. We, therefore, performed a prospective case-control study to analyze the

prevalence of factor V Leiden and prothrombin G20210A in patients with gastric cancer.

MATERIALS AND METHODS

One hundred and twenty-one consecutive patients (78 men, 43 women; mean age: 62 years, range: 51-76 years) with operable gastric carcinoma (TNM staging: T₁₋₃, N₀₋₂, M₀) and 130 healthy subjects, matched for age, sex and ethnic-background, were investigated for the presence of factor V Leiden and prothrombin G20210A gene mutation. All individuals were from central Italy, without any previous thrombotic event. Specifically, no control subject or cancer patient had a history of peptic ulcer or *H pylori* infection.

Genomic DNA was extracted from white blood cells according to standard procedures. Factor V Leiden was detected by using polymerase chain reaction and restriction enzyme digestion following the methods described by Bertina *et al*^[4]. Prothrombin G20210A gene mutation was detected by allele-specific PCR according to the methods described by Poort *et al*^[5].

Statistical analysis

Statistical analysis was performed using χ^2 test (with Yates correction).

RESULTS

Among the 121 cancer patients, factor V Leiden was found in 4 cases (GA genotype: 3.3%) and prothrombin G20210A variant in 10 cases (GA genotype: 8.3%). Among the 130 control subjects, factor V Leiden was detected in 6 cases (GA genotype: 4.6%) and prothrombin G20210A variant in 8 cases (GA genotype: 6.1%). No double heterozygous carriers of both mutations were found in both groups. The prevalence of both factor V Leiden and prothrombin G20210A was not statistically different between the cancer patients and the healthy subjects.

DISCUSSION

The present study suggests that, in gastric cancer patients, there is no increase in the prevalence of both fac-

tor V Leiden and prothrombin G20210A gene mutation. These data seem apparently in contrast with the results of Pihusch *et al*^[1], obtained in a cohort of patients with carcinoma of all the gastrointestinal tract (most patients with adenocarcinoma of the colon), and this could indicate a different, peculiar pathogenetic pathway of gastric carcinogenesis. To our knowledge, this is the first report about the prevalence of factor V Leiden and prothrombin G20210A in a cohort of gastric cancer patients. Moreover, the ethnic background of our subjects is different and this could partly explain our results. On the other hand, our data are in agreement with the findings by Paspatis *et al*^[2] who did not find a significant difference in the prevalence of the two prothrombotic polymorphisms in 74 colorectal cancer patients as compared to the controls. However, the limitation of our study is the low statistical power of our sample size.

In conclusion, our data strengthened the evidence that, in gastric cancer, the thrombophilic state is on acquired rather than on genetic basis and seem to suggest that the prothrombin G20210A is not involved in gastric cancer pathogenesis.

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S- Editor Wang J L- Editor Kumar M E- Editor Bi L