Factor V Leiden Mutation is not a Risk Factor for Myocardial Infarction in North-East Turkey

DOĞU KARADENİZ BÖLGESİNDE FAKTÖR V LEIDEN MUTASYONU MİYOKARD İNFARKTÜSÜ İÇİN BİR RİSK FAKTÖRÜ DEĞİLDİR

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Summary

Objective: The genetic defect of coagulation factor V known as factor V Leiden produces a resistance to degradation by activated protein C (APC) and increases the risk of venous thrombosis. The relationship between this genetic abnormality and myocardial infarction is still unresolved. Aim of this study was to investigate whether factor V Leiden is a risk factor for myocardial infarction in north-east Turkey.

Methods: We studied 112 patients who had a diagnosis of acute MI (94 males and 18 females, aged 55 ± 10 years), and 95 control subjects. The study population was identified by characteristic ECG changes and elevation of serum CK-MB, whereas the control subjects were anonymous healthy blood donors with no known history of coronary artery disease, stroke or thromboembolic disease. Blood samples from the patients and controls were analyzed for the factor V Leiden mutation by DNA analysis, using the polymerase chain reaction.

Results: Factor V Leiden mutation was found in 9 of 112 (8%) patients with miyocardial infarction and 7 of 95 (7.3 %) control subjects (p = 0.32).

Conclusion: This study showed no evidence of an association between factor V Leiden and myocardial infarction in north-east Turkey.

Key Words: Factor V Leiden, Myocardial infarction

T Klin J Cardiol 2001, 14:104-106

Özet

Amaç: Faktör V Leiden, aktive protein C'nin antikoagülan aktivitesinde azalmayla seyreden kalıtsal bir koagülasyon kusurudur. Faktör V Leidenin venöz tromboz riskini artırdığı açık bir şekilde gösterilmiştir. Ancak arteriyel trombozu dolayısıyla da miyokard infarktüsü gelişimini artırıp artırmadığı açık değildir. Bu çalışmada Doğu Karadeniz bölgesinde Faktör V Leiden mutasyonunun akut miyokard infarktüsü gelişimi için bir risk faktörü olup olmadığı araştırıldı.

Metod: Akut miyokard infarktüsü tanısı alan 18'i kadın, 94'ü erkek, yaş ortalamaları 55 ± 10 olan 112 hasta ve kontrol grubu olarak da bilinen koroner arter hastalığı olmayan 95 sağlıklı olgu çalışmaya alındı. Faktör V Leiden mutasyonu tüm hasta ve kontrol grubu olgularından alınan venöz kanda polimeraz zincir reaksiyonu kullanılarak analiz edildi.

Bulgular: faktör V Leiden Mutasyonu miyokard infarktüsü tanısı alan 112 hastanın 9 (%8)' unda, kontrol grubundaki 95 olgunun 7 (%7.3)'sinde saptandı (p=0.032).

Sonuç: Faktör V Leiden mutasyonunun Doğu Karadenizde sık olduğu ancak akut miyokard infarktüsü için bir risk faktörü olmadığı sonucuna vardık.

Anahtar Kelimeler: Faktör V Leiden Mutasyonu, Akut miyokard infarktüsü

T Klin Kardiyoloji 2001, 14:104-106

Geliş Tarihi: 23.08.2000

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Acute myocardial infarction (MI) is caused by thrombotic occlusion of coronary arteries triggered by atherosclerotic plaque disruption, leading to an activation of coagulation processes (1,2). However, a causal role for individual haemostatic factors in

the development of thrombotic occlusion has not been established.

The genetic defect of coagulation factor V known as factor V Leiden produces a resistance to degradation by activated protein C (APC) and increases the risk of venous thromboembolism (3). APC-resistance is present in 20-60% of venous thrombosis cases (4). Factor V Leiden is present in %4 to %6 of the general population (5). It is caused by a single point mutation in the factor V gene which substitutes arginine (R) at position 506 with a glutamine (Q) (6). The relationship between factor V Leiden and arterial disease is still unresolved. Factor V Leiden was found in 7.1 percent of the Turkish population (7). This high frequency suggests that screening for the Factor V mutation should be considered in patients with myocardial infarction in our population. We conducted a study in patients presenting with acute MI to assess whether factor V Leiden increases the risk of arterial thrombosis.

Methods

Patients

Between April 1999 and March 2000, we prospectively evaluated 112 consecutive patients with a first acute MI. The diagnosis of MI was based on the triad of chest pain, ECG changes, and raised plasma enzyme activity. The study also included 95 control subjects. Healthy age and sex matched subjects without a personal or family history of ischaemic heart disease, stroke or thromboembolic disease served as a control group.

Assays

Blood samples were drawn from cases and controls in the fasting state, and collected in EDTA-tubes (Vacutaine, Becton Dickinson, Meylon, France) centrifuged at 2000 g for 20 min. DNA was extracted from blood by nucleospin DNA extraction kit (Macherey-Nagel GmbH, Düren, Germany). DNA concentrations were measured spectrophotometrically at 260 nm, and concentrates stored at -70° C. All measurements were subsequently performed within 3 weeks of collection. Ten microliters of DNA were amplified by polymerase chain reaction (PCR) in Techne-Genius thermocycler (Techne-Cambridge UK) followed by digestion with the MnlI restriction enzyme (New England Biolabs) at 37° C for 16 hours. The products were then subjected to metaphor agarose gel electrophoresis. After completion of electrophoresis, gels were photographed under ultraviolet transillumination. The technicians were blinded to whether a specimen was from a case subject or control subject.

Statistical analysis

Data are presented as mean ± SD. A comparison between groups was performed by means of an unpaired t test for continuous variables. Categorical variables were analyzed with contingency tables using the chi-square test and the Fisher exact test when appropriate. A p value < 0.05 was considered statistically significant.

Results

The clinical characteristics of 112 patients and 95 controls are shown in Table 1. In the comparison of patients and control subjects, there were no significant differences in age and sex. Hypertension, diabetes, smoking were significantly more prevalent among patients. Of the patients with MI, 93 (83%) were smokers, compared with 64 (67%) of the controls. The infarct site was anterior in 46 patients, inferior in 41 patients, and multiple in 25 patients.

In this study, we found a similar prevalence of the factor V mutation between patients with MI and an age matched control group. The prevalence of the factor V mutation was 8 % (9/112) in patients with MI, and 7.3 % (7/95) in the normal control group.

Discussion

In recent years there has been increasing interest in the role of coagulation factors in myocardial infarction and there is little doubt that in the vast ma-

Table 1. Clinical Characteristics and Prevalence of the Factor V Leiden

	Patients (n =112)	Controls (n = 95)	p value
Age, y	55 ± 10	54 ± 9	NS
Male, n (%)	94 (84)	78 (82)	NS
Smoking, n (%)	93 (83)	64 (67)	< .05
Hypertension, n (%)	14 (13)	9 (10)	NS
Diabetes Mellitus, n (%)	11 (10)	3 (3)	<.05
Factor V Leiden, n (%)	9 (8)	7 (7.3)	NS

jority of cases the final stages of coronary occlusion are via activation of the coagulation system (1,2). However, a causal role for individual haemostatic factors in the development of thrombotic occlusion is not established. Factor V Leiden has recently emerged as an important cause of venous thrombosis (6), and it is associated with a single point mutation in the factor V gene (FVQ 506 or factor V Leiden), which removes an important cleavage site for activated protein C. It is still unclear whether the factor V Leiden predisposes patients to arterial thrombosis and MI. Several reports, including a controlled study among patients with coronary heart disease, are suggestive of an association with coronary heart disease (8-10), but in several other controlled studies no relationship was observed (11-13).

One of the largest studies to look at the relation between factor V Leiden and MI is the health physicians study in which no difference was found in the prevalence of factor V Leiden between those who did and did not develop MI (13). Emmerich et al also found similar prevalence of the factor V Leiden between 609 men who had had a myocardial infarct and 692 controls (5.1 % vs 4.6 ; NS) (11). On the other hand, Marz et al found that prevalence of the factor V Leiden was more common (9 %) in 89 patients with myocardial infarction than in controls (4 %, p =0.032) (9). In our study we found that prevalence of factor V Leiden was not more common in patients with MI than in control subject.

The reason for the lack of consistency among studies is unclear but may result from differences regarding other risk factors such as smoking that act synergistically with factor V Leiden (14), or differences in grade of coronary heart disease, or small number of observations.

One of the most important aspects of factor V Leiden is their very high prevalence in the populations first studied. In most of Europe, the factor V Leiden heterozygote frequency is 5-10% (being particularly high in Scandinavia and Greece) but it is virtually absent in other populations such as in the Japanase and most Africans (5,15). In the Turkish populations, the factor V Leiden frequency was reported as 7 %. In our study, it was 8 %.

In conclusions, there appears to be no significant difference between the prevalence of factor V Leiden in patients with MI and normal control subjects in north-east Turkey. However, The most important limitation of our study involves the small number of patients studied. Large prospective studies are needed to establish the factor V Leiden as a risk factor for LV thrombus formation in acute MI.

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