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About authors:
Orazov Mekan, MD, PhD, associate Professor of Department of obstetrics and gynecology with a course of Perinatology; tel.: +79152375292; e-mail: omekan@mail.ru
Radzinskiy Victor, MD, PhD, Professor, an honored scientist of Russia, Head of Department of obstetrics and gynecology with a course of Perinatology; tel.: +79037232212
Nosenko Elena Nikolaievna, MD, PhD, Professor, Department of obstetrics and gynecology; tel.: +380506383828; e-mail: nosenko.olina@gmail.com

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CORRELATION BETWEEN FIBRINOGEN BETA-CHAIN GENE POLYMORPHISM, PLASMA FIBRINOGEN AND THROMBOEMBOLIC COMPLICATIONS IN PATIENTS WITH ATRIAL FIBRILLATION

Bulgakova N. E. 1, Baikulov M. Kh. 2, Scheglova E. V. 1, Kolesnikov V. N. 2, Yagoda A. V. 1, Boeva O. I. 1

1 Stavropol State Medical University, Russian Federation
2 Stavropol Regional Clinical Cardiology Centre, Russian Federation

В проспективном когортном исследовании изучено влияние полиморфизма -455G-A гена фибриногена В и уровня фибриногена плазмы крови на риск развития инсульта и системных тромбоэмболий у 102 пациентов (83.3 % men, mean age 52.9±8.4 yrs) with non-valvular atrial fibrillation. Identification of fibrinogen B gene 455G-A polymorphism can be useful to customize the anticoagulation strategy in patients with atrial fibrillation.

Key words: atrial fibrillation, fibrinogen, thromboembolic complications, genetic polymorphism, fibrinogen beta-chain gene

In a prospective cohort study the effect of the fibrinogen β-chain gene polymorphism -455G-A and fibrinogen plasma levels on the risk of stroke and systemic thromboembolism in 102 patients (83.3 % men, mean age 52.9±8.4 yrs) with non-valvular atrial fibrillation. Identification of fibrinogen B gene 455G-A polymorphism can be useful to customize the anticoagulation strategy in patients with atrial fibrillation.

Key words: atrial fibrillation, fibrinogen, thromboembolic complications, genetic polymorphism, fibrinogen β-chain gene

The key focus in treating patients with atrial fibrillation (AF) is prevention of thromboembolic complications (TEC) [5]. Currently, assessment of TEC risk in patients with AF is done employing the CHA2DS2-VASc clinical scale, which leaves the doctor with no precise recommendation regarding tactics for antithrombotic therapy in case the number of points scored on the scale belongs to the 0-to-1 range [2]. The issue of identifying certain additional TEC risk factors in this group of patients yet remains unresolved. Gene polymorphism of coagulation factors has a significant impact on the hemostatic system. Proper attention paid to the genetic parameters may facilitate developing individual
forecast and respective tactics for antithrombotic therapy in patients with AF who reveal low and moderate TEC risk subject to the data obtained through the \( \text{CHA}_2\text{DS}_2\text{-VASc} \) scale.

Fibrinogen is known to be involved in platelet adhesion and aggregation, and factor XIII activation [4]. Of all the fibrinogen \( \beta \)-chain gene (FGB) polymorphisms described until now, the -455-G-A type stands out as the most studied one. We performed a prospective cohort study in order to examine the effect that the FGB gene -455G-A polymorphism and levels of fibrinogen in blood plasma have on the risk of TEC development in patients with AF.

Material and Methods. The study included 102 patients with non-valvular type of AF (83.3% men, mean age 52.9±8.4 yrs). The inclusion criteria embraced non-valvular AF, lack of recently suffered traumas, surgeries, inflammatory diseases; voluntary consent to join the study; ability to maintain contact after discharge from hospital.

The patients were subject to follow up for 24 months. The endpoints implied the development of acute cerebrovascular accident (CVA) and/or systemic embolic events. The plasma fibrinogen level was identified through the Clauss method on an automatic coagulometer Sysmex CA-500. FGB gene 455G-A polymorphism was identified with polymerase chain reaction using a set of agents (SNP-Express).

The statistical processing of the data was performed using IBM SPSS Statistics 20 for Windows. The distribution normality was evaluated using the Kolmogorov – Smirnov test. In case of normal distribution the signs were expressed as median and interquartile range (Me\((Q_1\text{-}Q_3))\); the differences between groups were analyzed using Student’s t-test in view of Levene’s test for dispersions equality. In the event of abnormal distribution, the data were expressed as median and interquartile range (Me (Q1–Q3)); the differences between groups were analyzed using the Mann – Whitney U test. The \( \chi^2 \) test and Fisher’s exact test were employed to compare fractions. The evaluation of the prognostic role played by a particular feature was carried out through the odds ratio (OR) with a 95% confidence interval (CI). Differences were considered statistically significant at \( p<0.05 \).

Results and Discussion. In the group, 72 (70.6%) patients were homozygous carriers of the wild type allele of FGB gene G-455, with another 6 (5.9%) patients have on the risk of TEC development in patients with AF.

Among the patients with TEC, there were significantly more homo- or heterozygous carriers of the -455A allele (64.3% vs. 23.9%); OR 5.74; (CI 1.73; 19.03), \( p=0.006 \), while the average level of plasma fibrinogen was higher in the group where the patients reached no endpoints; this trend, however, failed to reach any statistically significant levels (2.87±0.69 g/l vs 2.56±0.31 g/l, respectively, \( p=0.121 \)).

Our study, just like the case with the investigation carried out by V.A. Shulman and N.V. Aksyutina in central Russian population of patients, confirmed a relationship between the homo- or heterozygous carrier status of the mutant -455A FGB allele and the development of TEC in patients with AF in South Russian population [1,3]. Lack of accurate association of fibrinogen level with endpoints may be due to a high variability of plasma fibrinogen concentration subject to impact from numerous factors (from inflammatory diseases to the vitamin B12 and C levels), which are not always easy to detect and take into consideration.

Conclusions. The carriage of the fibrinogen B gene mutant -455A allele is associated with an increased risk of stroke and systemic thromboembolism in patients with atrial fibrillation. No significant relationship between the plasma level of fibrinogen and the TEC was found. Evaluation of fibrinogen B gene 455G-A polymorphism may be recommended in order to customize the anticoagulation strategy in patients with atrial fibrillation, especially in cases of low risk based on the \( \text{CHA}_2\text{DS}_2\text{-VASc} \) scale assessment.

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About authors:

Bulgakova Natalya, MD, Assistant Professor, Department of Hospital Therapy; tel.: +79034401287; e-mail: natabulgakova@yandex.ru

Baikulova Madina, MD, Cardiologist; tel.: +79283213267; e-mail: m.baykulova@mail.ru

Shcheglova Elena, MD, Assistant Professor, Department of Hospital Therapy; tel.: +79034401287; e-mail: natabulgakova@yandex.ru

Kolesnikov Vladimir, Chief physician of Stavropol Regional Clinical Cardiology Centre; tel.: +79624402777; e-mail: skkb@inbox.ru