

## Association of rs10507391 polymorphism with the development of acute cerebrovascular accident in patients with cardiovascular pathology

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### ABSTRACT

The aim of the study was to investigate the association of single-nucleotide polymorphism (SNP) rs10507391 (A>T) with the acute cerebrovascular accident (CVA) development in patients of the East Siberian population with cardiovascular pathology and its risk factors.

**Material and methods.** The study involved 260 patients with acute CVA (age [57.0; 51.0–62.0]) and 272 patients of the control group (age [55.0; 51.0–62.0]). Among the patients who had acute CVA there were 157 men and 103 women. The control group included 170 men and 102 women. The examination of the experimental group included: collection of complaints, anamnesis, clinical examination, computed tomography of the brain, electrocardiography, echocardiography, ultrasound duplex scanning of extracranial brachiocephalic arteries, daily blood pressure and heart rate monitoring, and analysis of the blood coagulation system. In patients of the experimental group, the following cardiovascular pathology and risk factors were present: arterial hypertension, paroxysmal supraventricular tachycardias, dyslipidemia, atherosclerosis of the brachiocephalic arteries, and disorders of the hemostatic system. The control group was surveyed in the framework of the international “HAPIEE” project. Molecular genetic research was performed by real-time PCR. Statistical processing of the material was carried out using the following software: Statistica for Windows 7.0, Excel and SPSS 22.

**Results.** When studying the association of SNP rs10507391 (A>T) with the acute CVA development in all the analyzed groups and subgroups of patients, a link was established between the rare TT genotype and the T allele and an increased risk of acute CVA.

**Conclusion.** TT genotype and T allele of the SNP rs10507391 (A>T) increase the risk of acute CVA in patients regardless of previous cardiovascular pathology and its risk factors, including patients with arterial hypertension, supraventricular tachyarrhythmias, atherosclerosis of brachiocephalic arteries, impaired lipid metabolism and hemostasis system.

**Key words:** acute CVA, supraventricular tachycardia, arterial hypertension, dyslipidemia, atherosclerosis, hemostasis, rs10507391.

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## Ассоциация полиморфизма rs10507391 с развитием острого нарушения мозгового кровообращения у пациентов с сердечно-сосудистой патологией

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### РЕЗЮМЕ

**Цель.** Изучить ассоциацию однонуклеотидного полиморфизма (ОНП) rs10507391 (A>T) с развитием острого нарушения мозгового кровообращения (ОНМК) у пациентов с сердечно-сосудистой патологией и факторами риска ее развития, являющихся представителями восточносибирской популяции.

**Материалы и методы.** В исследовании приняли участие 260 пациентов с ОНМК, (возраст [57,0; 51,0–62,0]) и 272 пациента контрольной группы (возраст [55,0; 51,0–62,0]). Среди пациентов, перенесших ОНМК, – 157 мужчин и 103 женщины. Контрольная группа – 170 мужчин и 102 женщины. Обследование основной группы включало: сбор жалоб, анамнеза, клинический осмотр, компьютерную томографию головного мозга, электрокардиографию, эхокардиоскопию, ультразвуковое дуплексное сканирование экстракраниальных брахиоцефальных артерий, суточное мониторирование артериального давления и сердечного ритма, анализ свертывающей системы крови. У пациентов основной группы присутствовала следующая сердечно-сосудистая патология и факторы риска: артериальная гипертензия, пароксизмальные наджелудочковые тахикардии, дислипидемия, атеросклероз брахиоцефальных артерий, нарушения системы гемостаза. Контрольная группа обследована в рамках международного проекта HAPIEE. Молекулярно-генетическое исследование проводили методом полимеразной цепной реакции в реальном времени. Статистическая обработка материала проводилась с применением набора прикладных программ Statistica for Windows 7.0, Excel и SPSS 22.

**Результаты.** При изучении ассоциации ОНП rs10507391 (A>T) с развитием ОНМК во всех анализируемых группах и подгруппах пациентов установлена связь между редким генотипом TT и аллелем T и повышенным риском ОНМК.

**Заключение.** Генотип TT и аллель T ОНП rs10507391 (A>T) повышают риск развития острого нарушения мозгового кровообращения у пациентов вне зависимости от предшествующей сердечно-сосудистой патологии и факторов риска, в том числе у пациентов с артериальной гипертензией, наджелудочковыми тахикардиями, атеросклерозом брахиоцефальных артерий, нарушением липидного обмена и системы гемостаза.

**Ключевые слова:** ОНМК, наджелудочковая тахикардия, артериальная гипертензия, дислипидемия, атеросклероз, гемостаз, rs10507391.

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## INTRODUCTION

The single-nucleotide polymorphism (SNP) rs10507391 (A> T) is located on chromosome 13, position 30737959, at the locus of the ALOX5AP gene. The gene encodes a protein necessary for the synthesis of leukotrienes, which are metabolites of arachidonic acid and are involved in various types of inflammatory reactions. ALOX5AP genotypes are associated with a risk of developing such cardiovascular diseases as myocardial infarction (MI) and ischemic stroke [1].

The relationship between SNP rs10507391 of the ALOX5AP gene and five other polymorphisms (ALOX5 rs12762303 and rs12264801, LTA4H rs2072512, rs2540487, rs2540477) and myocardial infarction and risk factors for its development (dyslipidemia, alcohol consumption, smoking) were studied in the Chinese population. 401 patients with history of myocardial infarction (MI) and 409 people in the control group were genotyped according to these polymorphisms. SNP rs10507391 was significantly associated with lipid levels in patients with MI ( $p < 0.006-0.008$ ) [2].

The associations of ALOX5AP gene polymorphisms with subclinical atherosclerosis in families of type 2 diabetes (T2D) patients were studied by K.P. Burdon et al. (2010, USA). The study involved 998 patients, of whom 828 suffered from

T2D and 170 did not have diabetes. As a result of the study, associations of the ALOX5AP gene single-nucleotide polymorphisms (rs9506352 and rs4769060) with subclinical atherosclerosis of the coronary and carotid arteries were revealed. Regarding the rs10507391 polymorphism, no statistically significant results were obtained [3].

A number of studies have confirmed the association of ALOX5AP gene polymorphisms with stroke among the Chinese population.

In the Chinese population, the relationship between ALOX5AP-SG13S114A/T (rs10507391), COX-2-765G/C and COX-1-50C/T polymorphisms and acute CVA was evaluated. The study included 411 patients with acute CVA and the same number of people in the control group. None of the genes showed significant associations with acute CVA in the isolated analysis. However, in carriers of the AA rs10507391 genotype of the ALOX5AP gene and the CC genotype of the COX-2-765CC polymorphism, the risk of acute CVA increased by 2.84 times (95% confidence interval (CI) 1.344–6.543). The obtained results confirm the polygenic etiology of acute CVA [4].

The effect of gene interactions on the risk of acute CVA in the Chinese population was confirmed by L.F. Chi et al. (2014). In 292 patients with acute CVA and 259 healthy people,

the authors conducted a study of 8 SNPs in five candidate genes. Multivariate analysis showed a pronounced interaction of the ALOX5AP gene rs10507391 and the CYP3A5 gene rs776746 ( $p = 0.0107$ ). This interaction was associated with an increased risk of acute CVA in patients (taking into account age, hypertension and diabetes; odds ratio (OR) = 1.804; 95% CI 1.180–2.759,  $p = 0.006$ ) [5].

Associations of six ALOX5A gene polymorphisms with acute CVAs were studied in the northeastern Chinese population. Genotyping by polymorphisms of the studied genes was carried out by real-time polymerase chain reaction (PCR) and DNA sequencing. The results showed that only the G allele of rs9579646 polymorphism was significantly associated with an increased risk of acute CVA. There were no statistically significant differences in the genotype frequencies of rs9551963, rs9315050, rs4769874, rs10507391 and rs4147064 polymorphisms in the experimental and control groups. However, association analysis of rs9579646 and rs10507391 polymorphisms showed that the increased risk of acute CVA was significantly associated with the GT and GA haplotype [6].

The association of ALOX5AP gene polymorphisms with stroke has been studied in a population of East China. By PCR, 507 patients with stroke and 510 healthy individuals were genotyped. A haplotype-based analysis of the rs10507391 and rs12429692 associations showed that the reduced risk of stroke was significantly linked to the AA haplotype (OR = 0.66; 95% CI 0.46–0.95) [7].

Single-nucleotide polymorphisms of the ALOX5AP gene were studied in individuals of the Taiwanese population with history of a atherothrombotic stroke. The results of the study showed that the rare allele combination of three polymorphisms – rs4293222, rs10507391 and rs12429692 – reduces the risk of atherothrombotic stroke by 44% (OR = 0.56; 95% CI 0.37–0.84,  $p = 0.005$ ) [8].

A study of SNP rs10507391 as a genetic marker of stroke risk was conducted in the Icelandic population. The study involved 639 patients with acute CVA and 736 patients in the control group. Twenty-two SNPs of the ALOX5AP gene were analyzed. The most statistically significant

association with acute CVA was demonstrated by SNP rs10507391 (OR = 1.24; 95% CI 1.04 to 1.55;  $p = 0.017$ ). Moreover, in the male subgroup with acute CVA, associations were more pronounced than in the female subgroup [9].

Thus, most studies confirm the association of the ALOX5AP gene with acute CVA. However, the independent effect of SNP rs10507391 on the risk of stroke is proved only in the European population, which makes this polymorphism attractive for further studies in various populations.

The aim of the research was to study the association of SNP rs556621 (G>T) with the acute CVA development in patients with cardiovascular disease and risk factors for its development. The patients are representatives of the East Siberian population.

## MATERIALS AND METHODS

The study included 260 patients with acute CVA (experimental group) and 272 patients in the control group. The study was carried out in accordance with Good Clinical Practice standards and the principles of the Declaration of Helsinki. Prior to inclusion in the study, a written informed consent was received from all participants. The age of patients in the experimental group ranged from 32 to 69 years [57.0; 51.0–62.0], the age of the control group – from 37 to 68 years [55.0; 51.0–62.0]. Among the patients who had an acute CVA there were 157 men (age [56.5; 51.0–62.0]) and 103 women (age [57.0; 51.0–62.0]). The control group included 170 men (age [55.0; 51.0–62.0]) and 102 women (age [55.0; 51.0–62.0]).

Patients of the main group were at inpatient treatment and under examination at the Krasnoyarsk Interdistrict Clinical Hospital No, 20 n. a. I.S. Berzon, Krasnoyarsk. Examination of individuals of the main group included: collection of complaints, anamnesis, clinical examination, computed tomography of the brain, electrocardiography, echocardiography, ultrasound duplex scanning of extracranial brachiocephalic arteries, daily monitoring of blood pressure and heart rhythm, and analysis of the blood coagulation system. Clinical and instrumental examination of patients from the experimental group was aimed at verifying the diagnosis and detecting the concomitant cardiovascular pathology and risk fac-

tors for the development of acute CVA. 199 patients (123 men and 76 women) of the main group had an ischemic stroke, 51 patients (28 men and 23 women) were diagnosed with hemorrhagic stroke, and 10 patients (6 men and 4 women) showed a mixed type of acute CVA.

Of 260 patients, 19 (13 men and 6 women) had a repeated stroke. None of the examined patients had clinical, anamnestic and instrumental data indicating the presence of coronary heart disease. Arterial hypertension (AH) (249 people, of which 153 men and 96 women) was the most common cardiovascular pathology preceding acute CVA. Heart rhythm disturbances of the paroxysmal supraventricular tachycardia type, including atrial fibrillation, were detected in 31 patients (20 men and 11 women). The following risk factors for stroke in the study group of patients were observed: dyslipidemia (159 patients, of which 95 men and 64 women), atherosclerosis of the brachiocephalic arteries (BCA) (160 patients, of which 94 men and 66 women), hemostatic disorders leading to hypercoagulability (90 patients, of which 53 men and 37 women), 28 patients (19 men and 9 women) had aggravated hereditary history of acute CVA.

The control group is represented by a population sample of the Novosibirsk city inhabitants examined in the framework of the international HAPIEE project [3]. The examination of the control group included: questionnaires (social economic conditions of life, chronic diseases, level of physical activity, mental health), anthropometry (height, body weight, waist, hips), a survey on smoking and alcohol consumption (frequency and typical dose), blood pressure measurement, lipid profile evaluation, a survey for the detection of exertional angina (Rose), resting ECG with 12 leads, and a study of respiratory and cognitive functions. In the control group, AH occurred in 177 patients, of which 98 were men and 79 were women. There were no other cardiovascular diseases and risk factors for their development at the time of the examination in the control group.

Molecular and genetic research of individuals from the experimental and control groups was carried out by real-time PCR at the Research Institute for Treatment and Preventive Medicine of the Siberian Branch of the Russian Academy of Medical Sciences.

Statistical processing of the material was carried out using the following software: Statistica for Windows 7.0, Excel and SPSS 22.

When performing a statistical analysis of the obtained material, standard operating procedures for conducting statistical exercises were used, while the methods of statistical processing were used in accordance with the nature of the accounting features and the number of comparison groups. Fisher's exact test was used when the desired frequencies were less than 5. The relative risk of disease probability for a particular allele or genotype was calculated as the odds ratio (OR). The value of the critical significance level ( $p$ ) when testing statistical hypotheses was designated 0.05 [10–12].

Correspondence of the distribution of the observed frequencies in the studied genotypes theoretically expected by the Hardy – Weinberg principle was checked using the  $\chi^2$  criterion. The counting was carried out using a calculator for statistics in case-control studies on the Gen Expert website (Russia, <http://www.oege.org/software/hwe-mr-calc.shtml>).

## RESULTS

The frequency distribution of SNP rs10507391 genotypes and alleles (A>T) among the patients with acute CVA and in control group is presented in Table 1. A statistically significant number predominance of the rare TT genotype and T allele carriers among the patients with acute CVA was compared with the control group. There was also a statistically significant decrease in the number of the AA genotype and A allele carriers in the group of patients who had acute CVA, compared with the control group. Differences in the frequencies of the heterozygous AT genotype in the compared groups were not statistically significant.

When analyzing the frequency distribution of SNP rs10507391 genotypes and alleles (A>T) in the subgroup of men with acute CVA and in the male control group, results similar to the experimental group were obtained. The TT genotype was statistically significantly more common among men with acute CVA ( $50.6 \pm 7.9\%$ ) than among men in the control group ( $11.2 \pm 4.74\%$ ;  $p = 0.000$ ; OR 8.1; 95% CI 4.60–14.45). The frequency of the AA genotype in the subgroup of

men with acute CVA was significantly lower ( $7.1 \pm 4.07\%$ ) than in the control group ( $46.5 \pm 7.5\%$ ;  $p = 0.000$ ; OR 11.2; 95% CI 5.71–22.22). The frequencies of the AT genotype were comparable in the subgroup of men with acute CVA ( $42.2 \pm 7.8\%$ ) and among men in the control group ( $42.4 \pm 7.43\%$ ;  $p = 0.98$ ). The frequency of the A allele in the subgroup of men with acute CVA was  $28.2 \pm 5.03\%$ , and in the control group of men it was  $67.6 \pm 4.97\%$ . T allele in the subgroup of men with acute CVA was found with a frequency of  $71.8 \pm 5.03\%$ , and with a frequency of  $32.4 \pm 4.97\%$  in the control group. The differences in alleles were also statistically significant ( $p = 0.000$ ; OR 5.34; 95% CI 3.79–7.46).

When analyzing the frequency distribution of genotypes and alleles of SNP rs10507391 (A>T) in the subgroup of women with acute CVA and in the female control group, results were obtained that are similar to the results in the exper-

imental group and in the subgroup of men with acute CVA. The frequency of the AA genotype among women with acute CVA was  $6.8 \pm 4.86\%$ , among women in the control group it was  $56.9 \pm 9.1\%$  ( $p = 0.000$ ; OR 18.18; 95% CI 7.63–43.48). The AT genotype in the subgroup of women with acute CVA was found with a frequency of  $34.0 \pm 9.15\%$ , and in the control group of women with a frequency of  $35.3 \pm 9.27\%$  ( $p = 0.84$ ). The TT genotype was identified in  $59.2 \pm 9.49\%$  of women with acute CVA and in  $7.8 \pm 5\%$  of women in the control group ( $p = 0.000$ ; OR 17.06; 95% CI 7.50–38.82). In the subgroup of women with acute CVA,  $23.8 \pm 5.81\%$  of patients were carriers of the A allele,  $76.2 \pm 5.81\%$  of patients were carriers of the T allele. In the control group,  $74.5 \pm 5.98\%$  of women were carriers of the A allele,  $25.5 \pm 5.98\%$  of women were carriers of the T allele ( $p = 0.000$ ; OR 9.34; 95% CI 5.98–14.70).

Table

Frequency distribution of SNP rs10507391 genotypes and alleles (A>T) among patients with acute CVA and in control group							
Genotypes and alleles	Patients with acute CVA ( <i>n</i> = 257)			Control group ( <i>n</i> = 272)			<i>p</i>
	total	%	<i>m</i>	total	%	<i>m</i>	
Genotypes							
AA	18	7.0	3.12	137	50.4	5.94	$p = 0.000$
AT	100	38.9	5.96	108	39.7	5.81	$p = 0.85$
TT	139	54.1	6.09	27	9.9	3.55	$p = 0.000$
Alleles							
A	136	26.5	3.81	382	70.2	3.84	$p = 0.000$
T	378	73.5	3.81	162	29.8	3.84	
OR A/T; 95% CI	6.53; 5.00–8.55						
Total alleles							
AA	18	7.0	3.12	137	50.4	5.94	$p = 0.000$
AT + TT	239	93.0	3.12	135	49.6	5.94	
OR; 95% CI	13.5; 7.87–23.25						
TT	139	54.1	6.09	27	9.9	3.55	$p = 0.000$
AA + AT	118	45.9	6.09	245	90.1	3.55	
OR; 95% CI	10.7; 6.70–17.05						

Note. OR – odds ratio; 95% CI – 95<sup>th</sup> confidence interval, *p* – significance level when comparing the distribution of genotypes with indices of the control group.

The frequencies of the SNP rs10507391 (A>T) genotypes and alleles in the subgroups of patients who suffered from acute CVA and with various cardiovascular pathologies and risk factors were analyzed. The analysis results of the frequencies and alleles distribution in all subgroups corresponded to the distribution in the experimental group of patients with acute CVA.

In the subgroup of patients with arterial hypertension (AH) and history of acute CVA, the genotypes were distributed as follows: the AA genotype –  $7.3 \pm 3.25\%$ , the AT genotype –  $39.0 \pm 6.10\%$ , the TT genotype –  $53.7 \pm 6.23\%$ . In the control group of patients without hypertension and acute CVA, the AA genotype was detected in  $46.3 \pm 10.03\%$  of patients, the AT

genotype in  $44.2 \pm 9.99\%$ , and the TT genotype in  $9.5 \pm 5.89\%$  of patients. Among patients with AH and acute CVA, compared with the control group, a statistically significant predominance of the number of TT genotype carriers ( $p = 0.000$ ; OR 11.06; 95% CI 5.33–22.98) and a statistically significant decrease in the number of AA genotype carriers were found ( $p = 0.000$ ; OR 10.87; 95% CI 5.85–20.41). Differences in the AT genotype were statistically insignificant ( $p = 0.38$ ) (Fig. 1). The A allele frequency in the subgroup of patients with AH and acute CVA was  $26.8 \pm 3.92\%$ , in the control group it was  $68.4 \pm 6.61\%$ . The T allele in the subgroup of patients with AH and acute CVA occurred with a frequency of  $73.2 \pm 3.92\%$ , and with a frequency of  $31.6 \pm 6.61\%$  in the control group. The differences were statistically significant ( $p = 0.000$ ; OR 5.92; 95% CI 4.09–8.55).

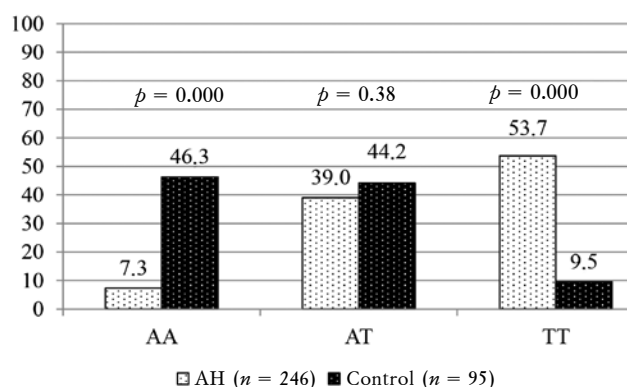


Fig. 1. Frequency distribution of SNP rs10507391 genotypes and alleles (A>T) among patients with AH and history of acute CVA and people in the control group without AH and acute CVA

In the subgroup of patients with cardiac rhythm disturbances (CRD) and history of acute CVA, the frequency of AA genotype was  $3.3 \pm 6.42\%$ , the history of the AT genotype was  $30.0 \pm 16.4\%$ , and that of the TT genotype was  $66.6 \pm 16.87\%$ . The frequencies of SNP rs10507391 genotypes and alleles (A>T) in the control group are presented in Table. Among patients with CRD and acute CVA, compared with the control group, a statistically significant predominance of the number of TT genotype carriers ( $p = 0.000$ ; OR 18.15; 95% CI 7.70–42.75) and a statistically significant decrease in the number of the AA genotype car-

riers were established ( $p = 0.000$ ; OR 29.41; 95% CI 3.95–200.0). Differences in the AT genotype were not statistically significant ( $p = 0.30$ ). A statistically significant predominance of the number of T allele carriers and a decrease in the number of A allele carriers in the subgroup of patients with CRD and acute CVA were compared with numbers in the control group ( $p = 0.000$ ; OR 11.11; 95% CI 5.32–20.83) (Fig. 2).

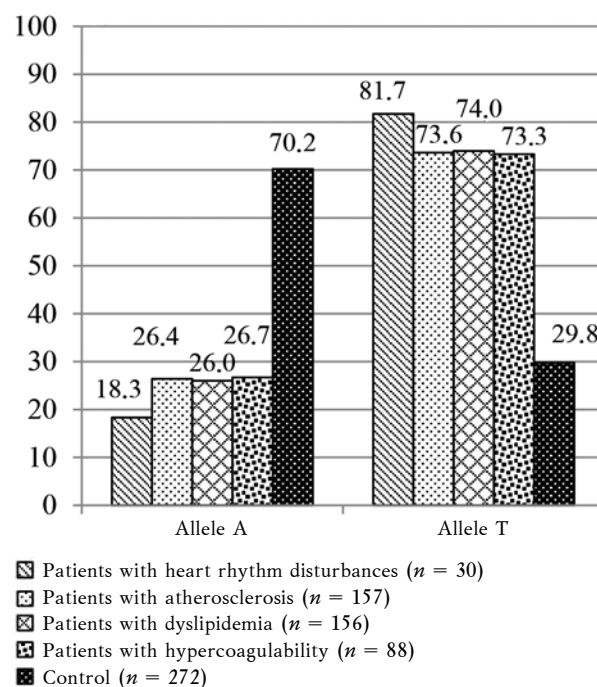


Fig. 2. Frequency distribution of SNP rs10507391 alleles (A>T) among the patients with cardiovascular pathology, its risk factors and history of acute CVA and individuals in the control group

In the subgroup of BCA atherosclerosis patients with history of acute CVA, the frequencies of genotypes and alleles were distributed as follows: AA genotype –  $5.7 \pm 3.64\%$ , AT genotype –  $41.4 \pm 7.70\%$ , TT genotype –  $52.9 \pm 7.81\%$ , A allele –  $26.4 \pm 4.88\%$ , T allele –  $73.6 \pm 4.88\%$ . The frequencies of SNP rs10507391 genotypes and alleles (A>T) in the control group are presented in Table 1. In the subgroup of patients with BCA atherosclerosis and acute CVA, compared with the control group, the TT genotype was statistically significantly more likely to be found ( $p = 0.000$ ; OR 10.18; 95% CI 6.13–16.88) and the AA genotype was statistically significantly less common ( $p = 0.000$ ; OR 16.67; 95% CI 8.19–34.48). The frequencies of the AT genotype were comparable

in the compared groups ( $p = 0.73$ ). The T allele significantly prevailed among patients with atherosclerosis of BCA and acute CVA in comparison with the control group ( $p = 0.000$ ; OR 6.58; 95% CI 4.81–8.93) (see Fig. 2).

In the subgroup of patients with dyslipidemia and history of acute CVA, the frequencies of genotypes and alleles were distributed as follows: AA genotype –  $5.1 \pm 3.46\%$ , AT genotype –  $41.7 \pm 7.74\%$ , TT genotype –  $53.2 \pm 7.83\%$ , A allele –  $26.0 \pm 4.86\%$ , T allele –  $74.0 \pm 4.86\%$ . The frequencies of SNP rs10507391 genotypes and alleles (A>T) in the control group are presented in Table 1. In the subgroup of patients with CRD and acute CVA, compared with the control group, the TT genotype was statistically significantly more frequent ( $p = 0.000$ ; OR 10.32; 95% CI 6.21–17.13) and the AA genotype was statistically significantly less common ( $p = 0.000$ ; OR 18.87; 95% CI 8.85–40.0). The frequencies of the AT genotype were comparable in the compared groups ( $p = 0.69$ ). The T allele significantly prevailed among patients with dyslipidemia and acute CVA compared with the control group ( $p = 0.000$ ; OR 6.571; 95% CI 4.93–9.17) (see Fig. 2).

In the subgroup of patients with impaired hemostasis system and history of acute CVA, the AA genotype was  $6.8 \pm 5.27\%$ , the AT genotype –  $39.8 \pm 10.23\%$ , and the TT genotype –  $53.4 \pm 10.42\%$ . The frequencies of SNP rs10507391 (A>T) genotypes and alleles in the control group are presented in Table. A statistically significant predominance of the number of TT genotype carriers ( $p = 0.000$ ; OR 10.40; 95% CI 5.84–18.53) and a statistically significant decrease in the number of AA genotype carriers were found ( $p = 0.000$ ; OR 13.89; 95% CI 5.85–33.33) in the subgroup of patients with hypercoagulation and acute CVA, compared with the control group. There were no significant differences when comparing the frequencies of the AT genotype ( $p = 0.99$ ). The T allele significantly prevailed among patients with hypercoagulation and acute CVA as opposed to individuals in the control group ( $p = 0.000$ ; OR 6.45; 95% CI 4.42–9.43) (see Fig. 2).

## DISCUSSION

When studying the association of SNP rs10507391 (A>T) with the development of acute CVA in all analyzed groups and subgroups of

patients, a connection was established between the rare TT genotype and the T allele and the increased risk of acute CVA. The results are consistent with published data and are determined by the mechanism by which the action of polymorphism is realized: participation in most types of inflammatory reactions. The uniqueness of this study is the confirmation of the SNP rs10507391 TT genotype (A>T) role as an independent predictor of acute CVA in individuals of the East Siberian population. Previously it was established only among patients of European origin [9].

## CONCLUSION

TT genotype and T allele of the SNP rs10507391 (A>T) increase the risk of developing acute cerebrovascular accident in patients regardless of previous cardiovascular pathology and its risk factors, including patients with arterial hypertension, supraventricular tachyarrhythmias, atherosclerosis of brachiocephalic arteries, impaired lipid metabolism and hemostatic system.

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Tretyakova S.S., Chernov V.N., Kelemenova A.N., Gurazheva A.A. – conception and design, analysis and interpretation of data. Nikulin D.A., Platonova I.M., Marilovtseva O.V., Maksimov V.N. – substantiation of the manuscript, critical revision for important intellectual content. Nikulina S.Yu., Shulman V.A., Chernova A.A., Prokopenko S.V. – final approval of the manuscript for publication.

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