

Clinical and Prognostic Significance of Ace Gene Polymorphisms in Cerebrovascular Disease

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Abstract

This article presents the prognostic significance of ACE gene polymorphisms in various degrees of cerebrovascular disease. The main aim of the ACE gene is to encode the angiotensin-converting enzyme, which catalyzes inactive angiotensin I into active angiotensin II. In 2001, the prevalence of brain pathological defects was 247,2 per 100.000 populations in the Republic of Uzbekistan.

Keywords: Stroke and Recurrent Stroke, Prognostic Significance, Investigations, Examinations, Chronic Cerebral Circulation Insufficiency, Ischemic Stroke.

INTRODUCTION

Objective: To investigate the prognostic significance of ACE gene polymorphisms in relation to the severity of CVDs.

Materials and Methods: Investigations related to cerebral angiodyplasia of extra- and intracranial areas of the brain were performed in the vascular surgery department of the second Tashkent Medical Academy Clinic. As a control group 105 patients diagnosed with CCCI (Chronic Cerebral Circulation Insufficiency) and 50 people without various types of abnormalities in this system were examined.

The majority of patients with cerebral circulatory pathology were aged 25-85 years. Statistical indicators of sick people varied: men in 69 (65.7%) cases, mean 58.4 ± 1.0 ; women in 36 (34.3%) cases, mean 60.9 ± 0.9 . Statistics for healthy individuals varied: men in 32 (64%) cases, mean 24.1 ± 1.4 ; women in 18 (36%) cases, mean 24.4 ± 1.4 . For the purposes of the experiment, the patients were monitored in the vascular surgery of the 2nd TMA Clinic and the anamnesis, clinical, laboratory investigations, examinations by the necessary medical specialists with their further recommendations were carried out.

Duplex color scanning, MSCT (multi-slice computer tomography) of the cerebral region with angiographic complementary examinations have been applied, and molecular genetic and morphological studies have been carried out.

Results: Patients were divided according to cerebral vascular lesions according to Schmidt's classification, 1985. [5].

No initial manifestations of cerebral hemorrhage were detected in the main group and in the control group of patients, TIA (Transient ischemic attack) prevailed in the main group, and amounted to 16 (21.3%) cases compared to the control group of patients 3 (10%). In the main group 45 (60%) patients had stroke in the control group in 20 (66,7%) cases. Of them all 45 (100%) patients in the main group had ischemic stroke (IS), in the control group IS was observed in 20 (100%) cases only (Table 1).

Table 1. Frequency of cerebral circulation disorders in the main and control group of patients

Manifestation	Patients with a pathological deformation of the internal carotid arteries n= 75		Patients without pathological deformation of the internal carotid arteries n= 30	
	abs	%	abs	%
Initial manifestations of N.C.	0	0	0	0
Progressive cerebrovascular disease				
DEP I	9	12	2	6,7
DEP II	64	85,3	27	90
DEP III	2	2,7	1	3,3
TIA	16	21,3	3	10
Stroke	45 (60%)		20 (66,7%)	
Minor stroke	27	60	11	55
Consequences of a previous stroke	18	40	9	45

Microstroke was observed in 27 (60%) cases in the main group and in 11 (55%) cases in the control group. Consequences of a previous stroke were detected in 18 (40%) patients in the main group and in 9 (45%) cases in the control group. Dyscirculatory encephalopathy (DEP) II occurred more frequently in both groups 64 (85.3%) and in the control group 27 (90%) cases.

Of 105 (100%) patients: 65 (62%) had acute stroke (TIA, stroke and recurrent stroke) and the remaining 40 (38%) had chronic cerebrovascular disease (Table 2).

Table 2. Incidence of acute cerebral haemorrhage

	TIA		Stroke		Stroke recurrence		TOTAL	
	Abs	%	abs	%	abs	%	abs	%
Patient group	19	29,7	30	46,9	15	23,4	64	100

Of these, a transient disorder (TIA) was observed in 19 (29.7%) patients, an acute disorder (ONMC stroke) in 30 (46.9%) and a recurrent acute disorder (recurrent stroke) in 15 (23.4%) patients.

Of 105 (100%) patients, 45 (43.8%) had a stroke and recurrent stroke, with 18 (39%) having regressed symptoms and 28 (61%) having residual findings.

The Rankin Scale [7] in patients with DEP and in patients with stroke showed moderate and severe impairment of vital functions, with an average score of 1.7 ± 0.5 and 2.6 ± 0.38 in the main group, and 1.4 ± 0.2 and 2.1 ± 0.3 in the control group of patients. Patients with TIA with no significant impairment and with mild impairment averaged 1.6 ± 0.5 in the study group and 1.2 ± 0.3 in the control group (Fig. 1).

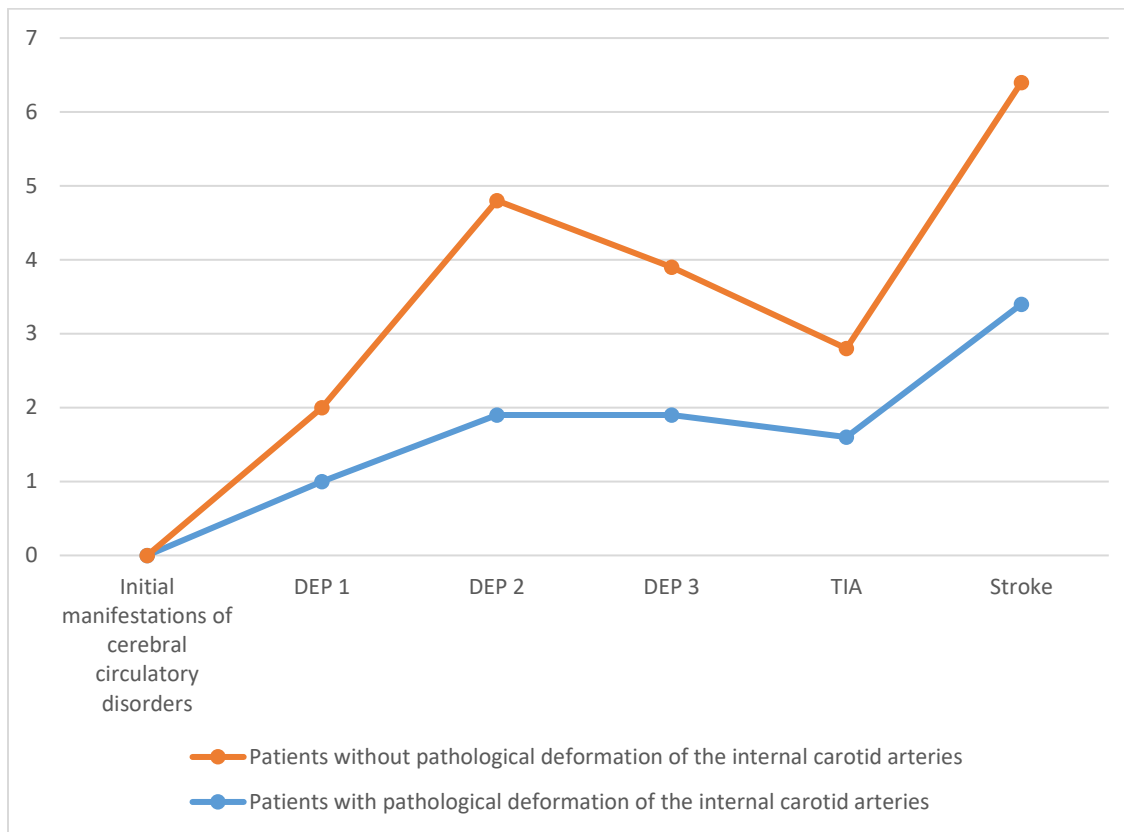


Figure 1. Assessment of the functional status of patients using the Rankine Scale [7]

In patients, the clinical course of CCCI manifests itself by multiple subjective and objective neurological manifestations (Fig. 1). The analysis of subjective symptoms in patients in the main group revealed that the most frequent symptoms in stage II of DEP were: [1] headache 40 (53.3%), dizziness 22 (29.3%), numbness in extremities 28 (37.3%) and decreased memory and sleep disturbance 17 (22.7%) and 19 (25.3%) cases compared to the control group of patients where subjective symptoms were more frequent with stage II DEP 14 (46.7%), 7 (13.3%), 16 (53.3%) and 8 (26.7%), 10 (33.3%) cases. Less commonly, patients complained of tinnitus 12 (16%) and decreased vision in 1 (1.3%) cases in the control group 9 (30%) and 1 (3.3%) respectively.

Analysis of objective symptoms in patients in the main group showed that common objective symptoms in the main group of patients with stage II DEP were central paresis and hemiparesis [2] in 60 (80%) and 10 (13.3%) cases in the control group, and central paresis and CN of XII pair of NMN in 26 (86.7%) cases, hemiparesis and CN of XII pair of NMN in 9 (30%) and 8 (26.7%) cases. Symptoms such as hemihypesthesia and aphasia were mostly uncommon with 6 (8%) and 4 (5.3%) cases in the main group and 2 (6.7%) cases in the control group.

A comparison of TIA and ischemic stroke patients was made [3], where the prevalence of symptoms in ischemic stroke patients was 43 (70.5%) central paresis of EMN pairs and hemiparesis in the control group and 18 (29.5%) in the control group; central paresis of XII CN (cranial nerve) pairs - 19 (82.6%), hemiparesis and CN of XII CN pairs - 9 (39.1%). Such symptoms as hemihypesthesia and cerebellar ataxia were mostly uncommon in both groups of patients who underwent AI - 7 (11.5%), 7 (30.4%) and 8 (34.8%) cases, in the control group the hemihypesthesia and horizontal nystagmus were found in 2 (6.7%) cases each. Horizontal nystagmus and aphasia occurred in the main group of patients in 2 (3.3%) and 6 (9.8%) cases (Figure 2).

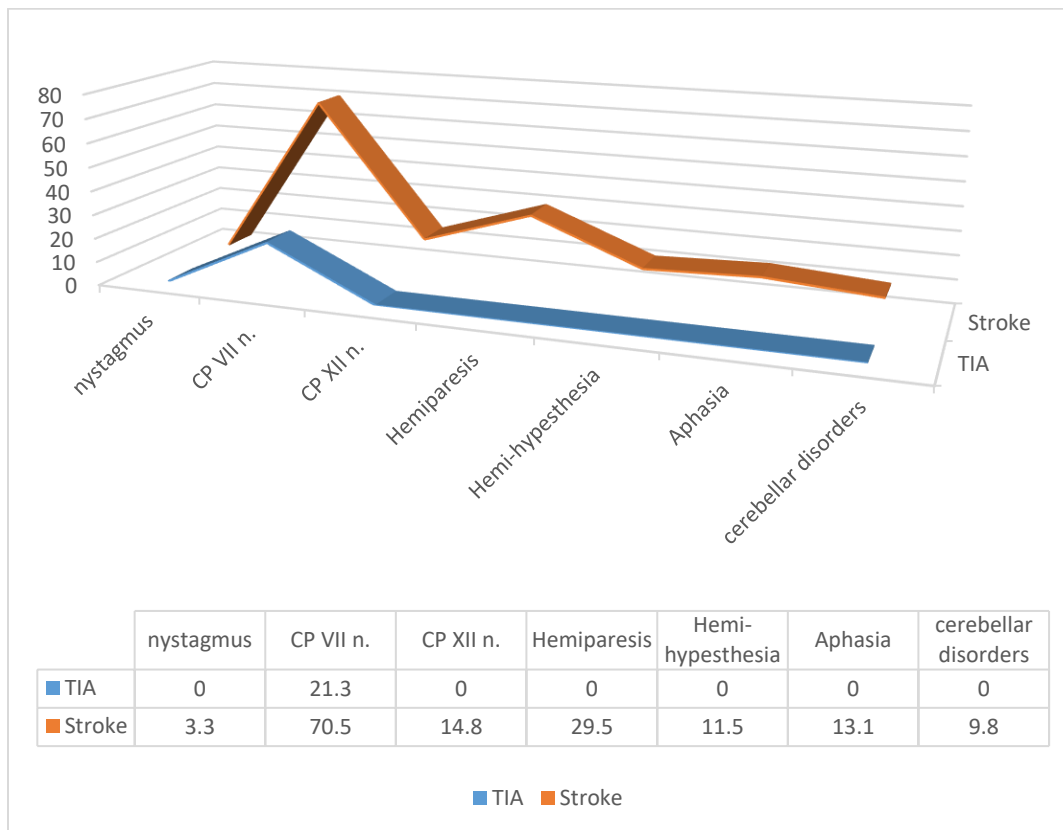


Figure 2. Frequency of objective symptoms in patients in the main group with impaired cerebral circulation

The largest number of patients in the main and control groups occurred in stage II of DEP 64 (85.3%) and 27 (90%).

Analysis of ACE gene polymorphisms [4] depending on DE stage revealed that I/I 16 (21.3%) and I/D 15 (20%) genotypes and DD genotypes were more frequently encountered in II stage of DEP with prevalence of DD genotype 33 (44%) ($P < 0.05$; $\chi^2 = 8.0$; OR=1.8; CI 95%- 0.91-3.72) and carriers of D/D genotype had 1.8 times higher chance to develop CCHD compared with control group of patients, the incidence of genotypes was higher in stage II DEP I/I 9 (30%) and I/D 8 (26.7%) and DD 10 (33.3%) with prevalence of DD genotype ($P > 0.05$; $\chi^2 = 0.18$; OR=0.8; CI 95%- 0.34-2.31), which had no significant association with disease. (Figure 2).

A study of the distribution of ACE gene polymorphisms depending on cerebral circulation disorders (TIA, stroke) (Fig. 2) showed that D/D genotype 31 (50.8%) most frequently occurred in ischemic stroke patients, while microstroke type occurred in 14 (22.9%) patients and stroke outcomes in 17 (27.9%) patients ($P < 0.05$; $\chi^2 = 8.0$; OR=1.8; CI 95%- 0.91-3.72). Also in the control group of patients who had suffered ischaemic stroke, DD genotype was more frequently encountered in 17 (73.9%) cases, but with a small difference in patients who had suffered ischaemic stroke of the microstroke type in 9 (39.1%). At the same time, according to our data, carriage of the DD genotype in patients in the control group has no significant association ($P > 0.05$) with the development of stroke.

CONCLUSIONS

The most common complaints of patients in the main group were headache, dizziness, numbness in the extremities, memory loss, insomnia and tinnitus. These symptoms were most frequently observed in patients with stage II DE.

A study of the distribution of ACE gene polymorphisms depending on cerebral circulation disorders showed that the D/D 31 genotype (50.8%), which has a correlation ($r=0.8$), is the most common in patients who had an ischemic stroke with complicated forms of stroke. Carriage of this genotype increases the risk of stroke by a factor of 2.0.

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