MINISTRY OF HEALTH OF THE REPUBLIC OF UZBEKISTAN
TASHKENT STATE DENTAL INSTITUTE

ABDULLAEVA M.B.

PROGNOSTIC SIGNIFICANCE OF TRANSITORY ISCHEMIC ATTACKS IN THE DEVELOPMENT OF ISCHEMIC STROKE

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Authors:

M.B. Abdullaeva *PhD, Associate Professor of the Department of Neurology and Traditional Medicine at the Tashkent State Dental Institute*

Reviewers:

Haydarov N.K. *MD, Professor of the Department of Neurology and Traditional Medicine at the Tashkent State Dental Institute*

R.B. Azizova *MD, Associate Professor, Department of Neurology and Medical Psychology at the Tashkent Medical Academy*

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List of abbreviations

TIA - Transient Ischemic Attack

IS - Ischemic Stroke

UDG BCS - Ultrasonic Dopplerography of Brachiocephalic Vessels

TDG - Transcranial Dopplerography

BP - Blood Pressure

VBB - Vertebro-Basilar Basin

CB - Carotid Basin

CCA - Common Carotid Artery

ECA - External Carotid Artery

ICA - Internal Carotid Artery

ACA - Anterior Cerebral Artery

MCA - Middle Cerebral Artery

PCA - Posterior Cerebral Artery

CVD - Cerebrovascular Diseases

The monograph presents the results of a scientific research study that aimed to identify the clinical and differential diagnostic features of cerebrovascular diseases. The relevance of the study is undeniable as it is dedicated to the investigation of one of the most widespread pathologies in neurology, significantly affecting the quality of life of patients. The goal of the research was to determine, based on clinical-neurological, neuroimaging, and biochemical studies, the prognostic significance of transient ischemic attacks (TIAs) in the development of ischemic strokes, optimizing their primary prevention.

The scientific novelty of the work lies in the fact that, for the first time, the characteristics of TIAs have been established depending on the vascular territory and factors of vascular comorbidity—the combination of atherosclerosis, uncontrolled arterial hypertension, diabetes mellitus, and other conditions that exacerbate TIAs; the role of changes in cerebral hemodynamics in the development of ischemic strokes after a TIA and their impact on the clinical picture of TIAs has been proven; the influence of blood nitric oxide levels in the development of TIAs and subsequent ischemic strokes has been demonstrated; and the effectiveness of optimized therapeutic and preventive measures for the prevention of ischemic strokes has been proven.

The clinical material is sufficient in volume and is presented with data from the study of 114 patients with various forms of cerebrovascular pathology (CVP). Among them, Group I (main) consists of 80 patients with TIAs, and Group II (comparison) consists of 34 patients with ischemic strokes following TIAs. To achieve the goals and objectives of the study, well-founded methodologies were used: clinical-neurological examination, laboratory tests (blood coagulogram, blood nitric oxide level, blood lipid spectrum), instrumental examinations (Doppler ultrasound of the cerebral vessels, transcranial Doppler, MRI, CT of the brain), and statistical methods (using computer programs). To objectify cognitive impairments in patients with TIAs and strokes following TIAs, a detailed neuropsychological examination was conducted using the MMSE (Mini-Mental State Examination) mental status assessment scale. The risk of stroke in patients with TIAs was assessed using the ABCD2 scale.

The monograph is intended for neurologists, specialists dealing with this problem, master's students, clinical residents, and participants in continuing medical education courses.

INTRODUCTION

Transient ischemic attacks (TIAs), as precursors to acute cerebrovascular accidents—strokes—occupy an important place in the symptomatology of cerebrovascular diseases (CVDs). The complexity of diagnosing TIAs is primarily related to the symptoms that develop due to a significant reduction in blood supply to a part of the brain—local brain ischemia or retinal ischemia (retinal TIAs)—which quickly resolves within 24 hours, and patients do not attach much importance to these disturbances [67, 79]. The clinical outcome of ischemic cerebrovascular disturbances (TIAs or strokes) is determined by the caliber of the artery in which blood flow is disrupted, the location and speed of the occlusion of the cerebral artery, the state of collateral circulation, the rheological properties of the blood. On average, more than 50% of patients with TIAs will develop not only a stroke but also a myocardial infarction within the first year, 20% within the first month, and 50% in the following 5 years [29]. When observing patients who have had a TIA, half of the transient ischemic attacks occur against the background of ischemic heart disease, most patients have arterial hypertension, and 10-20% of patients have diabetes mellitus [29, 79]. Currently, there is an increase in the incidence and mortality of cerebrovascular diseases (CVDs), which confirms the need to change the approach to managing this group of patients. The application of modern clinical-neurological, neurophysiological, and instrumental research methods, with improved differential diagnosis and correction of the somatic status, will allow timely prediction and reduction of the risk of stroke, subsequently reducing disability and mortality from CVDs and cardiovascular diseases in patients with TIAs. "An important aspect of maintaining the health of the population is the early detection of pre-stroke cerebrovascular disturbances and the implementation of screening among the population." It should be noted that the screening of neurological diseases is included in the plan of measures PP-№3925 dated August 30, 2018. The primary tasks awaiting solution at present are timely prevention at all stages of medical care for patients with strokes, the provision of highly qualified and quality medical care through the expanded use of modern technologies, which will improve the quality of life in various strata of the population.

The development of predictive criteria has attracted researchers for many years. Risk scores for transient ischemic attack report that the risk of recurrent ischemic stroke after an episode of TIA is 5-10% and is particularly increased in the first days after the index event (European Stroke Initiative recommendations for stroke management). Clearly, all studies confirm that TIA is just as much a "vascular catastrophe" for the brain as a stroke and requires urgent measures to save patients' lives [17-19, 123, 129, 135]. Great importance was attached in the studies to the differential diagnosis of TIAs with diseases that have similar initial clinical symptoms [55, 58, 60, 67]. In the scientific work of Schwarzburg N.T., the "training" role of

TIAs in the development of acute ischemic stroke in patients was investigated. It should be noted that the results of these studies are quite contradictory. The risk of stroke after episodes of TIA has been proven in numerous epidemiological studies and certainly requires urgent measures to prevent the development of acute ischemic stroke in patients with TIAs. In a systematic review of the results of clinical studies by the Antithrombotic Trialists' Collaboration, clear evidence of the effectiveness of antiplatelet therapy is presented, which can reduce the risk of serious vascular episodes by about 25%. The J-STARS study demonstrated that low-dose pravastatin therapy reduces the frequency of atherothrombotic infarction in patients with a previous ischemic stroke. The SPARCL study demonstrated that high doses of atorvastatin prevent recurrent stroke and led to the AHA/ASA recommending statin therapy for patients with stroke or TIA of atherosclerotic origin.

Since early prediction of the risk of stroke in patients with symptoms within 24 hours of onset has become increasingly clinically relevant in stroke emergency units, the ABCD score was developed (for prognostic factors, age, blood pressure, clinical symptoms, duration of symptoms). The reliability was promising, and therefore additional assessments were developed, which led to a large number of studies aimed at testing these systems or improving them (e.g., ABCD(2), ABCD(2)I, ABCD(3), ABCD(3)I, CIP model, ASPIRE approach, ABCDE+) [103, 105, 106, 107, 136, 139, 143]. Based on the literature we have studied, we have concluded that the prognostic significance of TIAs in the clinic and course of brain strokes is insufficiently studied, and the results of various studies in this area are contradictory. Therefore, we have conducted research to study the prognostic significance of TIAs, with the subsequent development of measures for the primary prevention of brain strokes, aiming to improve patients' prognoses.

The aim of the research is to determine, based on clinical-neurophysiological and biochemical studies, the prognostic significance of TIAs in the development of ischemic strokes, optimizing their primary prevention.

CHAPTER I. LITERATURE REVIEW.

Modern Concepts of Transient Ischemic Attacks.

1.1. Etiological Aspects and Definition of Transient Ischemic Attacks.

The problem of cerebrovascular diseases, specifically strokes, brings together many specialists and makes the issue of preventing the development of this disease multidisciplinary. Within the framework of PP39/25 dated August 30, 2018, "Improving the Neurological Service Provided to the Population," and PP40/63 dated December 18, 2018, "Prevention of Non-Infectious Diseases, Support for Health and Physical Activity of the Population," the development of preventive medicine, early diagnosis of diseases, and the development of therapeutic measures to reduce their complications are relevant issues in Uzbekistan's medicine. An important aspect of maintaining the health of the population is the early detection of pre-stroke cerebrovascular disturbances and the implementation of screening among the population. It should be noted that the screening of neurological diseases is included in the plan of measures PP-№3925 dated August 30, 2018. Currently, according to the Strategy for Action on Five Priority Areas for the Development of the Republic of Uzbekistan in 2017-2021, further improvement of medical care for the population of the country is planned. The primary tasks awaiting solution at present are timely prevention at all stages of medical care for patients with strokes, the provision of highly qualified and quality medical care through the expanded use of modern technologies, which will improve the quality of life in various strata of the population.

Transient cerebral circulatory disturbances (TCCD) are conditions characterized by neurological focal or generalized symptoms, retinal dysfunction, depending on the vascular territory, which are not accompanied by the formation of a brain infarct according to MRI. It is necessary to note that this condition develops suddenly, the developing organic neurological manifestations persist and resolve within 24 hours [40]. However, after the patient's condition is restored, the risk of stroke increases. Transient ischemic attacks (TIAs), as precursors to such an acute cerebrovascular disturbance as a stroke, occupy an important place in the symptomatology of cerebrovascular diseases (CVDs). The syndrome of TIA today is the main syndrome that can subsequently lead to the development of a stroke. According to recent years' research, on average, 40% of patients with TIAs may develop a stroke in the following 5 years, more than 50% in the first year, and 20% within the first month [23, 55, 56, 87]. Thus, the risk of stroke in patients with TIAs is approximately 10% in the first year, and then about 5% annually. The probability of a stroke increases with the age of the patient, and recurrent TIAs bring the probability of an acute cerebrovascular accident closer [27, 55, 57]. This requires therapeutic measures to prevent the development of ischemic strokes in this category of patients. According

to the literature, numerous cohort studies in the United States and other countries show varying incidence and prevalence of TIAs, which is up to 1.1 per 1000 people per year, among Americans, the incidence is 2.3%, and with age, the incidence of stroke increases to 4.6% [18]. In a British study, the incidence of TIAs increases with age, reaching 6.41 per 1000 population among those over 85 years old. It should be noted that a history of TIAs in patients suffering from strokes ranges from 7 to 40% [16, 94]. In Russia, the diagnosis of TIA is made annually in 40,000 people [18]. According to Gafurov B.G., in Uzbekistan, the incidence of TIAs is up to 40,000 cases per year [45]. These figures could be much higher, as TIAs are characterized by rapidly passing clinical symptoms and can be isolated, which reduces patients' seeking medical help [27]. Many researchers note that the episode of TIA quickly passes, leaving no organic disturbances, and both the patients themselves and their relatives do not attach much importance to these disturbances, reducing the appeal to medical institutions [57, 58]. Today, TIA is considered just as urgent a condition as a stroke. Experts from the European Stroke Organization (ESO) have revised the protocols for managing patients with TIAs [68, 103]. Therefore, stroke prevention is one of the priority areas of the strategy for managing patients with TIAs [57].

Concepts of TIAs began to form in the 1950s. In this regard, conferences were held with reports on the prevention of CVDs, descriptions of TIAs were given as a rapidly passing condition in which the emerging organic disturbances quickly disappeared [132]. Further, a classification of CVDs was adopted, compiled by experts from the National Institute of Neurological Diseases of the United States [96]. At the third Princeton Conference (1961), the British neurologist J. Marshall defined the duration of TIAs as 24 hours [131]. Over time, especially with the development of neuroimaging and interventional technologies, the 24-hour time window became increasingly inadequate as a diagnostic criterion [117]. There were many cases where neurological organic symptoms lasted up to 24 hours, and neuroimaging revealed signs of brain infarction [94].

Of course, today's clinical protocols recommend conducting the same plan of examination and therapy for patients with TIAs as for acute CVDs [18, 20]. It should be noted that a complication of TIAs is not only a stroke but also a myocardial infarction, which is possible within 10 years after an episode, observed in 30% of patients [113]. In this case, fatal outcomes in 20-25% of cases are related to myocardial infarction, not a brain infarction [17, 85].

The definition of TIA has also undergone changes with the development of instrumental and neuroimaging methods. TIA is a sudden neurological or retinal deficit of ischemic nature, corresponding to the territory of a particular artery, which completely regresses within 24 hours [128]. It should be noted that only 15% of neurological symptoms regressed within 24 hours, with the duration of the TIA episode being about 1 hour [94]. In 2002, G. W. Albers et al.

proposed a definition of TIA based on neuroimaging results: "TIA is a brief episode of neurological dysfunction caused by focal cerebral or retinal ischemia, with neurological symptoms lasting less than 1 hour and no signs of infarction [43, 16, 98].

Then the American Heart Association/American Stroke Association (AHA/ASA), which specializes in strokes, emphasized the absence of signs of infarction in TIAs caused by focal vascular ischemia of the brain [18, 67]. However, according to the literature, signs of focal brain damage are more often found in patients with prolonged neurological symptoms lasting more than 1 hour, the presence of paresis, aphasia, accompanied by stenosis of the internal carotid artery of more than 50% of the diameter on the side of the brain lesion [67], therefore the new definition of TIA is also disputed.

Clearly, TIA is just as much a "vascular catastrophe" for the brain as a stroke and requires urgent measures to save patients' lives [18, 19, 123, 129, 135].

1.1.1. Pathogenesis of TIAs

One of the first theories of the occurrence of transient disturbances of cerebral circulation and TIAs was the theory of vasospasm [17, 21]. Research in this area showed that cerebral arteries are the least reactive in the human body, and the decisive role of vasospasm receded into the background [91]. Then came the period of hemodynamic concepts—deterioration of cardiac activity in combination with damage to the coronary arteries and cerebral vessels could cause TIAs [44, 46]. The theory put forward for the occurrence of TIAs, known as "cerebral intermittent claudication," was unable to explain the causes of short-term attacks accompanied by organic symptoms that resolve within 24 hours [77].

Since the 1950s, the thromboembolic theory of TIAs has emerged and has increasingly attracted supporters [29, 72]. The development and implementation of instrumental research made it possible to determine the connection between neurological organic disturbances in TIAs with various types of atherosclerotic vascular damage, correspondingly associated with the development of arterial emboli [53, 59, 66]. A very important role is given to the anatomical features of the structure of the cerebral blood supply system—the presence of hypoplasias, pathological tortuosities, anomalies in the structure of the circle of Willis, as well as vertebrogenic anomalies and compression of vessels, which can also be the cause of TIAs [71, 73, 76, 77, 89, 94].

In discussing the clinical picture and prognostic significance of TIAs, there are also various points of view. As written in the Annals of Neurology by Hakam A. and his colleagues (Massachusetts General Hospital, Charlestown, 2005), transient ischemic symptoms (TIS), with

subsequent brain infarction, were considered as a minor ischemic stroke, a variety of transient ischemic attack (TIA), or as an independent syndrome [24, 80]. Studies were conducted on 87 patients with TIAs and 74 patients with ischemic strokes, who underwent brain tomography upon admission [40]. In this case, an acute brain infarction was observed in 36 patients with TIAs (41.3%), but they were smaller than in patients with ischemic strokes—0.7 versus 27.3 ml; nevertheless, the volume of brain damage could not distinguish TIS from ischemic stroke. Neurological symptoms persisted longer in patients with TIS than in patients with a single TIA without brain infarction, but these differences were not statistically significant. The frequency of recurrent stroke or TIA during hospitalization was significantly higher among those with TIS, compared to patients with TIAs without brain infarction, or patients with ischemic stroke: 19.4% versus 1.9% and 1.3%, respectively. Based on the data obtained, the researchers suggest considering TIS (TIA with subsequent brain infarction) as a separate clinical syndrome [83, 124].

Today, the pathogenetic types of TIAs can include atherothrombotic—with damage to large cerebral arteries, associated with atherothrombosis or arterio-arterial embolism; cardioembolic, lacunar—with damage to small cerebral arteries, and caused by rarer causes—in hematological diseases (sickle cell anemia, leukemia, erythremia), venous thromboses, dissection of pre- and cerebral arteries, in immunological disorders (antiphospholipid syndrome) [57, 58, 85, 89, 93]. Often, concomitant arterial hypertension leads to the development of TIAs, causing lipogialinosis and fibrinoid necrosis in the perforating arteries of the brain, which leads to atherosclerotic changes in the cerebral arteries, contributes to the development of cardiac pathology, which is often complicated by cardiogenic embolism. It is precisely the damage to small cerebral arteries as a result of age-related changes, diabetes mellitus, or hypertensive disease that leads to thrombosis with the development of transient local brain ischemia, being the cause of TIAs in 15-30% of patients [57, 69, 82, 85].

In 20% of patients, a TIA attack is associated with cardioembolism, with the formation of embolic fragments on the heart valves or the formation of an intracardiac thrombus. It should be noted that in this case, risk factors for embolism, according to research data, can be atrial fibrillation, an artificial heart valve, a recent myocardial infarction, an intracardiac thrombus, a myxoma [22, 92, 77, 78].

Thus, the mechanism of TIA onset is associated with a focal decrease in cerebral hemodynamics due to damage to cerebral vessels. It should be noted that the main difference between TIAs and acute ischemic stroke lies in the instability of neurological disturbances and the reversibility of the pathological process [68].

1.1.2. Risk Factors for TIAs and TIAs as a Risk Factor for Stroke.

TIAs, as precursors to the development of stroke, in turn, are accompanied by the same risk factors as acute cerebrovascular accidents. According to literary sources, the mechanism of TIA development involves a focal decrease in brain hemodynamics due to damage to cerebral vessels. Pathogenetically, TIAs differ from ischemic stroke and are characterized by regression of the pathological process and organic manifestations in TIAs. Atherosclerotic damage to large and medium-sized arteries plays a leading role in the formation of TIAs, with the carotid and vertebral arteries being predominantly affected [48, 57]. Often, episodes of TIAs are caused by the processes of destruction of atherosclerotic plaques, stenosis, and obliteration of the artery lumen by a plaque, embolism, thrombosis, complicating atherosclerosis in the area of the plaque (atherothrombosis). Sometimes TIAs can be caused by secondary structural changes in the vessels associated with hemodynamic disturbances [42, 57, 68].

Recent studies have shown that TIAs most often (in 25–50%) precede the development of ischemic stroke of the atherothrombotic subtype, in 11–30% of the cardioembolic, and in 9–11% of the hemorrhagic stroke [49]. In the scientific work of Schwarzburg N.T., the "training" role of TIAs in the development of acute ischemic stroke in these patients was investigated. It should be noted that the results of these studies are quite contradictory. The risk of stroke after episodes of TIAs has been proven in numerous epidemiological studies and certainly requires urgent measures to prevent the development of acute ischemic stroke in patients with TIAs [17, 43, 88]. According to research data, in the next 3-6 months after the development of TIAs, the risk of acute ischemic stroke ranges from 10 to 20%. It should be noted that TIAs are often the cause of acute myocardial infarction, and the mortality rate for this reason over 5 years is 20-25% [3, 40]. The risk of acute ischemic stroke after a TIA ranges from 1 to 15% per year, with a relative increase of 2-5 times [68, 100]. Research results show a dependence of the risk of acute ischemic stroke on the nature and duration of TIA symptoms [16, 67, 70, 94].

In patients with TIAs combined with non-valvular atrial fibrillation (risk increases almost 5 times) and arterial hypertension (risk increases 3-8 times depending on blood pressure levels) [10]. It should be noted that acute ischemic stroke in the shortest time after a TIA attack developed in patients who did not follow the doctor's prescriptions [8, 74, 78].

In order to improve the prognosis of patients who have had a TIA, clinical protocols recommend immediate hospitalization, with a full examination and the appointment of necessary treatment [19, 16]. According to the literature, one of the important symptoms indicating the formation of an atherosclerotic plaque in the carotid artery is transient blindness, which accompanies TIA attacks [31, 35].

For the prevention of cerebrovascular diseases, it is recommended to examine The ABCD2 scale is commonly used for sorting patients with transient ischemic attack (TIA) who are at high risk for subsequent stroke [103].

1.2. The Role of Occlusive Lesions of Major Head Arteries in the Development of Acute Forms of Cerebrovascular Insufficiency.

The clinical picture of TIAs is very diverse, but the most important thing is that there are no clear pathognomonic symptoms in this pathology, the presence of which would help clinicians in diagnosing and timely deciding on the treatment tactics of the detected lesions, including the question of surgical correction of the pathology [18, 19].

Transient cerebral circulation disorders are characterized by researchers with a variety of symptoms [62]. These are rapidly regressing symptoms associated with sensory deficits, visual disturbances, including ipsilateral monocular or homonymous field defects, headache, tinnitus, periodic dizziness, personality changes with progressive mental disorders, reduced intelligence, reduced understanding of logical-grammatical and semantic structures, signs of anxiety, depression, various phobias, and other manifestations of cerebral asthenia. The mentioned symptoms with varying degrees of intensity are manifestations of TIAs [20, 23]. A special place is occupied by the correct differential diagnosis of TIAs with other diseases that have transient neurological disturbances: migraine, epileptic seizure, Meniere's disease, vestibular neuritis, benign positional vertigo, the debut of multiple sclerosis, hypoglycemic state, brain tumors, etc. In all these conditions, symptoms of transient neurological disturbances similar to TIA attacks may be noted [13, 67]. It is necessary to note the importance of the correct differential diagnosis of a TIA attack with an acute ischemic stroke, which can be the cause of increased mortality due to acute cerebrovascular accident. A significant group (16.2%) consists of patients with discirculatory encephalopathy, in whom, along with cognitive impairments, general weakness, dizziness, instability when walking, and falls are noted [13, 60, 67]. Differential diagnosis with hypertensive crises, acute hypertensive encephalopathy, and minor stroke is of great importance [1].

Depending on the localization of the process in the internal carotid artery system, hemiparesthesias are noted on the opposite side of the focus, sometimes hemiparesthesias. There may be local pareses of central origin, affecting one group of muscles, with pathological symptoms, anisoreflexia, which are temporary in nature [1, 4, 64]. With the localization of the process in the basin of the left middle cerebral artery, transient aphasia with motor and sensory

disturbances in the right half of the body is noted, and the development of epileptic seizures is possible [71].

With impaired hemodynamics in the proximal part of the internal carotid artery, monocular blindness may develop on the side of vessel occlusion (due to retinal ischemia) in combination with a contralateral central paresis of the limbs [51, 90].

With predominantly cortical localizations of TIAs, a transient brachiofacial paresis may be fixed on the opposite side with a predominant weakness and/or numbness of the wrist and a slight central paresis of the facial nerve.

In cases of steno-occlusive lesions of the left internal carotid artery in right-handed patients, episodes of not severe aphasic disorders may occur—so-called cortical dysphasia [20, 95].

In the vertebrobasilar system (VBS), in addition to dizziness and tinnitus, vegetative disturbances such as nausea, vomiting, hiccups, pallor of the skin, and diffuse hyperhidrosis are manifested. Headaches often occur, usually in the occipital region, increasing with changes in head position. TIAs in the VBS are three times more common than in the carotid artery, being precursors of ischemic stroke in up to 50% of cases, with visual, coordination, and auditory disturbances [52]. Visual disturbances such as photopsias, metamorphopsias, field defects, scotomas, and a sensation of a "veil" before the eyes are noted. Disorders of ocular motor innervation with diplopia may occur. Relatively rarely, transient disturbances of the function of the bulbar part of the brainstem (dysphonia, dysphagia, dysarthria) arise. Alternating syndromes are also rarely observed [63].

Sometimes there are disturbances of consciousness, loss of orientation, short-term loss of memory. The disturbance of consciousness most often occurs in the form of stupor or fainting states with mono- or paraparesis. Such a state, which occurs with loss of consciousness, is called the Unterharnscheidt syndrome [51, 52, 63, 64, 90].

In recent years, special attention has been paid to cognitive impairments in TIAs. According to research, cognitive deficits are noted in 40% of patients with TIAs, although focal brain lesions are not observed. It should be noted that psycho-emotional disturbances progress with each subsequent TIA attack, thereby exacerbating the clinical course of the disease [15, 24, 75]. A comparative study of the cognitive sphere in patients with cerebral hypertensive crisis and TIAs showed complete restoration of cognitive sphere indicators in patients with CGK than with

TIAs, which confirms the fact of neuronal network malfunction in TIAs. Many authors come to the conclusion that the progression of cognitive impairments in TIAs makes it difficult to control the course of the disease, reduces the patient's ability to follow the doctor's recommendations for preventing acute ischemic stroke, thereby increasing the risk of recurrent TIAs and strokes [68].

Thus, the diversity of neurological symptoms, combined with their transient nature and progressive cognitive deficits, is often the cause of a non-serious attitude towards the diagnosis of TIAs, both on the part of the patient and medical workers.

1.3. Strategy for the Diagnosis and Treatment of TIAs.

The prevention of TIAs consists of preventing the development of ischemic stroke after TIAs [5, 40]. All methods of secondary prevention of TIAs and strokes are included in the recommendations for the management of patients with TIAs and strokes. Screening of patients with TIAs includes laboratory, biochemical (coagulogram, lipid spectrum, blood glucose level) and instrumental studies (electrocardiography, computed tomography of the brain, non-invasive visualization of extra- and intracranial arteries (ultrasound, tomographic methods) [125]. It is important to note the role of neuroimaging methods in TIAs, which help in differential diagnosis; detects cerebral ischemia in the history, thereby confirming the vascular nature of the process; allows the exclusion of acute brain infarction, which would speak in favor of TIAs. Auxiliary diagnostic methods include: transthoracic or transesophageal echocardiography, contrast arteriography, detailed study of hemocoagulation, determination of antiphospholipid antibodies, 24-hour Holter monitoring, cerebrospinal fluid studies, etc. [94].

In Russia, the diagnosis and treatment of TIAs are carried out in accordance with the Order for the Provision of Medical Care to Patients with Acute Cerebrovascular Accidents (approved by Order of the Ministry of Health of the Russian Federation No. 928n dated November 15, 2012), which is mandatory for implementation throughout the territory of the Russian Federation, and the Standard of Specialized Medical Care for TIAs (approved by Order of the Ministry of Health of the Russian Federation No. 1693n dated December 29, 2012), which correspond to international recommendations. According to the recommendations of the European Stroke Organization (ESO), the management tactics for patients with TIAs are conducted as in acute ischemic stroke [65]. The necessary instrumental studies include electrocardiogram (ECG), head computed tomography, non-invasive visualization of extra- and intracranial arteries. In the event of an acute onset of symptoms of an acute cerebrovascular accident, any patient should be delivered to a specialized department as soon as possible. In

cases indicating a history of TIA, an examination should be carried out (including MRI of the head, non-invasive visualization of extra- and intracranial arteries, ECG, echocardiography) within 24 hours [68]. The most important aspect in the management of patients with TIAs is the control of risk factors—diabetes, hypertension, hyperlipidemia, heart disease, the fight against obesity, smoking, and alcoholism [8]. According to research, the most dangerous period is from 48 to 72 hours after a TIA episode [9, 17].

To improve the prognosis of patients who have experienced a transient ischemic attack (TIA), doctors recommend immediate hospitalization. Additionally, to develop an effective treatment strategy, it is necessary to specify the specific transient symptoms of cerebral circulation impairment that the patient may have. For example, one important symptom indicating the formation of an atherosclerotic plaque in the carotid artery is transient blindness. According to English medical professionals, approximately one in five patients with cerebrovascular insufficiency manifests this symptom. As a primary preventive measure against TIAs, regular examination of patients over 40 years old by a neurologist to assess neck vessels is crucial. In some cases, surgery is recommended to prevent recurrent TIAs and strokes. Furthermore, targeted preventive measures aimed at reducing risk factors significantly improve the clinical picture. It is observed that stroke most commonly develops in patients who, in addition to atherosclerosis, have a history of conditions such as diabetes and hypertension. This association is due to the negative impact of these diseases on vascular health. The patient's lifestyle also plays a crucial role. Harmful habits such as smoking and improper diet leading to excess weight significantly increase the risk of stroke. Unfortunately, many patients only consider these factors after experiencing their first cerebral circulation attack [6, 7, 30, 32, 33, 34, 86].

Great importance in the prevention of atherosclerosis is given to non-drug methods, such as a low-fat diet (reducing fat intake to 30% of total caloric intake and cholesterol to 300 mg per day). In cases of detecting hyperlipidemia (an increase in total cholesterol levels above 6.5 mmol/L, triglycerides above 2 mmol/L, and phospholipids above 3 mmol/L, a decrease in high-density lipoproteins to less than 0.9 mmol/L), a stricter diet is recommended (reducing fat intake to 20% of total caloric intake and cholesterol to less than 150 mg per day) [116]. In the case of atherosclerotic lesions of the carotid and vertebral arteries, a very low-fat diet (reducing cholesterol intake to 5 mg per day) can be used to prevent the progression of atherosclerosis. If significant hyperlipidemia is not reduced within 6 months of the diet, the use of antihyperlipidemic drugs (lovastatin, simvastatin, pravastatin, or others) is recommended, but

only in the absence of contraindications to their use [84]. A healthy lifestyle without bad habits and combating physical inactivity is also of great importance.

The TIA syndrome is currently the main syndrome that can subsequently lead to the development of a stroke. According to recent studies, on average, 40% of patients with TIA may develop a stroke within the next 5 years, more than 50% within the first year, and 20% within the first month [23, 55, 56, 87]. The likelihood of developing a stroke increases with the patient's age, and recurrent TIAs bring the probability of acute cerebrovascular accident (ACVA) closer [27, 55, 57]. The clinical picture of TIA is highly variable, and to establish an accurate diagnosis, it is necessary to use instrumental diagnostic methods that confirm the diagnosis and allow for the selection of the optimal management strategy for patients with TIA [5]. Based on the literature we studied, we concluded that the prognostic significance of TIA in the clinic and the course of cerebral strokes is insufficiently studied, with contradictory results from various studies in this area. Therefore, we conducted studies to examine the prognostic significance of TIA, followed by the development of measures for the primary prevention of cerebral strokes.

CHAPTER II. CLINICAL MATERIAL AND RESEARCH METHODS

2.1 General Characteristics of the Material

To achieve the scientific goals and objectives set, the study included 114 patients with various forms of cerebrovascular pathology (CVP), who were treated in the neurology department of the 3rd clinic of TMA. Among them, Group I (main) consisted of 80 patients with TIA, and Group II (comparison) included 34 patients with ischemic stroke following TIA. It is important to note that all patients in Group II were in the acute and early recovery periods of stroke.

Regarding gender distribution, there was a predominance of males with a ratio of 1.5:1. The average age of the patients was 68.3±3.2 years. As shown by the presented data, the largest age group of patients with ischemic stroke were the elderly (53.8%), followed by middle-aged patients (34.1%), and those of advanced age (12.1%).

All subjects had satisfactory socio-economic conditions. Patients with metabolic, toxic, or drug-induced encephalopathies, Parkinson's disease, Alzheimer's disease, epilepsy, brain injuries, infectious, demyelinating, hereditary degenerative diseases of the CNS, and those with decompensated somatic pathology were excluded from the study.

Research methods included clinical and neurological examination, general clinical methods (general blood and urine analysis), and biochemical studies (blood coagulogram, blood nitric oxide level, blood lipid spectrum). Instrumental methods included ultrasound Dopplerography of the brachiocephalic vessels (USDG BCS), transcranial Dopplerography (TCDG), magnetic resonance imaging (MRI), and computed tomography (CT) of the brain. Statistical methods (using computer programs) were used for data analysis. For the objectification of cognitive impairments in patients with TIA and stroke after TIA, a detailed neuropsychological examination was conducted using the Mini-Mental State Examination (MMSE) scale. The risk of stroke in patients with TIA was assessed using the ABCD2 scale.

2.2 Clinical and Neurological Examination

The neurological status and medical history of all patients were thoroughly studied. In the medical history, attention was paid to the duration and frequency of transient ischemic attacks (TIA), and the severity of neurological symptoms during TIA. For patients who had experienced an ischemic stroke (IS), attention was given to the frequency of TIA before and after the stroke, the vascular territory where the TIA and IS occurred, and the impact of TIA frequency and severity on the severity and degree of neurological deficit in IS.

The neurological status examination focused on the presence and degree of cranio-cerebral innervation insufficiency, motor sphere characteristics, muscle tone, tendon reflex changes, presence of pathological signs, coordination disorders, sensitivity disorders, pelvic organ function, and higher brain functions impairments.

2.3 Ultrasound (USDG BCS) and Transcranial (TCDG) Dopplerography

Cerebral hemodynamics and the state of major arterial vessels (MAG) were studied using ultrasound Dopplerography with a "VAZOSKAN" device from "SONICAID" (UK), employing 2, 4, and 8 MHz sensors with diameters of 14, 10, and 6 mm. The studies were conducted in the GMC clinic. Examinations were performed with patients lying on their backs, heads turned to the opposite side of the examined vessels. A water-soluble gel from "Hewlett-Packard" (USA) was used for better skin contact. The common carotid artery was examined at the lower edge of the sternocleidomastoid muscle, and its bifurcation at the upper edge of the thyroid cartilage. The internal carotid artery was localized anterior to the angle of the mandible. The supraorbital artery was located by placing the sensor at the inner corner of the eye. Blood flow in the vertebral artery was studied by placing the sensor behind the earlobe on the mastoid process of the temporal bone.

The vertebral artery was localized in the supraclavicular and subclavian areas. The computer of the device recorded the data obtained from the study as a summary table or separately for each localization point.

The method of ultrasound Dopplerography is based on the Doppler effect, which posits that when ultrasound is reflected from a moving object (erythrocytes), its frequency changes according to the formula: $Fd = Fo - Fi = 2\ Fo \times V / Ci$, where Fd is the difference between the incident and reflected ultrasound frequencies, Fo is the incident ultrasound frequency, V is the speed of the reflecting surface, Fi is the reflected sound frequency, and Ci is the speed of ultrasound propagation in the medium, approximately 1450 m/s for body tissues [46, 47]. Using the Doppler effect and knowing the direct relationship between the Doppler frequency and the speed of the reflecting surface, we could evaluate the state of blood flow in the vessels.

The Doppler picture in patients was studied using spectral analysis of the Doppler signal. The Doppler gates were set to sizes no more than half the diameter of the examined vessel. The probing ultrasound beam was directed at the main blood flow at the most acute angle possible, not exceeding 60 degrees. The audio and spectrograms were evaluated during the study. The audiogram initially indicated the presence or absence of turbulence. In a normal vessel, the concentration of energy in the high-frequency range of the Doppler signal, especially during the systolic peak, gives the sound a smooth whistling tone, unlike the rough noise characteristic of

turbulence. This is because in areas of vessel narrowing or abrupt diameter changes, irregularities in blood flow occur, causing most erythrocytes to move at speeds different from normal. The spectrogram was assessed both qualitatively and quantitatively.

Qualitative analysis involved evaluating the shape of the enveloping curve, the state of the arterial "window" under the systolic peak, and the intensity of the wave energy spectrum. Quantitative analysis included calculating hemodynamic frequency parameters: the maximum systolic frequency, characterizing the maximum speed at the examined point during systole, and the maximum diastolic frequency, reflecting the minimum systolic speed at the examined point. These parameters were calculated in kilohertz, based on the curves derived from the device's computer as an arithmetic average over several consecutive heart cycles.

Other quantitative analysis parameters included the circulatory resistance index (CRI), characterizing circulatory resistance in the examined artery basin. The CRI was calculated using the formula: CRI = (MaxA - MaxD) / MaxA [46, 47].

The spectral broadening index (SB) reflects blood flow turbulence, indicating the increase in the difference between the maximum and linear blood flow speeds during systole. It serves as a quantitative characteristic of wave spectrum broadening, being one of the most sensitive parameters in determining the hemodynamic significance of the process in the examined vessel, calculated using the formula: SB = (MaxA - MaxD) / MaxA [46, 47].

TCDG was performed on 32 patients with TIA once every 6 months, on 18 patients once a month, and on 12 patients with stroke after TIA, as well as on 15 healthy individuals of the same age group as a control group, using an ultrasound device from "Philips." Quantitative blood flow characteristics were assessed: systolic and diastolic blood flow speeds, systolic-diastolic ratio, peripheral resistance index, and the asymmetry coefficient of blood flow velocities in corresponding arteries.

2.4 Biochemical Studies

2.4.1 Nitric Oxide Study

Biochemical studies were conducted at the Central Scientific Research Laboratory (CSRL). The assessment of biochemical parameters was carried out dynamically — before and at the end of treatment. The endothelial function in patients was evaluated by the content of nitric oxide (NO) in erythrocytes and the activity of enzymes regulating its metabolism.

The NO level in blood serum was determined by the sum of nitrate and nitrite metabolites (NO_2^- and NO_3^-) using the Grees reagent in a modified method. To this end, 0.5 ml of blood

serum was added to 0.3 g of cadmium dust impregnated with copper (metallic zinc granules were placed in a Petri dish and covered with a 2% cadmium sulfate solution. The resulting loose porous film of metallic cadmium on the zinc granules was scraped off with a thin glass spatula and transferred to a beaker of water. The obtained porous cadmium was washed three times with water, homogenized by light grinding in a porcelain mortar to obtain fine particles of about 0.3-0.8 mm. Then, the cadmium was copper-plated by shaking it in a 5% copper sulfate solution. Subsequently, the excess copper and formed $Cd(OH)_2$ were removed by washing the precipitate in 0.1N hydrochloric acid. After this, the mixture was centrifuged, the hydrochloric acid residue was decanted, and the precipitate was placed in a thermostat to dry). To determine the NO content, the samples were heated in a water bath for 60 minutes at 100°C. After cooling, the samples were centrifuged at 1200 rpm for 10 minutes. The NO metabolites were determined in the supernatant. To 0.1 ml of the supernatant, 0.05 ml of 5% NH_4Cl and 1.5 ml of Grees reagent (1% sulfanilamide, 0.1% naphthylethylenediamine, 2.5% phosphoric acid (Sigma, USA)) were added and incubated for 10 minutes at room temperature. The absorbance was measured at 546 nm on an SF-46 spectrophotometer (Russia). Sodium nitrite ($NaNO_2$) was used as the standard. The calculation was made using the formula:

$$A=k\cdot E \text{ (nmol/l)},$$

Where, k is the calculation coefficient, and E is the extinction index of the sample.

Nitrate reductase activity (NR) was determined by the method of Vavilova T.P. and Petrovich Y.A. [5]. For this, 0.5 ml of blood serum was added to 5×10^{-2} phosphate buffer pH 6.5 containing 0.1 ml dithionite (4.6×10^{-3} M in 95×10^{-3} M $NaHCO_3$), 0.1 ml 50 mM NADPH, and 0.1 ml $NaNO_3$ (1×10^{-1} M). The resulting mixture was incubated at 37°C in a water bath for 30 minutes. After incubation, the samples were shaken vigorously until complete decolorization and the volume was brought to 2.0 ml with distilled water. Then, reagents for nitrites, including the Grees reagent, were added. NR activity was calculated using the formula:

$$A=\frac{Eo-Eucx}{t\cdot V\cdot m} \text{ (nmol/min/mg)},$$

where E_o is the amount of nitrites (μmol/l) determined after incubation, E_{init}, is the initial amount of nitrites (μmol/l) before incubation, t is the incubation time (30 min), V is the sample volume (0.5 ml), and m is the protein content (mg/ml) determined by the method of O.H. Lowry et al. (1951).

NADPH-diaphorase activity was determined by the method of Hope V.T., Vincent S.R.S. (1989) modified by Komarin A.S. and Azimov R.K. (2005). For this, 0.1 ml of blood serum was added to 0.1 ml of a 0.1% glutaraldehyde solution and incubated for 2 hours in 0.1 M phosphate buffer pH 7.4. Under these conditions, only NADPH-diaphorase retained its activity. To 0.2 ml

of the mixture, 3 ml of 0.1 M phosphate buffer containing 0.3% Triton X-100 "Serva", 0.5 mM nitro blue tetrazolium (NBT) "Sigma", and 1 mM reduced nicotinamide adenine dinucleotide phosphate ($NADPH_2$) "Sigma" were added. The resulting composition was incubated for 10 minutes at 37°C in a water bath. Then, 0.5 ml of 15% trichloroacetic acid (TCA) was added, and the samples were centrifuged again at 3000 rpm for 15 minutes. The samples were identified on an SF-46 spectrophotometer (Russia) at 565 nm. The enzyme activity (A) was expressed in nmol/min/mg protein, calculated using the formula:

$$A = \frac{\Delta E \cdot 3{,}0}{k \cdot V \cdot t \cdot m},$$

where ΔE is the difference in extinction between the control (without protein) and the test sample, 3.0 is the volume (ml) of the substrate, k is the calibration coefficient equal to 6.52×10^3 $mM^{-1} \cdot cm^{-1}$, V is the sample volume (0.1 ml), ttt is the incubation time (10 min), and mmm is the protein content in the sample (mg/ml).

All studies on patients were conducted dynamically — before treatment, on the 10th, and 30th days. The obtained clinical and biochemical research results were statistically processed using the Student's t-test to check for normal distribution (kurtosis criterion) and equality of general dispersions (Fisher's F-test) in the StatSoft, Inc. (2001) STATISTICA software system, version 6. Differences between the compared values were considered significant at a 5% significance level. Pearson's correlation analysis was performed to identify the degree of correlation between the studied parameters.

2.5.1. Neuroimaging Diagnosis of the Brain

Neuroimaging studies were conducted using magnetic resonance imaging (MRI) and multislice computed tomography (CT) of the brain. These investigations were performed on all patients with transient ischemic attack (TIA) and stroke following TIA.

2.5.2. Magnetic Resonance Imaging (MRI)

The MRI studies were conducted in the radiology department of Clinic 3 at the Tashkent Medical Academy using a "Magnetom Open Viva" (Siemens) machine with a magnetic field strength of 0.2 Tesla. Imaging was performed in coronal and transverse projections using a general-purpose flexible radiofrequency body coil with the patient in a neutral supine position. The standard protocol for T1-weighted MRI in spin-echo mode in the coronal projection included an echo time of 13 ms, a repetition time of 37 ms, a flip angle of 45 degrees, a field of view of 180x180 mm, a matrix size of 256x256, 12 slices, and a slice thickness of 5 mm. T2-weighted spin-echo studies in the axial projection included an echo time of 13 ms, a repetition

time of 37 ms, a flip angle of 45 degrees, a field of view of 180x180 mm, a matrix size of 256x256, 12 slices, and a slice thickness of 5 mm.

Additionally, MRI was performed using a Siemens Magnetom Symphony machine equipped with a superconducting magnet system with a field strength of 1.5 Tesla. Tomograms were obtained using standard techniques in axial, sagittal, and coronal projections with pulse sequences T2, T1, FLAIR (Fluid-Attenuated Inversion Recovery), and DWI (Diffusion-Weighted Imaging).

Ventricular System Analysis

The analysis of the ventricular system was conducted on axial slices, as shown in Figures 1 and 2. The following measurements were taken:

- A: Maximum distance between the anterior horns along the lateral edge (MFHD)
- B: Minimum size of the lateral ventricles (MWLV)
- C: Maximum size of the third ventricle (MV3)
- D: Inner cranial diameter at the level of the anterior horns of the lateral ventricles (IsdLFh)
- E: Inner cranial diameter at the level of the caudate nucleus (IsdhCn)
- F: Maximum inner cranial diameter (MISd)
- G: Outer cranial diameter at the level of the anterior horns (OsdFh)
- H: Maximum outer cranial diameter (MOSd)
- I: Minimum size of the lateral ventricles (at the level of the cella media) (MWLVc)
- K: Width of the fourth ventricle (maximum transverse diameter) (MV4)

To account for overall head size, the data were evaluated as ratios:

- Evan's ratio (ER): ER = A/F*100
- Bifrontal index (BFI): BFI = A/D*100
- Bicaudate index (BCI): BCI = B/E*100
- Central part lateral ventricle index (CMI): CMI = H/I
- Frontal horn index (FHI): FHI = G/A
- Ventricular index (VI): VI = B/A
- Hakman's number (HN): HN = B + A

These indices and measurements were used to assess the ventricular system's size and shape, providing a detailed view of brain structures and potential abnormalities.

2.6. Neuropsychological Examination of Patients with TIA and Stroke after TIA

Mini-Mental State Examination (MMSE)

The studies were conducted by a physician and a nurse in a separate room, in a trusting and calm environment. The evaluation of responses was based on the following criteria: the total score is 30. The MMSE assessment criteria are as follows: 30 - maximum score, 27-25 - moderate cognitive impairment, 24 and below - severe cognitive impairment (dementia) (Table 2.1) [15,24].

Table 2.1

Mini-Mental State Examination (MMSE)

Cognitive Domain

Cognitive Domain	Max Score	Description
1.	5	Ask the patient to name the year, season, date, day of the week, and month completely. A maximum score (5) is given if the patient independently and correctly names the date, month, and year. Each mistake or lack of response reduces the score by 1 point.
2.	5	Ask the patient: "Where are we?" The patient should name the country, region, city, institution where the examination is taking place, and the floor. Each mistake or lack of response reduces the score by 1 point.
3.	3	Give the patient the instruction: "Repeat and try to remember three words: apple, table, coin." You should say the words as clearly as possible at a rate of one word per second. Correct repetition of each word by the patient is scored as one point per word.
4.	5	Ask the patient to subtract 7 from 100 sequentially. Five subtractions (down to 65) are sufficient. Each mistake reduces the score by 1 point. If the patient is unable to perform this task, ask them to spell the word "world" backwards. Each mistake reduces the score by 1 point.
5.	3	Ask the patient to recall the words learned in step 3. Each correctly named word is scored as 1 point.
6.	2	Show the patient two simple objects, such as a pen and a watch, and ask them to name them.
7.	1	Ask the patient to repeat the sentence: "No ifs, ands, or buts."
8.	3	Give the patient a piece of paper and ask them to follow your commands sequentially: "Take the paper in your right hand, fold it in half, and place it on the table."
9.	1	Ask the patient to follow a written instruction on a piece of paper: "Close your eyes."
10.	1	Ask the patient to write any sentence independently (it should contain a subject and a predicate).
11.	1	Give the patient a piece of paper and ask them to copy a drawing. The task is considered complete if the patient's drawing shows all 10 angles, 2 of which intersect.

Determination of Stroke Risk Using the ABCD2 Scale

All patients with TIA should be evaluated using the ABCD2 scale to assess their risk of stroke. The ABCD2 scale (S.K. Johnston) is a rapid clinical tool that helps predict the early risk

of stroke within the first 2, 7, and 90 days after a transient ischemic attack (TIA) or minor stroke. The ABCD2 scale is based on five parameters:

- Age
- Blood Pressure
- Clinical Features
- Duration of TIA
- Diabetes

Each parameter is scored, and the results are summed, yielding a total score that ranges from 0 to 7.

2.7 Statistical Processing of Research Results

Statistical processing of the research results was conducted using standard methods of variation statistics. Quantitative characteristics of the studied traits, which follow the law of normal distribution, were presented as (M±σ), where M is the arithmetic mean value and σ is the standard deviation of these values. For comparing values, the Student's t-test and Chi-square test for contingency tables, as well as Pearson's linear correlation coefficient (r), were used. When the distribution of results differed from normal, analysis was conducted using non-parametric statistical methods. For comparing values, the Wilcoxon test (for assessing differences between quantitative data within groups) and the Mann-Whitney test (for assessing differences between groups) were used.

Differences were considered significant if the obtained p-value for the given criterion (test) was below the critical level of significance p=0.05. Statistical processing of the study was carried out on an IBM PC-compatible computer using the Microsoft Excel spreadsheet editor and IBM SPSS Statistics software version 22.0 (2013).

CHAPTER III. CLINICAL AND NEUROLOGICAL CHARACTERISTICS AND ANAMNESTIC FEATURES OF TRANSIENT ISCHEMIC ATTACKS

3.1. Clinical and Anamnestic Features of TIA in the Carotid Basin

We studied the clinical picture of TIA in 114 patients. In 80 patients, TIAs were considered as manifestations of pre-stroke forms of cerebrovascular insufficiency, while in 34 patients, TIAs preceded the development of ischemic stroke. Based on this, all patients were divided into two groups: the first (main) group consisted of 80 patients with TIA, and the second (comparison) group consisted of 34 patients with ischemic stroke following TIAs. When distributed by gender, we found a predominance of males with a ratio of 1.5:1. The average age of the patients was 68.3±3.2 years. As shown by the data, the largest age group of patients with ischemic stroke comprised elderly individuals (53.8%), middle-aged patients made up 34.1%, and the very elderly constituted 12.1%.

Comorbid somatic disorders play an important role, as they can aggravate the course of TIA and contribute to the development of ischemic stroke in patients with TIA. Therefore, an analysis of the spectrum of comorbid diseases in the somatic status of the examined patients was conducted (Table 3.1).

Table 3.1

Comorbid Diseases

Disease	Patients with TIA (n=80)		patients with II (n=34)	
	abc	%	abc	%
Hypertensive disease	75	93,75	34	100
Atherosclerosis	52	65	20	58,82
Ischemic heart disease	22	27,5	11	32,35
Diabetes mellitus	9	11,25	9	26,47
Rhythm disturbance	2	2,5	4	11,76
Chronic heart failure		0	1	2,94
Acquired heart defect	1	1,25	2	5,88

As seen from the table, the most common comorbid conditions associated with TIA and II in our observations were hypertensive disease, which was present in almost all patients (93.7% and 100% respectively). Atherosclerosis was observed in more than half of the patients in both groups (65% and 58.2% respectively). Additionally, almost one-third of patients with TIA and II

had ischemic heart disease (22% and 11% respectively). Furthermore, an analysis of treatment compliance in patients before the onset of TIA was conducted, showing that regular intake of antihypertensive drugs was only observed in 11 patients (14.67%), and only 6 patients (11.53%) with atherosclerosis received lipid-lowering therapy.

As demonstrated by the conducted clinical-neurological studies, the clinical picture of TIA was characterized by the presence of focal symptoms and global brain symptoms. The variety of clinical symptoms depended mainly on the localization of the ischemic focus. Therefore, all TIAs were divided into two groups: carotid and vertebrobasilar.

The clinical picture of ischemic strokes consisted of focal and global brain symptoms. An analysis of the medical history revealed a qualitative change in this form of transient cerebral ischemia. Specifically, in 79.4% of patients with II after a previous TIA (n=27), we identified the presence of recurrent TIAs, with 38.2% (n=13) experiencing them less frequently but for longer durations. This indicates worsening cerebrovascular insufficiency in these patients.

Our research showed that the symptoms of TIA in the carotid basin were characterized by the polymorphism of organic symptoms and had a transient nature, which is consistent with the literature [1, 4, 64]. However, as shown in the table below (Table 3.1.1), they occurred with varying frequencies.

Table 3.1.1

Subjective focal symptoms in patients with TIA in the carotid basin (n=56)

Complaints	TIA Carotid (n=56)	
	abc.	%
Monocular transient blindness	27	48,21
Speech impairment	25	44,64
Transient hemiparesis	21	37,50
Transient monoparesis	8	14,29
Transient amnesia	5	8,93
Swallowing disorder	4	7,14
Facial asymmetry	4	7,14
Walking disturbance	4	7,14

As seen from the presented Table 3.1.1, the subjective focal symptoms of carotid TIA were characterized by polymorphism. 48% of patients (n=27) reported transient blindness in one eye, known in the literature as amaurosis fugas. In 26% of cases, it was associated with transient hemiparesis. The development of this clinical syndrome is caused by thrombosis of the proximal part of the ophthalmic artery before its branching from the internal carotid artery, leading to the development of a hemisyndrome. Speech disorders in the form of aphasia or dysarthria, observed in 44.64% (n=25) of patients, followed in frequency. Transient hemiparesis and monoparesis were next, at 37.5% and 14.3%, respectively. Patients reported transient amnesia in 8.93% of cases (n=5). Four patients (7.14%) complained of swallowing disorders, facial asymmetry, and walking disturbance.

According to the literature, one of the important prognostic criteria for the development of ischemic stroke is the frequency of TIAs [17,43,88]. In this regard, we studied the anamnestic features of carotid TIA. The data are presented in Table 3.1.2.

Table 3.1.2.

Anamnestic features of TIAs in the carotid basin.

Frequency of TIAs	Once a year		Once every 6 months		Once a month		Once a week	
	abc.	%	abc.	%	abc.	%	abc.	%
n=(56)	15	24	24	42,86	12	21,43	5	8,93

From the presented table, it is evident that TIAs were most frequently observed with a frequency of once every 6 months and once a year. TIAs were less commonly reported with a

frequency of once a month (21.43%) and very rarely with a frequency of once a week. However, patients in these groups were under closer observation by doctors due to a higher risk of developing an ischemic stroke. It is important to note that in this category of patients, indicators of cerebral hemodynamics and the rheological properties of blood were somewhat worse than in other patients. Next, for a more detailed analysis of the anamnestic features of TIAs, we studied their duration, which according to modern literature [3,40,68,100] and our opinion, could serve as an indicator of cerebral blood flow and autoregulation of cerebral vascular tone. The analyzed data are presented in Table 3.1.3.

Table 3.1.3

Average duration of TIAs in the carotid basin.

Duration of TIA	**Up to 10 minutes**		**Up to 1 hour**		**More than 1 hour**	
	abc.	%	abc.	%	abc.	%
(n=56)	6	10,71	13	23,214	37	66,07

The analysis of TIAs according to duration revealed an uneven distribution of patients. Specifically, there were only 6 patients with short-duration TIAs (up to 10 minutes), slightly more – 23.14% (n=13) – experienced TIAs lasting up to 1 hour, and the majority of observations were for TIAs lasting up to 1 day – 66% (n=37). The duration of TIAs was largely determined by factors such as the degree of stenosis of major head arteries, the number of atherosclerotic plaques, the severity of arterial hypertension, and the state of autoregulation of cerebral vascular tone. These factors largely influenced the clinical picture of TIAs. For example, transient blindness lasted from 1 minute to 1 day, transient hemiparesis typically lasted no more than 2 hours, speech disturbances also regressed within 1 hour, and symptoms such as transient amnesia or monoparesis lasted no more than 1 hour. In our opinion, the polymorphism of clinical symptoms indirectly reflects the state of cerebral blood flow and can serve as a prognostic criterion for the development of ischemic stroke after TIAs, as noted in subsequent prospective observations. The aforementioned symptoms were characteristic of TIAs in the carotid basin.

In 45% of cases in our observations, TIAs developed against the background of a combination of two etiological factors – atherosclerotic cerebrovascular disease (ACVD) and stage II hypertension. This prompted us to study the relationship between the development of TIAs in the context of combined arterial hypertension and cerebral atherosclerosis. Analysis of the medical history of patients with TIAs revealed that the latter usually developed against the background of hypertension. The average blood pressure values at the time of TIA were

156.7±16.3 mmHg, and were often interpreted by primary care physicians as hypertensive cerebral crises. The predominance of focal symptoms over global cerebral symptoms served as a differential diagnostic criterion characteristic of TIAs. It is important to note that our research revealed a correlation between the duration of transient attacks and blood pressure values. The data analysis of the correlation between the duration of TIAs and blood pressure values is presented in Table 3.1.4.

Table 3.1.4

The dependence of the duration of TIA in the carotid basin on systolic blood pressure parameters.

Duration of TIA	Up to 10 minutes		Up to 1 hour		More than 1 hour	
	abc.	%	abc.	%	abc.	%
Systolic BP						
120-139	3	5,36	1	1,79		
140-159	2	3,57	4	7,14	17	30,36
160 and more			8	14,29	21	37,50

Our research has shown that high systolic blood pressure values influence the duration of transient ischemia. As evident from the presented Table 3.1.4, the presence of hypertension led to an increase in the duration of TIAs. That is, against the backdrop of systolic blood pressure above 140 and higher, TIAs more often lasted from 1 hour to a day. This is due to the dual mechanism of cerebral transient ischemia. Firstly, it involves thromboembolism of small cerebral vessels, and secondly, it involves persistent cerebral vasoconstriction due to hypertension, which is consistent with data from literary sources [8, 10].

Transient cerebral ischemia is accompanied by various clinical symptoms. It is known that the clinical picture of TIAs consists of focal and global cerebral symptoms. Typically, transient ischemia manifests with a predominance of focal symptoms over global ones. The focal symptoms are largely determined by the localization of the vascular territory in which the transient ischemia occurs. For convenience of description, all focal symptoms have been grouped by us into syndromes. Specifically, these include cognitive impairments, monocular blindness, pyramidal syndrome, speech disturbance, brachiofacial syndrome, and sensory disorders. The distribution of these syndromes is presented in Table 3.1.5.

Table 3.1.5

Structure of focal symptoms of TIA in the carotid basin.

Name of symptom or syndrome	(n=56)	%
Cognitive impairments	31	55,36
Monocular blindness	25	44,64
Pyramidal syndrome	24	42,86
Speech impairment	24	42,86
Sensory disturbances	12	21,43
Brachiofacial syndrome	9	16,07

Most frequently (55.36%), among patients with TIAs in the carotid territory, we encountered cognitive impairments, accompanied by memory loss, attention deficit, and spatial and temporal disorientation. Following in prevalence (44.64%), among patients with TIAs in the carotid territory, we observed monocular blindness, which was accompanied by decreased vision or complete loss of vision on the side of the stenosed artery. Complaints of feeling a "curtain" or "shade" in the eye, sometimes triggered by bright sunlight or glare, were noted in 25% of patients.

In 12 patients (21.43%), we diagnosed sensory disorders in the form of hypoesthesia and paresthesia. In 9 cases (16.07%), transient brachiofacial paresis with monoparesis of the arm and slight central paresis of the facial nerve on the opposite side of the ischemic focus was encountered.

In all cases, transient amnesia developed during TIAs in the context of uncontrolled arterial hypertension and resolved several hours after blood pressure reduction. Transient mono- or hemiparesis most often occurred in combination with monocular blindness or facial nerve palsy and were symptoms of optico-pyramidal or brachiofacial paresis.

3.2. Clinical and Anamnestic Features of TIAs in the Vertebrobasilar Territory.

Investigating the clinical picture of TIAs is associated with certain difficulties. Primarily, diagnosis is established retrospectively. Secondly, there are often challenges in differential diagnosis between TIAs and syncopal states. In the latter case, an important diagnostic criterion favoring TIAs is the presence of systemic vascular disease, instrumental study data confirming the vascular etiology of transient disorders, and, in some cases, focal symptoms indicating organic brain damage or chronic brain ischemia [31, 35, 52, 90]. In this regard, to clarify the clinical picture of TIAs in the vertebrobasilar territory, we examined the clinical features of TIAs in 24 patients, as presented in Table 3.2.

Table 3.2

Comorbidities in TIA patients in the vertebrobasilar basin.

Diseases	Patients with TIA (n=24)	
	abc	%
Hypertension	21	87,5
Atherosclerosis	12	50
Cervical osteochondrosis	9	37,5
Diabetes mellitus	4	16,67
Ischemic heart disease	4	16,67

The main accompanying comorbid conditions were: hypertension (87.5% of cases), cerebral atherosclerosis (50% of cases), and cervical spondylosis (37.5% of cases), as presented in Table 3.2.

Furthermore, for a more detailed analysis of the anamnestic features of TIAs, we studied their duration, which, according to modern literature and our opinion, may serve as an indicator of cerebral blood flow and autoregulation of cerebral vascular tone [16, 7, 14, 30, 32]. The analyzed data are presented in Table 3.2.1.

Table 3.2.1

Average duration of TIA in the vertebrobasilar basin.

Duration of TIA	Up to 10 minutes		Up to 1 hour		More than 1 hour	
	abc.	%	abc.	%	abc.	%
n=(24)	5	20,83	13	54,17	6	25,00

In the case of TIAs in the vertebrobasilar system, they were shorter in duration, typically lasting no more than an hour. The analysis of TIAs based on their duration revealed an uneven distribution of patients. Specifically, there were only 4 cases of TIAs with a duration of less than 10 minutes, while slightly more, 25% (n=6), lasted over an hour. The majority of observations, 54.2% (n=13), were TIAs lasting up to 1 hour. Meanwhile, in cases of carotid localization, TIAs lasted from several minutes to a day and were accompanied by confusion, such as dizziness or simple hallucinations, which some authors interpret as symptoms of "irritation".

Through our observations, we identified the peculiarities of the clinical picture of TIAs in the vertebrobasilar system. This was manifested in the polymorphism of clinical, focal symptoms of TIAs in the vertebrobasilar system, as presented in Table 3.2.1.

Table 3.2.2

Subjective symptoms in patients with TIA in the vertebrobasilar basin (n=24)

Complaints	TIA Carotid n=24	
	abc	%
Dizziness	24	100,00
Ataxia	17	70,83
Unsteadiness while walking	15	62,50
Nausea	15	62,50
Feeling of "falling into a pit"	9	37,5
Dysarthria	8	33,33
Dysphagia	8	33,33
Diplopia	5	20,83
Tinnitus	4	16,67

As evident from Table 3.2.1, all patients exhibited the symptom of dizziness (100% of cases). Typically, it was nonsystematic and lasted no more than 3-4 minutes. Additionally, we noted focal symptoms of TIAs such as ataxia (70.8%), staggering and nausea (both 62.5%), moderate dysarthria and dysphagia (33.3%), and diplopia (20.8%). In some cases, we observed the development of TIAs against the background of cervical spondylosis, which, as known, has a dual mechanism of development. Firstly, narrowing of the vertebral artery canal leads to a decrease in blood flow velocity, and secondly, reflexive angiospasm occurs as a result of irritation of the vascular wall by osteophytes. Drop attacks were observed in 9 patients (37.5%), characterized by sudden falls without loss of consciousness and subsequent postural tone loss.

For descriptive convenience, we categorized all these symptoms into a group of syndromes of vertebrobasilar TIA. The data are presented in Table 3.2.3.

Table 3.2.3

Structure of focal symptoms of TIA in the vertebrobasilar basin (n=24)

Name of symptom or syndrome	(n=24)	%
Dizziness	24	100,00
Cerebellar-ataxic syndrome	20	83,33
Bulbar syndrome	9	37,5

If monocular blindness syndrome was obligatory in carotid basin TIAs, then in vertebrobasilar basin TIAs, dizziness syndrome was present in 100% of cases, which in most instances was nonsystematic. Following in frequency was the cerebellar-ataxic syndrome (83.3%), manifested more commonly by gait instability, ataxia, and coordination impairment. Additionally, in 37.5% of cases (n=9), bulbar syndrome was noted, characterized by dysarthria and dysphagia.

Our studies revealed the polymorphism and course of the clinical picture of TIAs. Analysis of the clinical and anamnestic features of TIAs revealed their dependence on several factors. Specifically, these included etiological factors, the dependence of focal symptoms on the vascular basin in which transient ischemia occurred, the level of systolic blood pressure, which determined not only the polymorphism of symptoms but also the duration of the TIA itself. Furthermore, we determined the average duration of TIAs in the carotid basin, which was on average more than 1 hour and up to a day with a frequency of once every 6 months. In the clinical picture of TIAs depending on the vascular basin, either the monocular blindness syndrome, characteristic of TIAs in the carotid basin, or the dizziness syndrome, characteristic of TIAs in the vertebrobasilar basin, predominated. While the etiological factors of TIAs in the carotid basin more frequently involved the combination of hypertension and cerebral atherosclerosis, in patients with TIAs in the vertebrobasilar basin, in addition to the aforementioned comorbidities, we also noted cervical spondylosis.

Next, we studied the clinical and anamnestic features of ischemic strokes following a previous transient ischemic attack, presented in section 3.3.

3.3. Clinical and Anamnestic Features of Ischemic Strokes after a Previous Transient Ischemic Attack.

To study the clinical and anamnestic features of ischemic strokes (IS) following a previous transient ischemic attack (TIA), we examined 34 patients with IS who had a history of TIA. It is important to note that we observed strokes only in the carotid basin. An analysis of the spectrum

of concomitant diseases in the somatic status of the examined patients was conducted (Table 3.3).

Table 3.3

Comorbidities in patients with ischemic stroke

Diseases	Patients with IS (n=34)	
	abc	%
Hypertension	34	100
Atherosclerosis	20	58,82
Ischemic heart disease	11	32,35
Diabetes	9	26,47
Arrhythmia	4	11,76
Acquired heart defect	2	5,88
Chronic heart failure	1	2,94

As seen from the table, the most common comorbid conditions in our observations with ischemic strokes (IS) were represented by hypertension, which was present in all patients. Atherosclerosis was observed in more than half of the patients (58.8%). Approximately one-third of the patients with IS had ischemic heart disease and diabetes mellitus (32.3% and 26.4% respectively).

When studying the anamnestic features of IS after a previous TIA, we noted the following. The frequency and severity of the clinical picture of TIA determine the probability and severity of the course of ischemic stroke. As our research showed, all patients who had a stroke had a history of TIA in the carotid or vertebrobasilar basin. Analysis of the data from the medical history regarding the frequency of ischemic strokes after a previous TIA revealed differences, both in terms of the timing of the acute cerebrovascular event and in terms of the vascular catastrophe basin. The duration between the occurrence of TIA ranged from 1 year to 5 years. The distribution of the frequency of ischemic stroke according to the duration of TIA is presented in Table 3.3.1.

Table 3.3.1

Frequency of ischemic strokes in the carotid basin developed after a previous TIA.

Duration since TIA (n=34)	**1 year**	**2 years**	**3 years**	**4 years**	**5 years**
abc	4	9	11	5	5
%	11,76	26,47	32,35	14,71	14,71

The obtained anamnestic data allow us to state that strokes in the carotid basin more often developed in the second to third year after a previous TIA. However, summing up the results, we have concluded that the proportion of IS after a previous TIA accounts for more than half of all stroke cases, and they tend to occur more frequently in the 2nd and 3rd years after a previous TIA.

The low frequency of strokes in the first year after TIA may be due to the therapeutic measures implemented, which have had a certain preventive effect. According to the medical history, up to 88.2% of patients after TIA were taking antihypertensive, antiplatelet, and lipid-lowering medications for several months or a year, affecting blood rheology, etc. However, by the end of the first year, the number of patients receiving medication therapy had decreased to 20%, which may be a contributing factor to the development of stroke. Another significant factor in the development of stroke after TIA is the presence of concomitant comorbid conditions. According to several authors, the frequency and timing of stroke development in the context of systemic vascular disorders vary.

According to our data, ischemic strokes more frequently developed in the left carotid basin (55.82%).

Table 3.3.2

Distribution of patients with ischemic strokes in the carotid basin developed after a previous TIA based on the infarct basin.

Infarct basin (n=34)	**abc**	**%**
Right MCA (Middle Cerebral Artery)	14	41,18
Left MCA (Middle Cerebral Artery)	20	58,82

For the purpose of clarifying the features of the clinical presentation of ischemic strokes (IS) after a previous TIA, we studied the clinical picture of IS. It consisted of subjective symptoms and objective clinical signs. The data are presented in Table 3.3.3.

Table 3.3.3

Subjective symptoms in patients with ischemic strokes after a previous TIA (n=34)

Complaints	**IS (n=34)**	
	abc	%
General weakness	32	94,12
Weakness in limbs	31	91,18
Dizziness	28	82,35

Increased blood pressure	28	82,35
Headaches	27	79,41
Speech impairment	24	70,59
Numbness in limbs	19	55,88
Cognitive impairments	3	8,82
Vision disturbances	2	5,88
Not reported due to severity of condition	2	5,88

Analysis of subjective symptoms in patients who experienced IS after TIA showed a predominance of complaints of general weakness and weakness in the limbs (94.12% and 91.18% respectively). Around 80% of patients complained of dizziness (non-systemic), elevated blood pressure, and headaches. The next most frequent were sensory and cognitive impairments (55.88% and 8.82% respectively). The localization of IS occurred in the same vascular territory as TIA. The average period between TIA and subsequent stroke in our observations was 2.4 years. This has significant importance in stroke prevention; during this time interval, patients who have experienced TIA should be under close observation by neurologists, which can help reduce the risk of stroke.

Next, we conducted an analysis of focal clinical symptoms in patients with IS after TIA. All cases of IS noted in our observations occurred in the carotid territory. Out of 20 cases of IS, 14 occurred in the left carotid territory, and 14 occurred in the right. Only in 4 cases did the territory of IS not coincide with the territory of TIA. This indicates the significance of TIA not only in predicting the stroke itself but also in determining the localization of the ischemic focus. The variety of focal neurological symptoms depends on the latter factor, as illustrated in Table 3.3.4.

Table 3.3.4

Focal neurological symptoms in patients with ischemic strokes after a previous TIA (n=34).

Complaints	**IS n=34**	
	abc	%
Hemiparesis	31	91,18
Central paresis of VII and XII cranial nerves	30	88,24
Cognitive impairments	28	82,35
Aphasia	26	76,47
Pathological plantar reflexes	23	67,65
Changes in muscle tone	22	64,71
Hemihypaesthesia	18	52,94
Bulbar syndrome	7	20,59
Cerebellar-ataxic disorders	4	11,76

From the presented table, it can be seen that the most common focal symptoms were hemiparesis and speech impairment (in 91.18% and 88.24% of cases respectively). In the structure of speech impairments, we noted motor aphasia (26.9%), sensory aphasia (15.3%), but most often cases of mixed or total aphasia were observed (57.7%). Muscle strength in the paretic limbs averaged 2.4±0.7 points and corresponded to paresis. Muscle tone on the paretic side was usually increased (61.76%), and muscle hypotonia in the acute phase of IS was observed in only 26.4% of cases. Pathology of the cranial nerves in the form of central paresis of the facial and hypoglossal nerves was observed in 79.4%. Pyramid insufficiency was expressed not only as hemiparesis but also accompanied by pathological foot signs in 67.65%.

Thus, our research showed that strokes more often (58.82%) occur 2-3 years after TIA. The lowest percentage (11.76%) of morbidity occurs 1 year after TIA. The territory of IS coincided with the TIA territory in 88.32% of cases.

Among subjective complaints, weakness in the limbs was the most common (about 90%). Other complaints included speech and sensory disturbances, dizziness, headaches, and memory impairment. In the structure of focal neurological symptoms in our observations, hemisyndrome and speech disorders were often encountered (in 91.18% and 88.24% of cases). Of the speech disorders, motor aphasia (26.9%) and sensory aphasia (15.3%) were noted, but cases of mixed or total aphasia were most common (57.7%).

The correspondence of vascular territories between TIA and IS after TIA indicates an atherothrombotic or embolic mechanism of persistent cerebral ischemia (IS) and underscores the need for primary stroke prevention measures aimed at altering blood rheological parameters, which also undergo certain changes. This is indicated by both literary sources [30,32,57,89] and our observations presented in Chapter 4.1.

3.4. Features of Neuropsychological Manifestations in TIA and Ischemic Stroke after TIA.

Neuropsychological impairments associated with cognitive and psychomotor functions are significant complications of TIA and ischemic stroke. These impairments, especially in the cognitive domain, influence the rehabilitation process, the quality of life of the patient, and determine the severity of disability in patients who have experienced not only a stroke after TIA but also in those with TIA itself [15,24,68,75].

Cognitive impairments in patients who have had a stroke are characterized by diverse clinical and behavioral disturbances, which are determined by organic brain damage [57,58,85,89].

Assessment of the cognitive domain using scales and questionnaires allows not only the degree of organic impairments to be identified but also positive dynamics from the therapy conducted during the recovery period of the disease [15,68].

Cognitive deficit was assessed using the MMSE scale, the results of which are presented in Table 3.4.

Table 3.4

Structure of cognitive impairments

Degree of impairment	No cognitive impairments	Mild cognitive impairments	Moderate cognitive impairments	Mild dementia	Moderate dementia	Severe dementia
TIA VBB (n=24)	4 (16,7%)	8 (33,3%)	7 (29,2%)	4 (16,7%)	1 (4,2%)	
TIA CAROTID (n=56)	10 (17,9%)	14 (25,0%)	13 (23,2%)	11 (19,6%)	8 (14,3%)	
IS (n=34)		4 (11,8%)	13 (38,2%)	8 (23,5%)	7 (20,6%)	2 (5,9%)
Total	14 (12,2%)	26 (22,8%)	33 (28,9%)	23 (20,2%)	16(14,1%)	2 (1,8%)

As seen from Table 3.4, moderate cognitive impairments predominated among patients overall. While this trend persisted in the stroke group, milder cognitive impairments were more common in the TIA group. Cognitive impairments were observed in all patients who had experienced a stroke, whereas in the TIA group, cognitive impairments were absent in 14 patients (17% and 18% in VBB and CB, respectively). There were no cases of severe dementia in the TIA group, whereas it occurred in 2 patients (1.8%) in the stroke group. Mild to moderate dementia was more frequent in patients with stroke than in those with TIA. Additionally, in patients with TIA in the carotid basin, mild to moderate dementia was more common than in patients with TIA in VBB (19.6% and 14.3% vs. 16.7% and 4.2%, respectively). Thus, the most pronounced cognitive impairments were observed in the ischemic stroke group. Moreover, differences between the groups of patients who had experienced TIA showed that cognitive

deficits were more prevalent in patients with TIA in the carotid basin than in those with TIA in VBB.

CHAPTER IV. PARACLINICAL FEATURES OF TRANSIENT ISCHEMIC ATTACKS AND STROKES AFTER TRANSIENT ISCHEMIC ATTACKS

The clinical picture of TIA is very diverse, but most importantly, this pathology lacks clear symptoms that would assist clinicians in diagnosing and promptly deciding on treatment strategies for identified lesions, including the question of surgical correction of the pathology. According to several authors [85,89,93], TIAs develop against the background of stenotic or occlusive lesions of the major arteries of the head (MAA), the diagnosis of which is crucially aided by ultrasound methods, particularly Doppler ultrasound (US-D). Some authors [3,17,89,100] emphasize the role of ultrasound methods in the diagnosis of cerebral hemodynamics not only in diagnosing TIA but also in predicting ischemic strokes after a TIA.

4.1. Features of Cerebral Hemodynamics of Extracranial Arteries in TIA and Ischemic Strokes after TIA.

To determine the state of cerebral blood flow and all types of associated pathology, we used Doppler ultrasound of the brachiocephalic arteries (US-D of BCA) and transcranial Doppler ultrasound of the cerebral arteries (TCDG). The results of US-D of BCA are displayed in Table 4.1.

Table 4.1

Conditions of extracranial arteries in the head of patients who have had TIAs and ischemic strokes.

Type of impairment	IS (n=34)%	TIA (n=66)%
Stenosis and occlusion of right vertebral artery (VA)	55,9	47,0
Stenosis and occlusion of left vertebral artery (VA)	79,4	57,6
Stenosis of right vertebral artery (VA) up to 50%	41,2	42,4
Stenosis of left vertebral artery (VA) up to 50%	50,0	51,5
Stenosis of right vertebral artery (VA) from 50% to 70%	8,8	3,0
Stenosis of left vertebral artery (VA) from 50% to 70%	17,6	6,1
Stenosis of right vertebral artery (VA) more than 70%	2,9	1,5
Stenosis of left vertebral artery (VA) more than 70%	8,8	0,0
Occlusion of right vertebral artery (VA)	2,9	0,0
Occlusion of left vertebral artery (VA)	2,9	0,0
Stenosis and occlusion of right posterior cerebral artery (PCA)	17,6	18,2

Stenosis and occlusion of left posterior cerebral artery (PCA)	20,6	13,6
Stenosis of right posterior cerebral artery (PCA) up to 50%	11,8	18,2
Stenosis of left posterior cerebral artery (PCA) up to 50%	14,7	13,6
Stenosis of right posterior cerebral artery (PCA) from 50% to 70%	5,9	0,0
Stenosis of left posterior cerebral artery (PCA) from 50% to 70%	5,9	0,0
Stenosis of right posterior cerebral artery (PCA) more than 70%	0,0	0,0
Stenosis of left posterior cerebral artery (PCA) more than 70%	0,0	0,0
Occlusion of right posterior cerebral artery (PCA)	0,0	0,0
Occlusion of left posterior cerebral artery (PCA)	0,0	0,0
Deformation of right vertebral artery (VA) (without hemodynamic disorders)	50,0	43,9
Deformation of left vertebral artery (VA) (without hemodynamic disorders)	52,9	50,0
Pathological deformation of right vertebral artery (VA)	5,9	1,5
Pathological deformation of left vertebral artery (VA)	14,7	6,1
Deformation of right posterior cerebral artery (PCA) (without hemodynamic disorders)	41,2	39,4
Deformation of left posterior cerebral artery (PCA) (without hemodynamic disorders)	47,1	48,5
Pathological deformation of right posterior cerebral artery (PCA)	5,9	4,5
Pathological deformation of left posterior cerebral artery (PCA)	11,8	7,6
Vertebrogenic compression of right posterior cerebral artery (PCA)	11,8	9,1
Vertebrogenic compression of left posterior cerebral artery (PCA)	14,7	9,1
Hypoplasia of right posterior cerebral artery (PCA)	2,9	3,0
Hypoplasia of left posterior cerebral artery (PCA)	2,9	6,1
High origin of right posterior cerebral artery (PCA)	2,9	1,5
High origin of left posterior cerebral artery (PCA)	2,9	3,0

As seen from the table, stenoses and occlusions of the ICA were more frequently observed on the left side than on the right, with 79.4% versus 55.9% in patients with stroke and 57.6%

versus 47.0% in individuals who had experienced TIA. Stenoses up to 70% were also more commonly noted in the left carotid basin in both groups. Left-sided stenoses and occlusions of the PCA were more prevalent in patients who had suffered a stroke (20.6% versus 13.6%), while right-sided PCA impairments were approximately equal in both groups, at around 18%. Unlike patients with stroke, those with TIA exhibited stenoses of the PCA only up to 50%, whereas in the former group, stenoses of the PCA from 50% to 70% were observed in 5.9% of cases.

Deformities of the ICA without hemodynamic disturbances comprised 50.9% on the right side and 52.9% on the left side in the stroke group, and 43.3% and 50.0%, respectively, in the TIA group. Pathological deformities of the ICA in patients with stroke constituted 5.9% on the right side and 14.7% on the left side, while in the TIA group, these figures were 1.5% and 6.1%, respectively. Deformities of the PCA without hemodynamic disturbances constituted 41.2% on the right side and 47.1% on the left side in the stroke group, and 40.9% and 48.5%, respectively, in the TIA group. Pathological deformities of the PCA in patients with stroke were 5.9% on the right side and 11.8% on the left side, while in the TIA group, these figures were 4.5% and 7.6%, respectively.

Thus, hemodynamically significant vascular lesions were observed in 47% of patients with stroke and 20% in those with TIA. Otherwise, TIA and stroke developed in patients with hemodynamically insignificant stenoses, deformities, and additional hemodynamic factors, predominantly noted on the left side.

4.1.1. Comparative Characteristics of Cerebral Hemodynamics Parameters of Extracranial Arteries in Patients who Experienced Ischemic Stroke.

To compare hemodynamic parameters, patients with stroke were divided into 2 subgroups: Ia – group with stroke in the right vascular basin, and Ib – group with stroke in the left vascular basin. The study predominantly included patients with stroke in the left carotid basin - 21 individuals (61.8%), among whom were 14 men and 7 women; and in the right carotid basin - 13 cases (38.2%) - 4 men and 9 women. The age of patients in group Ia ranged from 49 to 82 years (mean age 64.07±10.5), and in group Ib from 47 to 72 years (mean age 59.6±7.6). Combined pathology of the MAA detected by US-D of BCA in groups Ia and Ib is presented in Table 4.1.1.

Table № 4.1.1

Condition of extracranial arteries in the head of patients who have had an ischemic stroke

Pathology of common carotid artery (CCA)	Ia % (n=13)	Pb % (n=21)
Stenosis of right vertebral artery (VA) up to 50%	53,8	33,3

Stenosis of left vertebral artery (VA) up to 50%	53,8	47,6
Stenosis of right vertebral artery (VA) from 50% to 70%	7,7	9,5
Stenosis of left vertebral artery (VA) from 50% to 70%	7,7	23,8
Stenosis of right vertebral artery (VA) more than 70%	7,7	0,0
Stenosis of left vertebral artery (VA) more than 70%	0,0	14,3
Occlusion of right vertebral artery (VA)	7,7	0,0
Occlusion of left vertebral artery (VA)	0,0	4,8
Stenosis of right posterior cerebral artery (PCA) up to 50%	15,4	9,5
Stenosis of left posterior cerebral artery (PCA) up to 50%	7,7	19,0
Stenosis of right posterior cerebral artery (PCA) from 50% to 70%	7,7	4,8
Stenosis of left posterior cerebral artery (PCA) from 50% to 70%	0,0	9,5
Stenosis of right posterior cerebral artery (PCA) more than 70%	0,0	0,0
Stenosis of left posterior cerebral artery (PCA) more than 70%	0,0	0,0
Occlusion of right posterior cerebral artery (PCA)	0,0	0,0
Occlusion of left posterior cerebral artery (PCA)	0,0	0,0
Deformation of right vertebral artery (VA) (without hemodynamic disorders)	61,5	42,9
Deformation of left vertebral artery (VA) (without hemodynamic disorders)	53,8	52,4
Pathological deformation of right vertebral artery (VA)	7,7	4,8
Pathological deformation of left vertebral artery (VA)	7,7	19,0

In patients who experienced stroke in the right carotid basin, stenosis of the ICA up to 70% was equally observed on both sides, accounting for 61.5%. In group Ib, stenosis of the left ICA up to 70% was present in 42.8% of cases, while stenosis of the right ICA was more frequent, constituting 71.4% of cases. Hemodynamically significant stenosis exceeding 70% and occlusion were encountered in 13% of cases in patients of group Ia in the right ICA and in 19% of cases in patients of group Ib in the left ICA. Therefore, the stenotic process predominantly prevailed in the site of stroke localization in patients.

Deformation (without hemodynamic disturbances) of the right ICA was observed in group Ia - 61.5%, Ib - 42.9%, while deformation of the left ICA in group Ia was 53.8% and in Ib was 52.4%. Pathological deformation of the right ICA was observed in group Ia - 7.7%, Ib - 4.8%, and deformation of the left ICA in group Ia was 7.7% and in Ib was 19.0%. Deformities of the MAA without hemodynamic disturbances were observed in all groups but predominated in group Ia (in patients with ischemic stroke in the left CB).

4.1.2. Comparison of Cerebral Hemodynamics Parameters in Extracranial Arteries in Patients who Experienced TIA.

To compare hemodynamic parameters, patients with TIA were divided into 3 subgroups: IIa - patients with TIA in the right carotid basin; IIb - patients with TIA in the left carotid basin; IIIc - patients with TIA in the vertebrobasilar basin.

The study predominantly included patients with transient ischemic attacks in the left carotid basin - 25 individuals (59.5%), among whom were 13 men and 12 women, and in the right carotid basin 17 patients (40.5%), including 10 men and 7 women. TIA in the vertebrobasilar basin was also present in 8 cases (17.0%) - 6 men and 2 women.

The age of patients in group IIa ranged from 35 to 80 years (mean age 57.4±12.9); in group IIb, from 25 to 84 years (mean age 62.4±12.03); and in group IIIc, from 33 to 78 years (mean age 58.9±11.7).

Combined pathology of the MAA detected by US-D of BCA in groups IIa, IIb, and IIIc is presented in Table 4.1.2.

Table № 4.1.2

Conditions of major arteries in the head of patients who have had a transient ischemic attack (TIA).

Carotid artery pathology (CCA)	IIa % (n=17)	IIb % (n=25)	IIc % (n=24)
Stenosis of right carotid artery (CCA) up to 50%	58,8	44,0	29,2
Stenosis of left carotid artery (CCA) up to 50%	47,1	60,0	45,8
Stenosis of right carotid artery (CCA) from 50% to 70%	5,9	4,0	0,0
Stenosis of left carotid artery (CCA) from 50% to 70%	0,0	16,0	0,0
Stenosis of right carotid artery (CCA) more than 70%	5,9	0,0	0,0
Stenosis of left carotid artery (CCA) more than 70%	0,0	0,0	0,0
Occlusion of right carotid artery (CCA)	0,0	0,0	0,0
Occlusion of left carotid artery (CCA)	0,0	0,0	0,0
Stenosis of right posterior cerebral artery (PCA) up to 50%	5,9	12,0	33,3
Stenosis of left posterior cerebral artery (PCA) up to 50%	11,8	12,0	16,7
Stenosis of right posterior cerebral artery (PCA) from 50% to 70%	0,0	0,0	0,0
Stenosis of left posterior cerebral artery (PCA) from 50% to 70%	0,0	0,0	0,0
Stenosis of right posterior cerebral artery (PCA) more than 70%	0,0	0,0	0,0
Stenosis of left posterior cerebral artery (PCA) more than 50%	0,0	0,0	0,0
Occlusion of right posterior cerebral artery (PCA)	0,0	0,0	0,0
Occlusion of left posterior cerebral artery (PCA)	0,0	0,0	0,0

Deformation of right carotid artery (CCA) (without hemodynamic disorders)	70,6	36,0	33,3
Deformation of left carotid artery (CCA) (without hemodynamic disorders)	35,3	64,0	45,8
Pathological deformation of right carotid artery (CCA)	5,9	0,0	0,0
Pathological deformation of left carotid artery (CCA)	0,0	16,0	0,0
Deformation of right posterior cerebral artery (PCA) (without hemodynamic disorders)	47,1	36,0	41,7
Deformation of left posterior cerebral artery (PCA) (without hemodynamic disorders)	35,3	56,0	50,0
Pathological deformation of right posterior cerebral artery (PCA)	0,0	0,0	8,3
Pathological deformation of left posterior cerebral artery (PCA)	5,9	8,0	8,3
Vertebral artery (VA) compression due to vertebrogenic issues (right)	5,9	4,0	16,7
Vertebral artery (VA) compression due to vertebrogenic issues (left)	0,0	4,0	20,8
Hypoplasia of right posterior cerebral artery (PCA)	5,9	0,0	4,2
Hypoplasia of left posterior cerebral artery (PCA)	0,0	4,0	12,5
High origin of right posterior cerebral artery (PCA)	0,0	0,0	4,2
High origin of left posterior cerebral artery (PCA)	0,0	0,0	8,3

As shown in Table 4.3, patients who experienced TIA more frequently exhibited stenoses of the ICA, as well as deformations of the ICA and PCA. Among the stenoses of the ICA and PCA, stenoses up to half of the vessel lumen predominated.

In group IIa, the most common manifestations of MAA pathology were deformation (without hemodynamic disturbances) and stenosis up to 50% of the right ICA (70.6% and 58.8%, respectively). Patients in group IIb most commonly exhibited deformation (without hemodynamic disturbances) and stenosis up to 50% of the left ICA (64.0% and 60.0%, respectively). In the VBB group, deformation (without hemodynamic disturbances) of the right PCA and stenosis of the left ICA were more frequently observed (54.2% and 45.8%, respectively).

Stenosis of the right ICA at 50-70% was encountered in 5.9% and 4.0% of cases in groups IIa and IIb, respectively. Stenosis of the left ICA at 50-70% was only present in 16% of individuals who experienced TIA in the left carotid basin. Among all three groups, only 5.9% of group IIa had stenosis of the right ICA exceeding 70%. Hemodynamically significant stenoses of the PCA were not observed in any of the groups. Stenoses of the PCA up to 50% were present in 5 to 12% of individuals who experienced TIA in the carotid basin and in 33.3% and 16.7% of

cases, right and left respectively, in patients with TIA in the VBB. Therefore, the stenotic process in the ICA predominated in the site of TIA localization.

Deformations of the PCA and ICA in groups IIa and IIb were always more predominant on the side of the lesion. In group IIc, deformation of the left ICA and PCA predominated over the right (45.8% versus 33.3% and 50.0% versus 41.7%, respectively). Pathological deformation of the right ICA was observed in 5.9% of group IIa, pathological deformation of the left ICA in group IIb was 16.0%, and pathological deformation of the PCA was not observed in groups IIa and IIb, but in group IIc, it occurred in 8.3% of cases. Pathological deformation of the left PCA was noted in approximately 8% of cases in groups IIb and IIc respectively, and in group IIa in 5.9% of cases. Vertebrogenic compression of the right PCA was detected in groups IIa and IIb in 5.9% and 4.0% of cases, respectively, and in group IIc in 16.7% of cases. Vertebrogenic compression of the left PCA was only observed in groups IIb and IIc (4.0% and 20.8% respectively).

4.2. Features of Cerebral Hemodynamics of Intracranial Arteries in TIA and Ischemic Strokes after TIA.

Transcranial Doppler ultrasonography was conducted on 72 patients (45 men and 27 women) aged 45 to 80 years (mean age 62.3 ± 5.1 years). The control group (12 patients) consisted of individuals of the same age who had experienced an ischemic stroke in the early recovery period. It is important to note that all stroke cases had a history of two or more TIAs. The etiological factors of TIA in our observations were cerebral atherosclerosis in 70.8% (51 patients) and a combination of cerebral atherosclerosis and hypertension in 29.2% (21 patients). The course of hypertension in our observations was uncontrolled, with mean blood pressure values of 170±6.4 mmHg and frequent systolic blood pressure elevations above 220 mmHg, which exacerbated the picture of cerebrovascular insufficiency.

The study of cerebral hemodynamics and the state of MAA was performed using transcranial Doppler ultrasonography with the "VAZOSKAN" apparatus from "SONICAID" (England) with probes of 2, 4, 8 MHz and diameters of 14, 10, and 6 mm.

To assess changes in autoregulation parameters against the background of hypo- and hypertonus of resistance vessels, studies were conducted at rest, under conditions of hyper- and hypocapnic stress, simulated by inhalation of 7% carbogen and hyperventilation, respectively, for 2-3 minutes. The obtained data were statistically processed.

In the clinical picture, outside of TIA attacks, complaints of a cerebral nature predominated, such as headaches, dizziness exacerbated by head movements and changes in body position, sleep disturbances, decreased performance, and memory impairment. With the presence of diffuse focal symptoms such as tendon areflexia, symptoms of oral automatism, pathological foot signs, the diagnosis of chronic cerebral ischemia with impaired circulation in the vertebrobasilar basin was made in the majority of our patients, 80.2%. According to Spiridonov A.A. (1996), pathology of only one carotid artery leads to the development of TIA in 51.7% of cases. Damage to one vertebral artery occurs in 38% of cases. The frequency of multiple lesions of the BCAs during TIA ranges

Table 4.2

Cerebral hemodynamics in patients with TIA and ischemic stroke (in cm/s).

Patient Groups	Brain Arteries			Basilar artery	Vertebral artery
	Anterior	Middle	Posterior		
I group (n=43)	47,6±2,3*	39,8± 4,1*	30,2± 2,6*	50,1±3,4	30,6±3,5
	50,3 ±2,7*	35,3±4,0*	40,2 ±3,4		29,4± 2,4*
II group (n=29)	40,5± 3,6	37,4±3,5*	27,3± 4,1	41,6±6,4*	26,7±2,68*
	43,3± 3,6*	34,3±3,2*	40,7 ±3,1		26,4± 3,4*
Control (n=12)	36,2±2,8	31,2±2,6	26,7±3,9	38,4±4,3	21,4±2,4
	32,1±2,4	30,4±2,2	35,7±3,8		22,6±2,6
Healthy individuals (n=15)	44,7± 5,7	38,6±5,2	39,6± 4,5	57,3±3,9	36,6±5,9
	56,8 ±3,7	43,3± 2,8	44,6 ±4,6		38,7±6,1

Note: numerator - right side, denominator - left side;
* - significant differences from control ($p < 0.05$).

The analysis of blood flow velocity parameters in intracranial vessels showed significant differences in patients with TIA occurring once every 6 months compared to the group of patients with ischemic stroke. Parameters in patients with a higher frequency of acute cerebral ischemic episodes (once a month) were closer to those of the stroke group. Based on this, we hypothesize that the highest risk of stroke development is in this group of patients. In our opinion, this is not only due to the severity of cerebral hemodynamic decompensation and depletion of compensatory mechanisms but also to the exhaustion of cerebral blood flow autoregulation mechanisms.

Cerebral blood flow autoregulation is a complex physiological phenomenon, implemented by at least three interactively regulating mechanisms: myogenic, neurogenic, and metabolic. The myogenic mechanism manifests itself in the early, dynamic phase of sharp changes in systemic arterial pressure. It is well known that myogenic autoregulation is carried out by regulating the

function of the juxtaglomerular apparatus of the kidneys, which participates in the synthesis of angiotensin-converting enzyme. The concentration of the latter in the blood affects the level of angiotensin in the blood. The content of angiotensin in the blood influences the tone of the smooth muscle layer of the brain arteries during TIA. (Semi-quantitative assessment of cerebral blood supply autoregulation under normal conditions by B.V. Gaidar, D.V. Svistov, K.N. Khrapov). The metabolic mechanism of autoregulation is realized in the lungs, brain, and coronary vessels. At the heart of this mechanism lies the known effect of O2 and metabolites on the tone of cerebral vessels. In hypoxemia (lack of O2) or hypercapnia (excess of CO2), the smooth muscles of the vessels relax, and vice versa. Mechanism: local action of metabolites on the ability of smooth muscles to regenerate impulses. The nervous regulation of cerebral vessel tone, which is carried out under the action of the vasomotor center, mediated through vasomotor nerves, also has significant importance.

In this regard, we further studied the reactivity of cerebral vessels as one of the main links in the compensatory mechanism of cerebral blood circulation. The data of the conducted studies on the coefficient of vasomotor reactivity are presented in Table 2.

The analysis of vasomotor reactivity parameters showed significant differences in patients of the first group compared to patients who had a stroke. The differences in these parameters in the second group of patients compared to those who had a stroke were not significant. It is important to note that the smallest differences in the coefficient of vasomotor reactivity in all three compared groups were in the basilar basin (main artery). This, in our opinion, indicates the greatest susceptibility (predisposition) of this vascular basin to TIA and explains the higher frequency of transient ischemia in the vertebrobasilar basin.

Table 4.2.1

Indicators of vasomotor reactivity coefficient in intracerebral arteries in patients with TIA.

Patient Groups	Middle cerebral artery		Basilar artery
	left	right	
I group (n=43)	90,6±6,2*	88,4±5,3*	81,9±4,0
II group (n=29)	80,9±4,1	82,7±3,0^	78,4±3,2 ^
Control (n=12)	73,5±3,2	78,1±2,4	76,3±2,6
Healthy individuals (n=15)	96,5±5,3	93,5±6,2	91,5±4,8

Note: * - significant differences from control ($p < 0.05$).
^ - significant differences from healthy individuals ($p < 0.05$).

Thus, our studies have shown that the clinical picture and course of TIA are largely determined by the state of cerebral hemodynamics. The clinical picture of TIA, as our research has shown, also depends on this parameter, as well as on the vascular basin.

The analysis of blood flow velocity parameters in intracranial vessels revealed significant differences in patients with a frequency of TIA once every 6 months compared to the group of patients with ischemic stroke. Parameters in patients with a higher frequency of acute cerebral ischemic episodes (more than once a month) were closer to those of the stroke group. Based on this, we hypothesize that the highest risk of stroke development is in this group of patients. This is due to the severity of cerebral hemodynamic decompensation and exhaustion of compensatory mechanisms, which was confirmed in studies on the state of cerebral vasomotor reactivity.

The vasomotor reactivity parameters in the second group of patients were insignificantly different from those in patients who had a stroke. It is important to note that the smallest differences in the coefficient of vasomotor reactivity in all compared groups were in the vertebrobasilar basin. This, in our opinion, indicates the greatest susceptibility of this vascular basin to TIA and explains the higher frequency of transient cerebral ischemia in the vertebrobasilar basin. Furthermore, a decrease in this parameter may indicate a higher risk of developing an acute cerebrovascular event, which has important prognostic value in the early diagnosis and prognosis of ischemic stroke.

Thus, as our research has shown, the severity and variety of clinical symptoms of transient ischemic attacks, as well as their frequency, indicate a greater likelihood of subsequent ischemic stroke. This, in turn, is associated with indicators of cerebral hemodynamics. A decrease in cerebral blood flow in patients with TIA, approaching those indicators in ischemic stroke, as detected by Doppler studies, is a risk factor for its development. In addition, as our studies have shown, the development of stroke after a TIA is significantly influenced by the state of cerebral blood flow autoregulation, the indicators of which, with a higher frequency of TIA, were also close to those of patients with stroke. In our opinion, an important aspect in the features of cerebral hemodynamics is that indicators of cerebral blood flow in the vertebrobasilar basin were the closest to the hemodynamic indicators of the stroke group, confirming the vulnerability of this vascular basin to transient hypoperfusion, which explains the predominance of dizziness syndrome or cerebellar-vestibular syndrome in the clinical picture of TIA.

4.3. Neurovisualization indicators in patients with TIA and ischemic stroke after a TIA.

The development of the scientific and technical process, and in particular the invention of computer tomography (CT) and magnetic resonance imaging (MRI) studies, allowed for the diagnosis of changes in the brain, with determination of the state of the ventricular system, brain substance density, and degree of brain atrophy. CT was performed to differentially diagnose and exclude hemorrhagic stroke in the examined patients.

It is known that both TIA and ischemic stroke are conditions accompanied by chronic cerebral ischemia. In addition to qualitative analysis, we studied the condition of the ventricular system, in particular, the calculation of linear parameters of the ventricular system in the examined patients. Magnetic resonance imaging studies were conducted in the radiology department of the 3rd clinic of the Tashkent Medical Academy on the "Magnetom Open Viva" apparatus (Siemens) with a magnetic field intensity of 0.2 Tesla in the coronal and transverse projections using a flexible radiofrequency coil for the body in the neutral position of the patient on the back. The standard protocol for T1-weighted MRI examination in spin-echo mode in the coronal projection included an echo time of 13 seconds, a repetition time of 37 msec, a spin deviation angle of 45 degrees, a field of view of 180x180, a matrix size of 256x256, and 12 slices with a thickness of 5 mm. T2-weighted spin-echo studies in the axial projection included an echo time of 13 seconds, a repetition time of 37 msec, a spin deviation angle of 45 degrees, a field of view of 180x180, a matrix size of 256x256, and 12 slices with a thickness of 5 mm.

The obtained data were compared with the indicators of individuals (n=20) of the same age without signs of cerebrovascular insufficiency.

Based on the conducted MRI studies, we obtained results indicating the state of brain tissue. The main parameters in this case were such linear indicators as the expansion of the subarachnoid space, the index of the lateral and third ventricles, as well as such densitometric indicators as the presence of foci of reduced density. The features of linear and densitometric indicators are presented in Table 4.3.

It should be noted that foci of reduced density were located in the white matter, periventricularly, and their number in patients with TIA ranged from 1 to 6. Their density averaged 18.4±2.7 HU, which is lower than the density of white matter in the norm (24 HU).

Features of linear and densitometric indicators on MRI in examined patients.

Table 4.3

Indicators	Control (n=20)	Patients		Total
		TIA (n=20)	IS (n=20)	
Enlargement of subarachnoid space	0%	64±1,78%**	100±0%**	70±0,87%**
Width of lateral ventricle	1,6±0,1	2,2±0,2**	2,7±0,04**	2,4±0,08**
Lateral ventricle index	12,1±0,2	15,6±0,8**	21,2±0,6**	18,2±0,60**
Low-density foci	0%	4,0±1,99%**	82±0,3%**	62,5±0,97%**

Analysis of patients by the number of foci of reduced density showed approximately equal numbers in the group of patients with ischemic stroke (IS) after a previous TIA and in patients with frequent (once a month) TIAs. This suggests that a large number of foci of reduced density may represent a specific MRI pattern, both of TIA and as an indicator of the risk of developing IS after TIA.

Significant differences were found in the analysis of linear parameters of the ventricular system and subarachnoid space of the brain in the examined patients. It is known that brain atrophy can be predominantly external when it comes to the expansion of the subarachnoid space, or internal when there is an expansion of the brain ventricles, leading to an increase in the ventricular index. In our observations, both external and internal atrophy were noted, manifested in the expansion of the subarachnoid space and an increase in the volume and index of the ventricles. It is important to note that the linear parameters of the ventricular system and subarachnoid space in both examined groups were different. For instance, while subarachnoid space expansion was noted in 64±1.78% of cases in patients with TIA, it was present in all observations in the IS group and constituted 100%. The lateral ventricle width in IS patients was larger, measuring 2.7±0.04 mm compared to 2.2±0.2 mm in the TIA group. A similar pattern was observed in the lateral ventricle index, with values also being higher in the IS group - 21.2±0.6 compared to 15.6±0.8 in the TIA group.

Summarizing the MRI findings, it can be said that the MRI pattern in TIA and IS after TIA has its own characteristics. These include the presence of foci of reduced brain tissue density located in the white matter around the lateral ventricles. Their number does not always correspond to the number of ischemic attacks experienced. In patients with IS after a previous TIA and in patients with TIA, their number is approximately equal, indicating that they represent not only an MRI pattern of TIA but also a risk factor for developing IS after TIA. Analysis of linear and volumetric parameters of the brain ventricular system showed that TIA and IS after a previous TIA develop against the background of chronic cerebral ischemia. This is manifested in

the increase in linear and volumetric parameters of the subarachnoid space and brain ventricular system in both patients with TIA and those with IS after a previous TIA, placing these two nosological units in the same category based on morphological changes.

4.4. The role of nitric oxide in the development of TIA and strokes after TIA

According to modern literature, nitric oxide (NO) plays an important role in regulating the function of the central nervous system. As a free radical, it is currently considered a universal regulator of many physiological processes in the body. Shifts in homeostasis often lead to dysfunction in the regulation of blood flow, which involves inadequate nitric oxide production by vascular endothelium and is termed endothelial dysfunction (ED). Several studies have demonstrated the role of nitric oxide (NO) in disrupting neuronal signaling, as well as in the pathophysiological mechanisms of seizure and ischemic brain disorders. High concentrations of NO significantly contribute to the disruption of physicochemical homeostasis, characterized by DNA cell mutations and subsequent initiation of apoptosis.

The level of NO in endothelial cells is determined by the activity of nitric oxide synthase (NOS), among which endothelial NOS (eNOS) is particularly important. ED is accompanied by a decrease in NO production, in which case inducible NOS (iNOS) can be involved in NO synthesis. For the assessment of iNOS activity, its marker - nitrate reductase (HP) - is usually used, which functions synchronously with iNOS. High iNOS activity in tissues and cells leads to an increase in NO content, which, in conditions of hypoxia and the resulting high concentration of superoxide anion oxygen O2, forms a toxic and highly reactive compound - peroxynitrite (ONOO"). Changes in the levels of NO, eNOS, iNOS, and ONOO" reflect the state of the endothelial NO synthase mechanism of vascular tone regulation, i.e., indicate the presence or absence of ED.

ED creates conditions for enhanced ONOO" synthesis and leads to a significant increase in its local concentration in the vascular wall. High concentrations of ONOO" are cytotoxic, induce apoptosis, and by blocking prostacyclin synthesis while enhancing thromboxane synthesis, disrupt prostacyclin synthase system function, thereby causing protein fragmentation through amino acid and lipoprotein nitration. Induction of low-density lipoprotein oxidation leads to irreversible suppression of tissue respiration.

As noted above, there are studies devoted to the role of NO metabolism in the pathomechanism of cerebral ischemia. However, as the analysis of modern literature has shown, the role of NO metabolism indicators in the pathogenesis of TIA and strokes after a previous TIA in a comparative aspect has not been studied. This served as the basis for our biochemical research.

We studied the state of ED in patients with TIA (40 individuals) - Group I, with IS after a previous TIA (30 individuals) - Group II. The control group consisted of 20 individuals of comparable age and gender without pathological changes in blood serum. The level of NO was determined by the sum of the main metabolites (NO2" and NO3"), the activity of endothelial NO synthase (eNOS), nitrate reductase (HP), and peroxynitrite (ONOO").

The level of NO was determined by the sum of the main metabolites (NO2" and NO3"), the activity of endothelial NO synthase (eNOS), nitrate reductase (HP), and peroxynitrite (ONOO").

As our research showed, the level of NO in the blood serum of patients in Group I was 26.6% higher and in Group II patients was 22.5% higher compared to the data from the control group. The activity of endothelial eNOS in Group I was 28.2% lower, and in Group II patients it was 21.6% lower, while the content of nitrate reductase (HP) increased by 62.1% in Group I patients and by 31.1% in Group II patients compared to the control (Table 4.4).

This trend persisted in the analysis of peroxynitrite (ONOO") content, which in turn increased to 3.64 ± 0.13 nmol/ml in Group I patients and to 3.03 ± 0.13 nmol/ml in Group II patients, significantly exceeding the values of the control group.

The analysis of nitric oxide metabolism indicators in our observations revealed differences compared to the parameters of the control group; however, the indicators in the patient groups were not significantly different.

Table 4.4

Indicators of the state of NO and its metabolites in the blood serum of patients with TIA and ischemic stroke after TIA.

Indicators	Control group (n=20)	I group (n=40)	II group (n=30)
NO, nmol/ml	5,36±0,24	7,31±0,26* **	6,92±0,26*
eNOS,	7,98+0,33	5,73+0,21* **	6,25±0,26*
HP, нмоль/мин/мл	10,16±0,32	16,47±0,67* **	13,32±0,50*
ONOO", нмоль/мл	2,26±0,10	3,64+0,13* **	3,03±0,13*

Note: * - significant compared to the control group ($p < 0.001$)
** - significant compared to the II group of patients

In our opinion, this indicates the presence of signs of endothelial dysfunction (ED) in patients of the first and second groups, with the degree of ED being slightly lower in patients with ischemic strokes (IS) after a transient ischemic attack (TIA). In this regard, to further clarify the

role of ED in the pathogenesis of TIA, we further analyzed the indicators of NO metabolism in the group of patients with TIA depending on the frequency of TIA (Table 4.5).

Table 4.5.

Indicators of NO and its metabolites in the serum of patients with TIA depending on the frequency of attacks.

Indicators	Once in 6 mon. (n=24)	Once in a mon. (n=12)
NO, nmol/ml	6,08±0,23	7,42±0,83***
eNOS, nmol/min/ml	4,17±0,32	5,13+0,17**
HP, nmol/min/ml	12,39±0,14	17,24+0,35***
ONOO-, nmol/ml	2,32+0,10	3,83±0,13***

Note: * - significant compared to the data for TIA once every 6 months (* - $p < 0.05$, ** - $p < 0.01$, *** - $p < 0.001$)

Patients with a higher frequency of endothelial nitric oxide production impairment significantly differed ($P<0.001$) from those with a frequency of TIAs every 6 months. Changes induced by frequent (once a month) TIAs were more pronounced than in patients with TIAs every 6 months. Importantly, differences were noted both in NO content and in the level of its metabolites in the blood. For instance, the HP content in patients with TIAs every 6 months was 12.39±0.14 nmol/min/ml, whereas in patients with monthly TIAs, this indicator was 17.24+0.35 nmol/min/ml, showing significant differences. This trend was also observed in comparing ONOO" levels in the blood of TIA patients. The content of this metabolite in the blood of patients also varied and depended on the frequency of transient cerebral ischemia. In patients with rare TIAs (every 6 months), this indicator was 2.32+0.10 nmol/ml. As the frequency of TIAs increased, this indicator also rose, reaching 3.83±0.13 nmol/ml in patients with monthly TIAs, which significantly differed from the group of patients with less frequent TIAs.

Based on our studies, we concluded that TIA, as well as IS after a TIA, are associated with endothelial dysfunction. This was confirmed by our results. In particular, there were significant differences in NO metabolism indicators in patients with TIA and IS after a TIA compared to those in the control group. The indicators themselves in the TIA patient group depended on the frequency of vascular paroxysms and were higher in patients with TIAs occurring once a month. In our opinion, this indicates a higher degree of membrane-destructive processes in this group of patients and is crucial for predicting IS after a TIA. Increased free-radical oxidative activity may

indicate a higher likelihood of IS with persistent neurological deficits and, consequently, disability in the patient.

CHAPTER V. QUESTIONS OF OPTIMIZING THERAPY FOR PATIENTS WITH TIA

5.1. Influence of complex therapy with acetylsalicylic acid (Cardiomagnyl®) on indicators of blood rheological properties, nitric oxide, and cerebral hemodynamics

Changes in blood rheological properties are one of the most common causes [6,7,12,81] of acute cerebrovascular diseases, including TIA. Signs of blood hypercoagulability indicate a high risk of thrombus formation, which, in turn, can lead to thrombosis or cerebral vascular embolism. In this regard, to clarify the role of blood rheological properties in the development of TIA and IS after a TIA, we conducted biochemical blood studies in patients from both groups. We examined coagulation profiles of 80 patients with TIA and 34 patients with IS after a TIA. The obtained data were compared with the indicators of 20 healthy individuals of similar age. From the indicators, we selected such parameters as fibrinogen, prothrombin index, and INR. The results of the studies are presented in Table 5.1.

Table 5.1

Indicators of the blood coagulation system

Indicators, average values	Patient group		Control (n=20)
	Group I TIA (n=80)	Group II IS after TIA (n=34)	
FG, g/L	3,83±0,4*	3,2±0,6*	3,2±0,2
PTI, %	90,8±2,42*	85,3±2,1* **	94,9±7,3
INR	0,96±0,05*	1,09±0,04* **	1,0±0,02
Hematocrit, %	44,7±3,2*	43±3,2*	41,3±1,5

Note: * - significant compared to the control group
** - significant compared to the first group of patients

Upon analyzing the nature of blood rheological and coagulation properties in patients with TIA and IS after a TIA, we found that blood viscosity did not significantly differ at high hematocrit and INR values compared to control indicators. The increase in blood viscosity in the TIA patient group was primarily associated with elevated levels of fibrinogen and PTI. In the group of patients with IS after a TIA, this indicator was lower than the control values, with relatively similar hematocrit levels and slight elevation of fibrinogen compared to the control group. Additionally, a comparative analysis of coagulation parameters in both patient groups revealed low PTI values in patients with IS after a TIA compared to patients with TIA and the control group. Importantly, the differences from the TIA patient group had significant values. In

our opinion, the differences in coagulation parameters in patients with IS after a TIA are associated with antiplatelet therapy, including aspirin derivatives.

We conducted an analysis of the results of the effect of antiplatelet therapy with acetylsalicylic acid (Cardiomagnyl) on the rheological properties of blood during treatment dynamics (Table 5.1.1).

Table 5.1.1

Dynamics of hemorheological parameters in patients with TIA undergoing treatment with acetylsalicylic acid (aspirin)

Parameters	Patient group	Time of examination	Results
Blood clotting time according to Bürgers (start in minutes)	IS	Before treatment	3'16"
		After treatment	3'58" (11,0)
	TIA	Before treatment	3'00"
		After treatment	4'17" (28,0)
Prothrombin Index (%)	IS	Before treatment	90,8%
		After treatment	94,2% (1.7)
	TIA	Before treatment	88% (3.7)
		After treatment	84,8%
Fibrinogen (g/L)	IS	Before treatment	3,83
		After treatment	3,68(4)
	TIA	Before treatment	4,55 (19)
		After treatment	3,8
Thrombotest (sec)	IS	Before treatment	5,16 (4.6)
		After treatment	4,93
	TIA	Before treatment	5,3 (6)
		After treatment	5

Our research on the rheological properties of blood conducted during treatment with acetylsalicylic acid (Cardiomagnyl®) revealed a tendency towards hypercoagulability in both patient groups, which in turn was identified as one of the factors contributing to the development of both TIA and IS. Studying the dynamics of these blood rheology indicators showed less improvement in the group of patients who had experienced IS. Parameters such as prothrombin index and fibrinogen levels were particularly resistant to the effects of antiplatelet therapy. In our view, this is one of the factors determining the risk of developing IS after a TIA. In the TIA patient group, the dynamics of rheological parameters significantly improved with acetylsalicylic acid (Cardiomagnyl®) treatment, highlighting the importance of prescribing this medication for secondary prevention of ischemic strokes.

From the data provided, it is evident that our observations included abnormalities in the blood coagulation profile, such as shortened blood clotting time, increased prothrombin index, elevated fibrinogen levels, and changes in thrombotest results. This justifies the prescription of antiplatelet therapy for these patients.

The improvement in blood rheological properties, in turn, had an impact on subjective complaints of patients, the frequency of TIAs, and in some cases, the duration of transient cerebral ischemia. Therefore, to further clarify the effect of acetylsalicylic acid (Cardiomagnyl®) treatment on nitric oxide metabolism indicators, we analyzed the indicators of nitric oxide metabolism and cerebral hemodynamics in patients from both groups who received this medication. It's worth noting that the studies were conducted twice, before treatment and at 6 months of medication intake, as these periods, according to literature [28,72,81,126,140], are when the most persistent changes in blood coagulation properties occur. The data on the status of nitric oxide metabolism in patients from both groups receiving acetylsalicylic acid (Cardiomagnyl®) therapy are presented in Table 5.1.2.

Table 5.1.2

Dynamics of nitric oxide indicators in the groups of examined patients undergoing Cardiomagnyl therapy.

Parameters	Control Group (n=20)	Group I (n=40)		Group II (n=30)
NO, nmol/mL	5,36±0,24	Before treatment	7,31±0,26* **	6,92±0,26*
		After treatment	7,04±0,21* **	6,41±0,23*
eNOS, nmol/min/mL	7,98+0,33	Before treatment	5,73+0,21* **	6,25±0,26*
		After treatment	5,1+0,21* **	6,07±0,26*
HP, nmol/min/mL	10,16±0,32	Before treatment	16,47±0,67* **	13,32±0,50*
		After treatment	16,11±0,13* **	13,05±0,20*
ONOO", nmol/mL	2,26±0,10	Before treatment	3,64+0,13* **	3,03±0,13*
		After treatment	3,1+0,04* **	2,8±0,08*

Note: * - statistically significant compared to the control group (P<0.001)
** - statistically significant compared to Group II

The analysis of the dynamics of nitric oxide metabolism indicators did not reveal significant changes during antiplatelet therapy. From the presented table, it is clear that treatment

with the antiplatelet agent acetylsalicylic acid (Cardiomagnyl®) had little impact on free radical oxidation indicators. Moreover, any insignificant changes observed were consistent across all nitric oxide metabolism parameters. For instance, the level of NO in the blood serum of patients in Group I decreased by only 3.7% after treatment, while in Group II, it decreased by 7.3% compared to baseline, with a significant difference from the control group. The activity of endothelial eNOS decreased by 10.1% in Group I during treatment and by 2.9% in Group II, while the level of nitrate reductase (HP) decreased by 2.2% in Group I and by 2.02% in Group II. The reduction in ONOO" also showed an insignificant trend. While the dynamics of this indicator were 14.8% in Group I, it was 7.6% in Group II.

Summarizing the dynamics of nitric oxide metabolism indicators in patients with TIA and IS after a TIA, it can be noted that there was no significant change in these indicators during treatment with acetylsalicylic acid (Cardiomagnyl®). The minor changes observed may have been due to the concurrent traditional therapy including neurotropics, antihypoxants, and other medications, which to some extent affect nitric oxide metabolism and the level of free radicals in the blood. However, based on our findings, it can be concluded that comprehensive therapy including acetylsalicylic acid (Cardiomagnyl®) had a minor impact on the course of TIA in terms of reducing attack duration and frequency.

Endothelial dysfunction is accompanied by vasospasm, leading to insufficient blood supply to the brain. Therefore, to clarify the state of cerebral hemodynamics during treatment with acetylsalicylic acid (Cardiomagnyl®), we conducted Doppler ultrasound studies on cerebral hemodynamics. The results are presented in Table 5.1.3.

Table 5.1.3

Cerebral Hemodynamic Status in Patients with TIA and IS during Treatment with Acetylsalicylic Acid (Cardiomagnyl®) (in cm/s)

Patient Groups	Cerebral Arteries			Main Artery	Vertebral Artery
	Anterior	middle	posterior		
Group I (n=23)	48,95±2,3	37,55±2,3	35,2±2,3	50,1±3,4	30±2,3
	49,62±1,7	39,04±1,3	43,1±1,9		32,7±1,5
Group II (n=19)	41,9±2,3	35,85±2,3	34±2,3	41,6±6,4*	26,55±2,3
	43,1±2,4	37,4±1,8	35,2±2,1		27,9±1,7
Control (n=12)	34,15±2,3	30,8±2,3	31,2±2,3	38,4±4,3	22±2,3
	36,4±2,6	33,5±2,3	32,9±1,4		23,7±1,2
Healthy Individuals (n=15)	50,75±2,3	40,95±2,3	42,1±2,3	57,3±3,9	37,65±2,3
	52,36±1,9	42,6±1,7	43,8±1,3		39,3±1,8

Note: In the numerator - before treatment, in the denominator - after treatment;
* - significant differences compared to the control group ($p < 0.05$).

From the presented Table 5.5, it can be seen that long-term comprehensive therapy including acetylsalicylic acid (Cardiomagnyl®) does not affect cerebral hemodynamics, despite a significant improvement in blood coagulation parameters. The investigations into cerebral hemodynamics conducted by us over a 6-month period of comprehensive treatment revealed insignificant changes in the linear blood flow velocity in major vascular basins, and the differences observed in the parameters before and after treatment were of minor significance and were not statistically significant. Based on these findings, we concluded the effectiveness of acetylsalicylic acid (Cardiomagnyl®) in improving blood coagulation parameters and in altering the duration and frequency of transient ischemic attacks (TIAs). However, no significant differences in cerebral hemodynamics and nitric oxide metabolism parameters were detected during the studies. Nevertheless, according to literature data, acetylsalicylic acid (Cardiomagnyl®) can be used at doses ranging from 80 to 1300 mg/day, with lower doses of 80 to 325 mg/day considered preferable due to a lower risk of gastrointestinal complications and the absence of suppression of vascular endothelial prostacyclin, which has antithrombotic effects. There are more effective drugs than acetylsalicylic acid, but the therapy is considerably more expensive and requires regular monitoring of prothrombin time and complete blood count.

However, despite this, considering the medication's influence on the frequency and duration of TIAs, it can be considered an effective therapeutic and prophylactic agent for TIAs and, consequently, for primary and secondary stroke prevention.

5.2. Stroke Prognosis in Patients with Transient Ischemic Attack (TIA)

To assess the stroke prognosis and evaluate the degree of vascular comorbidity, the ABCD2 scale was used. On average, during the year of observation following a TIA, 9 ischemic strokes occurred (19.6% of cases in the observation group). The majority of strokes occurred within the first month (first seven days) after the TIA, and they occurred significantly more frequently ($p<0.001$) in patients at moderate and high stroke risk according to the ABCD2 scale than in patients at low stroke risk according to this scale, as reflected in Table 5.2. Strokes occurred significantly more frequently ($p<0.01$) in patients who presented with unilateral limb weakness (mono- or hemiparesis) during the TIA episode and in patients with a stenosis of more than half the diameter of the carotid artery.

Ischemic strokes occurred in patients who had experienced TIAs in both the carotid and vertebrobasilar basins. There was no significant difference in the frequency of stroke occurrence ($p>0.05$).

After hospital discharge, strokes occurred only in patients who refused regular intake of the recommended medications. None of the 23 patients who continued regular medication intake after a TIA experienced a stroke. The differences in stroke development frequency between the group of patients regularly taking medication and the group who refused regular intake were statistically significant ($p<0.001$).

SUMMARISING

The problem of cerebrovascular diseases, particularly stroke, unites many specialists and makes the issue of preventing the development of this disease multidisciplinary. Transient ischemic attacks (TIAs) are conditions characterized by neurological focal or global symptoms, retinal dysfunction, depending on the affected vascular territory, which are not accompanied by the formation of brain infarction on MRI. It should be noted that this condition develops suddenly, and developing organic neurological manifestations persist and subside within 24 hours [40]. However, after the patient's condition stabilizes, the risk of stroke increases. Transient ischemic attacks (TIAs), as precursors to acute cerebrovascular accidents such as stroke, play an important role in the semiology of cerebrovascular diseases (CVD). TIA syndrome is currently the main syndrome that can lead to stroke development. According to recent studies, on average, 40% of patients with TIA may develop a stroke within the next 5 years, with more than 50% occurring in the first year and 20% within the first month [23, 55, 56, 87]. Thus, the risk of stroke development in patients with TIA is approximately 10% in the first year, and then about 5% annually. The probability of stroke development increases with the patient's age, and recurrent TIAs increase the risk of stroke [27, 55, 57].

Based on this, the dynamic analysis of the clinical-neurological characteristics of TIA, the neuropsychological state of patients, the degree of cerebral blood flow impairment, with the determination of vascular comorbidity factors and biochemical blood tests, is an urgent issue that we have attempted to address in our study.

To achieve the set scientific goals and objectives, the results of the study of 114 patients with various forms of cerebrovascular pathology (CVP) treated in the neurological department of the 3rd clinic of TMA are presented in the work. Of these, Group I (main) comprised 80 patients with TIA, and Group II (comparison) comprised 34 patients with ischemic stroke following TIA. It should be noted that all patients in Groups I and II were in the early or late recovery, or residual periods of stroke. The neurological status features and medical history of all patients were thoroughly studied. When studying the medical history, we paid attention to the duration and frequency of transient ischemic attacks, the severity of neurological symptoms during TIA. In patients who had experienced ischemic stroke (IS), we focused on the frequency of TIAs before and after the stroke, as well as on the vascular basin where the TIA and IS occurred. The influence of TIA frequency and severity on the severity and degree of neurological deficit in IS.

In examining the neurological status, attention was paid to the presence and degree of cranial nerve dysfunction, motor sphere, muscle tone, changes in tendon reflexes, presence of pathological signs, coordination disorders, sensory disturbances, function of pelvic organs, and presence of higher brain function disorders.

When distributing by gender, we found a predominance of males over females in a ratio of 1.5:1. The average age of patients was 68.3±3.2 years. The age structure of the examined patients is presented in Table 2.1. As seen from the data presented, the largest age group of patients with IS comprised elderly individuals (53.8%), middle-aged patients accounted for 34.1%, and elderly patients accounted for 12.1%.

Methods of research included clinical-neurological examination, general clinical methods such as complete blood count and urinalysis. Biochemical studies included blood coagulation analysis, examination of blood nitric oxide levels, and lipid profile analysis. Instrumental methods included ultrasound Dopplerography of the brachiocephalic vessels (UZDG BCS), transcranial Dopplerography (TCDG), magnetic resonance imaging (MRI), and computer tomography (CT) of the brain. For the objective assessment of cognitive impairments in patients with TIA and stroke after TIA, a detailed neuropsychological examination was conducted using the Mini-Mental State Examination (MMSE). The risk of stroke development in patients with TIA was assessed using the ABCD2 scale. Statistical methods (with the use of computer programs) were employed for data analysis.

We studied the clinical picture of TIA in 114 patients. Of these, TIA preceded the development of ischemic stroke in 34 patients. In 80 patients, TIA was considered by us as a manifestation of pre-stroke forms of cerebrovascular insufficiency. Considering this, all patients were divided into two groups: the first consisted of 34 patients with ischemic stroke that developed after previous TIAs, and the second consisted of 80 patients with TIAs. The gender distribution was approximately equal, with a slight predominance of males over females (59 and 55 respectively). The average age of the patients was 60.13±11.4 years.

Comorbid somatic disorders play an important role, worsening the course of TIA and contributing to the development of ischemic stroke in patients with TIA. Therefore, an analysis of the spectrum of comorbid conditions in the somatic status of the examined patients was conducted.

As seen from the table, the most common comorbid conditions in our observations of TIA and ischemic stroke were hypertension, which was present in almost all patients (93.7% and 100% respectively). Atherosclerosis was observed in more than half of the patients in both groups (65% and 58.2% respectively). Additionally, almost a third of the patients with TIA and ischemic stroke had ischemic heart disease (22% and 11%). Furthermore, an analysis of patient compliance with treatment before the development of TIA showed that regular intake of antihypertensive drugs was only seen in 11 patients (14.67%), and only 6 patients (11.53%) with atherosclerosis received lipid-lowering therapy.

As demonstrated by the conducted clinical-neurological studies, the clinical picture of TIA was characterized by focal symptoms and global brain symptomatology. The variety of clinical symptoms depended mainly on the localization of the ischemic focus. Therefore, all TIAs were divided into two groups by us: carotid and vertebro-basilar.

The clinical picture of ischemic strokes consisted of focal and global brain symptoms. An analysis of the medical history revealed qualitative changes in this form of transient cerebral ischemia. Specifically, in 79.4% of patients with ischemic strokes after a previous TIA (n=27), we identified recurrent TIAs, of which 38.2% (n=13) became less frequent but longer in duration. This indicates a worsening of cerebrovascular insufficiency in these patients.

The subjective focal symptoms of carotid basin TIAs were polymorphic. Forty-eight percent of patients (n=27) described transient blindness in one eye, known in the literature as amaurosis fugax. In 26% of cases, it was combined with transient hemiparesis. The development of this clinical syndrome was due to thrombosis of the proximal portion of the ophthalmic artery before its branching from the internal carotid artery, resulting in the development of a hemisyndrome. Speech disorders such as aphasia or dysarthria, observed in 44.64% of patients, were the next most common symptoms. Transient hemiparesis and monoparesis followed at 37.5% and 14.3% respectively. Patients reported transient amnesia in 8.93% of cases (n=5). Four patients (7.14%) complained of swallowing disorders, facial asymmetry, and gait disturbances.

TIAs were most often observed every 6 months and once a year. TIAs occurring once a month were less common (21.43%), and those occurring once a week were very rare. However, patients in these groups were under closer observation by physicians due to their higher risk of developing ischemic strokes. In our view, it is important to note that patients in this category had somewhat worse cerebral hemodynamics and rheological properties of the blood compared to other patients. Furthermore, for a more detailed analysis of the historical features of TIAs, we studied their duration, which according to modern literature [3, 40, 68, 100] and our opinion, may serve as an indicator of cerebral blood flow and autoregulation of cerebral vessel tone.

As the analysis of TIAs depending on duration showed, the distribution of patients was uneven. In particular, there were only 6 patients with short-duration TIAs (up to 10 minutes), slightly more (23.14%) had TIAs lasting up to 1 hour, and the most common observations were of TIAs lasting up to 1 day (66% or 37 patients). The duration of TIAs was largely determined by factors such as the degree of stenosis of the major arteries of the head, the number of affected vascular plaques, the severity of arterial hypertension, and the state of autoregulation of cerebral vessel tone. These factors largely determined the clinical picture of TIAs. For example, transient blindness lasted from 1 minute to 1 day, transient hemiparesis lasted on average no more than 2 hours, speech disorders also regressed within 1 hour, and symptoms such as transient amnesia or

monoparesis lasted no more than 1 hour. In our opinion, the polymorphism of clinical symptoms indirectly indicates the state of cerebral blood flow and can serve as a prognostic criterion for the development of ischemic stroke after TIA, as we noted in subsequent prospective observations. The aforementioned symptoms were characteristic of carotid basin TIAs.

In 45% of our observations, TIAs developed against the background of a combination of two etiological factors – CAS and Grade II hypertension. This prompted the study of the relationship between the development of TIAs in the context of a combination of arterial hypertension and cerebral atherosclerosis. The medical history of patients with TIAs revealed that they usually occurred against the background of arterial hypertension. At the time of TIA, the average blood pressure figures were 156.7±16.3 mm Hg, and were often considered by primary care physicians as hypertensive cerebral crises. The predominance of focal symptoms in the clinical picture over global brain symptoms served as a differential diagnostic criterion typical of TIAs. It is important to note that during the studies, we identified a relationship between the duration of the transient attack and blood pressure values.

The presence of hypertension led to an increase in the duration of TIAs, i.e. against a systolic blood pressure of more than 140 and above, TIAs more often lasted from 1 hour to a day. This was due to the dual mechanism of cerebral ischemia. Firstly, it was thromboembolism of small

Most frequently (55.36%) in patients with TIA in the carotid basin, we encountered cognitive impairments, which were accompanied by memory impairment, attention deficit, spatial and temporal disorientation. The next most common symptom (44.64%) in patients with TIA in the carotid basin was monocular blindness, which was accompanied by decreased vision or complete loss of vision on the side of the stenosed artery. In 25% of patients, complaints of feeling a "curtain" or "shutter" in the eye were noted, which were sometimes provoked by bright sunlight or glare.

In 12 patients (21.43%), we diagnosed sensory disorders in the form of hypoesthesia and paresthesia. In 9 cases (16.07%), transient brachiofacial paresis with monoparesis of the arm and mild central facial nerve paresis on the opposite side of the ischemic focus was observed.

In all cases, transient amnesia developed as TIA against the background of uncontrolled arterial hypertension and subsided several hours after blood pressure reduction. Transient mono- or hemiparesis was most often associated with monocular blindness or facial nerve paresis and were symptoms of optico-pyramidal or brachiofacial paresis.

The main accompanying comorbid conditions were: hypertension (87.5% of cases), cerebral atherosclerosis (50% of cases), and cervical spondylosis (37.5% of cases), as presented in Table 3.2.

Furthermore, in order to conduct a more detailed analysis of the clinical and anamnestic features of TIA, we studied their duration, which according to modern literature and our opinion, could serve as an indicator of cerebral blood flow and autoregulation of cerebral vessel tone.

The duration of TIAs in the vertebrobasilar basin was shorter, lasting on average no more than an hour. As the analysis of TIAs according to duration showed, the distribution of patients was uneven. In particular, there were only 4 patients with short-duration TIAs (up to 10 minutes), slightly more – 25% (n=6) with TIAs lasting more than 1 hour, and the largest number of observations were TIAs lasting up to 1 hour – 54.2% (n=13). At the same time, in cases of carotid localization, they lasted from several minutes to a day and were accompanied by confusion, such as daze or simple hallucinations, which some authors regard as "irritation" symptoms.

As a result of our observations, we identified the peculiarities of the clinical picture of TIAs in the vertebrobasilar basin. Dizziness syndrome was observed in all patients (100% of cases). It was usually nonsystemic and lasted no more than 3-4 minutes. In addition, focal symptoms of TIAs such as: ataxia (70.8%), gait instability and nausea (both 62.5%), moderate dysarthria and dysphagia (33.3%), diplopia (20.8%) were noted. In some cases, we observed the development of TIA against the background of cervical spondylosis, in which, as is known, it has a dual mechanism of development. Firstly, narrowing of the vertebral artery canal leads to a decrease in blood flow velocity, secondly, reflex angiospasm, as a result of irritation of the vessel wall by osteophytes, is important. Drop attacks were observed in 9 patients (37.5%), accompanied by sudden falls without loss of consciousness and subsequent postural tone drop.

If monocular blindness syndrome was obligatory in carotid basin TIAs, then in the vertebrobasilar basin, dizziness syndrome was present in 100% of cases, which in most cases was nonsystemic. The next most frequent symptom was cerebellar-vestibular syndrome (83.3%), which often manifested as gait instability, ataxia, and coordination disorders. In addition, in 37.5% of cases (n=9), bulbar syndrome was noted, which manifested as dysarthria and dysphagia.

Our studies showed polymorphism in the clinical picture and course of TIAs. Analysis of clinical and anamnestic features of TIAs revealed their dependence on a number of factors. In particular, these are etiological factors, the dependence of focal symptoms on the vascular basin in which the transient ischemia occurred, the level of systolic blood pressure, which determined not only the polymorphism of symptoms but also the duration of the TIA. In addition, we determined the average duration of TIAs in the carotid basin, which was on average more than 1 hour and up to a day with a frequency of once every 6 months. In the clinical picture of TIAs depending on the vascular basin, either the monocular blindness syndrome, characteristic of

TIAs in the carotid basin, or the dizziness syndrome, characteristic of TIAs in the vertebrobasilar basin, predominated. If the etiological factors of TIAs in the carotid basin

Next, we conducted an analysis of focal clinical symptoms in patients with ischemic infarction (II) after a previous transient ischemic attack (TIA). All cases of II noted in our observations occurred in the carotid basin. Out of 20 cases of II, 20 occurred in the left carotid basin and 14 in the right. Only in 4 cases did the basin of II not coincide with the basin of TIA. This indicates the significance of TIA not only in terms of predicting the II itself but also in determining the localization of the ischemic focus. The most commonly encountered focal symptoms included hemiparesis and speech impairment (in 91.18% and 88.24% of cases, respectively). In the structure of speech impairments, we observed motor aphasia (26.9%), sensory aphasia (15.3%), but most commonly encountered mixed or total aphasia (57.7%). The muscle strength in the paretic limbs averaged 2.4±0.7 points and corresponded to paresis. Muscle tone on the side of the paresis was usually increased (61.76%), and muscle hypotonia in the acute period of II was noted in only 26.4% of cases. Pathology of cranial nerves in the form of central paresis of the facial and hypoglossal nerves was observed in 79.4%. Pyramid insufficiency, in 67.65% of cases, was expressed not only as hemiparesis but also accompanied by pathological foot signs.

Thus, our research showed that II more often (58.82%) develops 2-3 years after a previous TIA. The lowest percentage (11.76%) of incidence was observed 1 year after TIA. More often (58.82%), the basin of II coincided in 88.32% of cases with the basin where the TIA occurred.

The most frequently reported subjective complaint was weakness in the limbs (about 90%). Other complaints included speech and sensory disturbances, dizziness, headaches, and memory loss. In the structure of focal neurological symptoms in our observations, hemisyndrome and speech disturbances (91.18% and 88.24% of cases) were often encountered. Motor aphasia (26.9%), sensory aphasia (15.3%), but most commonly mixed or total aphasia (57.7%) were noted among speech impairments.

The correspondence of vascular basins between TIA and II after a previous TIA indicates an atherothrombotic or embolic mechanism of persistent cerebral ischemia (II) and underscores the need for primary stroke prevention measures aimed at altering blood rheology parameters, which also undergo certain changes.

Neuropsychological disorders associated with cognitive and psycho-emotional sphere lesions are serious complications of TIA and ischemic stroke, which significantly influence the rehabilitation period, quality of life, and severity of disability in patients.

Cognitive impairments in stroke patients represent heterogeneous disorders of cognitive functions, different in clinical and neuropsychological manifestations, and are caused by organic damage to brain structures, more pronounced in patients with atherothrombotic stroke.

Cognitive deficit was assessed using the MMSE scale. Predementia cognitive impairments and mild dementia predominated in all groups. The most pronounced cognitive impairments were observed in the group with ischemic stroke. Differences between groups of patients who had experienced TIA showed that patients with TIA in the carotid basin had a higher prevalence of cognitive deficit compared to those with TIA in the vertebrobasilar basin.

In conclusion, our research showed that II more often (58.82%) develops 2-3 years after a previous TIA. The lowest percentage (11.76%) of incidence was observed 1 year after TIA. More often (58.82%), the basin of II coincided in 88.32% of cases with the basin where the TIA occurred. According to the data, predementia cognitive impairments and mild dementia predominated in all groups. The most pronounced cognitive impairments were observed in the group with ischemic stroke. Differences between groups of patients who had experienced TIA showed that patients with TIA in the carotid basin had a higher prevalence of cognitive deficit compared to those with TIA in the vertebrobasilar basin.

The clinical picture of TIA is very diverse, but the most important thing is that there are no clear pathognomonic symptoms in this pathology, the presence of which would help clinicians in diagnosing and timely decision-making regarding the treatment tactics for detected lesions, including the question of surgical correction of the pathology. According to a number of authors, TIA develops against the background of stenotic or occlusive lesions of the major arteries of the head (MAH), the diagnosis of which is important, including ultrasound methods of investigation, particularly Doppler ultrasound (DUS).

To determine the condition of cerebral blood flow and all types of associated pathology, we used Doppler ultrasound of the brachiocephalic arteries (DUS BCA) and transcranial Doppler ultrasound of the cerebral arteries (TCDG).

The studies showed that stenoses and occlusions of the internal carotid artery (ICA) were more frequently encountered on the left side than on the right, 79.4% versus 55.9% in patients with II, and 57.6% versus 47.0% in those who had experienced TIA. Stenoses up to 70% were also more common in the left carotid basin in both groups. Stenoses and occlusions of the posterior cerebral artery (PCA) were more frequently encountered on the left side in patients who had experienced II (20.6% versus 13.6%), while right-sided PCA abnormalities were approximately the same in both groups, around 18%. Unlike patients who had experienced II, patients with TIA had PCA stenoses only up to 50%, whereas in the former, PCA stenoses of 50% to 70% were observed in 5.9% of cases.

Deformations of the ICA without hemodynamic disturbances were observed in the II group: 50.9% on the right and 52.9% on the left; in the TIA group, respectively, 43.3% and 50.0%. Pathological deformations of the ICA in patients with II were 5.9% on the right and 14.7% on the left, while in the TIA group they were 1.5% and 6.1%, respectively. Deformations of the PCA without hemodynamic disturbances were observed in the II group: 41.2% on the right and 47.1% on the left; in the TIA group, respectively, 40.9% and 48.5%. Pathological deformations of the PCA in patients with II were 5.9% on the right and 11.8% on the left, while in the TIA group they were 4.5% and 7.6%, respectively.

Thus, hemodynamically significant vascular lesions were observed in 47% of patients with II and 20% of those with TIA. Otherwise, TIA and II developed in patients with hemodynamically insignificant stenoses, deformations, and additional hemodynamic factors, which were predominantly noted on the left side.

For comparison of hemodynamic parameters, patients with II were divided into 2 subgroups: Ia – group with II basin on the right, Ib – group with II basin on the left. The study predominantly included patients with II in the left carotid basin - 21 individuals (61.8%), among whom were 14 males and 7 females; in the right carotid basin - 13 cases (38.2%) - 4 males and 9 females.

The age of patients in group Ia ranged from 49 to 82 years (mean age 64.07±10.5), in group Ib from 47 to 72 years (mean age 59.6±7.6).

Among patients who had experienced II in the right carotid basin, ICA stenosis up to 70% was equally prevalent on both sides and accounted for 61.5%. In group Ib, stenosis of the left ICA up to 70% occurred in 42.8% of cases, while left ICA stenosis was more prevalent, accounting for 71.4% of cases. Hemodynamically significant stenosis of more than 70% and occlusion occurred in 13% of cases in group Ia in the right ICA and in 19% of cases in group Ib in the left ICA. Therefore, the stenotic process predominantly prevailed in the site of stroke localization in patients.

Deformation (without hemodynamic disturbances) of the right ICA was observed in group Ia - 61.5%, Ib - 42.9%, deformation of the left ICA in group Ia - 53.8%, Ib - 52.4%. Pathological deformation of the right ICA was observed in group Ia - 7.7%, Ib - 4.8%, deformation of the left ICA in group Ia - 7.7%, Ib - 19.0%. Deformations of the MAH without hemodynamic disturbances were observed in all groups, but predominated in group Ia (in patients with ischemic stroke in the left carotid system).

For comparison of hemodynamic parameters, patients with TIA were divided into 3 subgroups: IIa – patients with TIA in the right carotid basin; IIb – patients with TIA in the left carotid basin on the left; IIIc – patients with TIA in the vertebrobasilar basin.

The study predominantly included patients with transient ischemic attacks in the left carotid basin - 25 individuals (59.5%), among whom were 13 males and 12 females, in the right carotid basin 17 patients (40.5%), including 10 males and 7 females. TIA in the vertebrobasilar basin was also observed in 8 cases (17.0%) - 6 males and 2 females.

The age of patients in group IIa ranged from 35 to 80 years (mean age 57.4±12.9); in group IIb from 25 to 84 years (mean age 62.4±12.03); in group IIIc ranged from 33 to 78 years (mean age 58.9±11.7).

Stenosis of the right ICA of 50-70% was encountered in 5.9% and 4.0% of cases in groups IIa and IIb respectively. Stenosis of the left ICA of 50-70% was observed only in 16% of individuals who had experienced TIA in the left carotid basin. Among all three groups, stenosis of the right ICA of more than 70% was noted only in 5.9% of group IIa. Hemodynamically significant stenoses of the PCA were not observed in any of the groups. PCA stenoses of up to 50% were encountered in 5 to 12% of individuals who had experienced TIA in the carotid basin, and in 33.3% and 16.7% of cases among patients with TIA in the vertebrobasilar basin, on the right and left sides respectively. Thus, the stenotic process predominated in the site of TIA localization in the ICA.

Deformation (without hemodynamic disturbances) of the right ICA was observed in group Ia - 61.5%, Ib - 42.9%, deformation of the left ICA in group Ia - 53.8%, Ib - 52.4%. Pathological deformation of the right ICA was observed in group Ia - 7.7%, Ib - 4.8%, deformation of the left ICA in group Ia - 7.7%, Ib - 19.0%. Deformations of the MAH without hemodynamic disturbances were observed in all groups, but predominated in group Ia (in patients with ischemic stroke in the left carotid system).

For comparison of hemodynamic parameters, patients with TIA were divided into 3 subgroups: IIa – patients with TIA in the right carotid basin; IIb – patients with TIA in the left carotid basin on the left; IIIc – patients with TIA in the vertebrobasilar basin. The study predominantly included patients with transient ischemic attacks in the left carotid basin - 25 individuals (59.5%), among whom were 13 males and 12 females, in the right carotid basin 17 patients (40.5%), including 10 males and 7 females. TIA in the vertebrobasilar basin was also observed in 8 cases (17.0%) - 6 males and 2 females. The age of patients in group IIa ranged from 35 to 80 years (mean age 57.4±12.9); in group IIb from 25 to 84 years (mean age 62.4±12.03); in group IIIc ranged from 33 to 78 years (mean age 58.9±11.7).

Patients who experienced TIA more often had stenoses of the ICA, as well as deformations of the ICA and PCA. Among the stenoses of the ICA and PCA, stenoses of up to half of the vessel lumen predominated. In group IIa, deformation (without hemodynamic disturbances) and stenosis of up to 50% of the right ICA were most frequently noted (70.6% and 58.8%

respectively). For patients in group IIb, the main manifestation of MAH pathology was deformation (without hemodynamic disturbances) and stenosis of up to 50% of the left ICA (64.0% and 60.0% respectively). In the IIIc group, deformation (without hemodynamic disturbances) of the PCA and stenosis of the left ICA were most frequently observed (54.2% and 45.8% respectively).

Stenosis of the right ICA of 50-70% was encountered in 5.9% and 4.0% of cases in groups IIa and IIb respectively. Stenosis of the left ICA of 50-70% was observed only in 16% of individuals who had experienced TIA in the left carotid basin. Among all three groups, stenosis of the right ICA of more than 70% was noted only in 5.9% of group IIa. Hemodynamically significant stenoses of the PCA were not observed in any of the groups. PCA stenoses of up to 50% were encountered in 5 to 12% of individuals who had experienced TIA in the carotid basin, and in 33.3% and 16.7% of cases among patients with TIA in the vertebrobasilar basin, on the right and left sides respectively. Thus, the stenotic process predominated in the site of TIA localization in the ICA.

Deformations of the PCA and ICA in groups IIa and IIb were always predominant on the side of the lesion. In group IIIc, deformation of the left ICA and PCA predominated over the right (45.8% vs. 33.3% and 50.0% vs. 41.7% respectively). Pathological deformation of the right ICA was observed in group IIa in 5.9%, pathological deformation of the left ICA in group IIb - 16.0%. Pathological deformation of the PCA was not observed in groups IIa and IIb, but was observed in 8.3% of cases in group IIIc. Pathological deformation of the left PCA was noted in groups IIb and IIIc in approximately 8% of cases each, and also in group IIa in 5.9% of cases. Vertebrogenic compression of the right PCA was detected in groups IIa and IIb in 5.9% and 4.0% of cases respectively, and in group IIIc - in 16.7% of cases. Vertebrogenic compression of the left PCA was observed only in groups IIb and IIIc (4.0% and 20.8% respectively).

Transcranial Dopplerography was performed on 72 patients (45 males and 27 females) aged 45 to 80 years (mean age - 62.3 ± 5.1 years). The control group (12 patients) consisted of individuals of the same age who had experienced an ischemic stroke in the early recovery period. It is important to note that all cases of stroke had a history of two or more TIAs. The etiological factors of TIA in our observations were: cerebral atherosclerosis 70.8% (51 patients) and a combination of cerebral atherosclerosis and hypertension 29.2% (21 patients). The course of hypertension in our observations was uncontrolled, with average blood pressure values of 170±6.4 mmHg and frequent increases in systolic blood pressure above 220 mmHg, which exacerbated the picture of cerebrovascular insufficiency.

The study of cerebral hemodynamics and the condition of the MAH was conducted using the method of ultrasound Dopplerography on the "VAZOSKAN" apparatus from "SONICAID" (England) using sensors with frequencies of 2, 4, 8 MHz and diameters of 14, 10, and 6 mm.

To assess changes in autoregulation parameters against the background of hypo- and hypertonus of resistive vessels, studies were conducted at rest, under conditions of hyper- and hypocapnic load, simulated by inhalation of 7% carbogen and hyperventilation, for 2-3 minutes. The obtained data were processed statistically.

In the clinical picture, outside the TIA attack, cerebral complaints predominated, including headaches, dizziness exacerbated by head turns and changes in body position, sleep disturbances, decreased performance, and memory impairment. In the presence of diffuse focal symptoms such as tendon areflexia, symptoms of oral automatism, pathological plantar reflexes, the diagnosis of chronic cerebral ischemia with impaired circulation in the vertebrobasilar basin was made in the majority of our patients, 80.2%.

Patients with TIA, depending on the frequency of ischemic episodes, were divided into 2 groups: Group I (32 patients) with a TIA frequency of 1 time every 6 months, Group II (18 patients) with a TIA frequency of 1 time per month. As noted above, the indicators of cerebral hemodynamics and reactivity of cerebral vessels were compared with those of patients with ischemic strokes in the early recovery period (12 patients).

The analysis of the indicators of linear blood flow velocity in intracranial vessels showed significant differences in patients with a TIA frequency of 1 time every 6 months compared to the group of patients with ischemic stroke. Closer to the indicators of patients with stroke were the indicators in patients with a higher frequency (1 time per month) of acute cerebral ischemic episodes. Based on this, we hypothesized that it is in this group of patients that the risk of stroke development is highest. In our opinion, this is due not only to the severity of decompensation of cerebral hemodynamics and exhaustion of compensatory mechanisms but also to the exhaustion of mechanisms of autoregulation of cerebral blood flow.

The autoregulation of cerebral blood supply is a complex physiological phenomenon, implemented by at least three interrelated regulatory mechanisms: myogenic, neurogenic, and metabolic nature. The myogenic mechanism manifests itself in the early, dynamic phase of sharp changes in systemic arterial pressure. It is well known that myogenic autoregulation is carried out by regulating the function of the juxtaglomerular apparatus of the kidneys, which is involved in the synthesis of angiotensin-converting enzyme. The concentration of the latter in the blood affects the level of angiotensin in the blood. The content of angiotensin in the blood affects the tone of the muscular layer of the cerebral arteries during TIAs.

In this regard, we further studied the state of vascular reactivity of the brain as one of the main links in the compensatory mechanism of cerebral blood circulation. The data of the conducted studies on the study of the vasoconstrictor reactivity coefficient are presented in table 2.

The analysis of vasoconstrictor reactivity parameters showed significant differences in patients of Group I compared to patients who had a stroke. The differences in these parameters between patients in the second group and those who had a stroke were not significant. It is important to note that the smallest differences in the vasoconstrictor reactivity coefficient in all three compared groups were in the basilar basin (main artery). This, in our opinion, indicates the greatest susceptibility (predisposition) of this vascular basin to TIA and explains the higher frequency of transient ischemia in the vertebrobasilar basin.

Thus, our studies have shown that the clinical picture and course of TIAs are largely determined by the state of cerebral hemodynamics. According to our research, both this parameter and the vascular basin determine the clinical picture of TIAs.

The analysis of linear blood flow velocity parameters in intracranial vessels revealed significant differences in patients with a TIA frequency of 1 time every 6 months compared to the group of patients with ischemic stroke. Patients with a frequency of acute cerebral ischemic episodes of more than 1 time per month had indicators closer to those of the stroke group. Based on this, we hypothesize that it is in this group of patients that the risk of stroke development is highest. This is due to the severity of cerebral hemodynamic decompensation and exhaustion of compensatory mechanisms, which was confirmed in studies on the state of cerebral vascular reactivity.

The indicators of vascular reactivity in patients of the second group compared to patients who had a stroke were not significantly different. It is important to note that the smallest differences in the vascular reactivity coefficient in all compared groups were in the vertebrobasilar basin. In our opinion, this indicates the greatest susceptibility of this vascular basin to TIAs and explains the higher frequency of transient brain ischemia in the vertebrobasilar basin. Moreover, a decrease in this indicator may indicate a greater risk of developing acute cerebrovascular accidents, which has important prognostic value for early diagnosis and prognosis of ischemic stroke.

Thus, as our studies have shown, the severity and variety of clinical symptoms of transient ischemic attacks, as well as their frequency, indicate a higher likelihood of subsequent ischemic stroke. This is, in turn, associated with indicators of cerebral hemodynamics. Therefore, a decrease in cerebral blood flow in patients with TIAs, approaching those indicators during ischemic stroke, as revealed by Doppler studies, is a risk factor for its development.

Additionally, as our research has shown, the state of cerebral blood flow autoregulation is important in the development of stroke after a TIA, with indicators in patients with a higher frequency of TIAs also approaching those of stroke patients. In our opinion, an important aspect of cerebral hemodynamics is that indicators of cerebral blood flow in the vertebrobasilar basin were most similar to the hemodynamic indicators of the stroke group, indicating the susceptibility of this vascular basin to transient dysgeusia, which explains the predominance in the clinical picture of TIAs of vertigo syndrome or cerebellar dyscoordination syndrome.

Based on the conducted MRI studies, we obtained results indicating the condition of brain tissue. The main parameters in this case were such linear indicators as the expansion of the subarachnoid space, the lateral and third ventricle index, as well as such densitometric indicators as the presence of foci of reduced density. It is necessary to note that foci of reduced density were located in the white matter, periventricularly, and their number in patients with TIAs ranged from 1 to 6. Their density averaged 18.4±2.7 HU, which is less than the density of white matter in the norm (24 HU).

MRI findings in transient ischemic attack (TIA) and ischemic stroke (IS) after TIA

Linear and volumetric parameters of the ventricular system and subarachnoid space

It is important to note that the linear parameters of the ventricular system and subarachnoid space were different in both groups examined. Thus, if in patients with TIA, expansion of the subarachnoid space was noted by us in 64 ± 1.78% of cases, then in the group with IS it was noted in all observations and amounted to 100%. The width of the lateral ventricle in patients with IS was greater and was 2.7 ± 0.04 mm versus 2.2 ± 0.2, than in the group with TIA. A similar pattern was observed when comparing the lateral ventricle index, the values of which were also higher in the IS group - 21.2 ± 0.6, and 15.6 ± 0.8 in the TIA group.

Summarizing the data obtained from MRI studies, we can say that the MRI picture of TIA and IS after TIA has its own characteristics. They consist in the presence of foci of reduced density of brain matter located in the white matter around the lateral ventricles. Their number does not always correspond to the number of ischemic attacks suffered. In patients with IS after TIA and patients with TIA, their number is approximately the same, which represents them not only as an MRI pattern of TIA, but also as a risk factor for the development of IS after TIA. Analysis of the linear and volumetric parameters of the ventricular system of the brain showed that TIA and IS after TIA develop against the background of chronic cerebral ischemia. The latter was manifested by an increase in the linear and volumetric parameters of the subarachnoid space and ventricular system of the brain in both patients with TIA and patients with IS after TIA, which puts these two nosological units on a par in terms of morphological changes.

Endothelial dysfunction (ED) in patients with TIA and IS after TIA

The state of ED was studied in patients with TIA (40 people) - group I, with IS after TIA (30 people) - group II. The control group consisted of 20 people of comparable age and sex without pathological changes in the blood serum.

The level of NO was determined by the sum of its main metabolites (NO2- and NO3-), the activity of endothelial NO synthase (eNOS), nitrate reductase (HP), and peroxyni nitrite (ONOO-).

As our studies showed, the level of NO in the blood serum in patients of group I was 26.6% higher and in patients of group II - 22.5% relative to the control group. The activity of endothelial eNOS in group I was 28.2% lower and in patients of group II - 21.6%, and the content of nitrate reductase (HP) increased by 62.1% in patients of group I and by 31.1% in patients of group II compared to the control (Table 4.4).

This trend persisted when analyzing the content of peroxyni nitrite (ONOO-), which in turn increases to 3.64 + 0.13 nmol / ml in patients of group I and to 3.03 ± 0.13 nmol / ml in patients of group II, which significantly exceeded such indicators of the control group.

Analysis of the indicators of nitrogen oxide exchange in our observations revealed differences, in comparison with the indicators of the control group, however, the indicators in the groups of patients differed insignificantly. In our opinion, this indicates the presence of signs of ED in patients of the first and second groups, the severity of which was somewhat less in patients with IS after TIA.

In this regard, in order to clarify the role of ED in the pathogenesis of TIA, we further analyzed the indicators of NO exchange in the group of patients with TIA depending on the frequency of TIA. In patients with a higher frequency of violations in the production of nitric oxide by the vascular endothelium with high reliability ($P < 0.001$), it differs from that in patients with a frequency of TIA once every 6 months, the changes caused by frequent (once a month) TIA are more pronounced than in patients with TIA once every 6 months. It is important to note that the differences were observed both in terms of the content of NO and in terms of the level of its metabolites in the blood. For example, the content of HP in patients with a frequency of TIA once every 6 months was 12.39 ± 0.14 nmol / min / ml, while in patients with a frequency of once a month this indicator was 17.24 + 0.35 nmol / min / ml.

Based on our research, we have concluded that transient ischemic attacks (TIAs), as well as ischemic strokes (IS) following TIA, are associated with endothelial dysfunction. This has been confirmed by our findings. Specifically, there are significant differences in NO exchange indicators among patients with TIA and IS following TIA compared to those in the control group. The indicators in the TIA group were dependent on the frequency of vascular paroxysm and were higher in patients with a TIA frequency of once a month. In our opinion, this indicates

a greater degree of membranodestructive processes in this group of patients and is important in predicting IS following TIA. Greater activity of free radical processes may indicate a higher likelihood of IS with persistent neurological deficit and, consequently, disability.

Changes in blood rheological properties are one of the most common causes of acute cerebrovascular diseases, including TIAs. Signs of blood hypercoagulability indicate a high risk of thrombus formation, which can lead to thrombosis or embolism of cerebral vessels. Therefore, biochemical studies of blood in patients from both groups were conducted to clarify the role of blood rheological properties in the development of TIAs and IS following TIA. We examined coagulograms of blood from 80 patients with TIA and 34 patients with IS following TIA. The obtained data were compared with indicators from 20 healthy individuals of the same age. Parameters such as fibrinogen, prothrombin index (PTI), and international normalized ratio (INR) were selected from the indicators.

Analysis of the nature of blood rheological and coagulation properties in patients with TIA and IS following TIA revealed that blood viscosity did not significantly differ at high hematocrit and INR levels compared to control indicators. The increase in blood viscosity in the TIA group was primarily associated with elevated levels of fibrinogen and PTI. In the IS group following TIA, this indicator was lower than control values, with relatively equal hematocrit levels and a slight increase in fibrinogen compared to the control group. Comparative analysis of coagulation parameters in both patient groups revealed low PTI values in patients with IS following TIA compared to those with TIA and the control group, with significant differences from the TIA group. In our opinion, the differences in coagulation parameters in patients with IS following TIA are related to antiplatelet therapy, including aspirin derivatives.

We analyzed the results of the effect of antiplatelet therapy with acetylsalicylic acid (cardiomagnyl) on blood rheological properties during treatment. Our studies showed a tendency towards hypercoagulability in both patient groups during treatment with acetylsalicylic acid (cardiomagnyl), which in turn was one of the factors contributing to the development of both TIAs and IS. Studying the dynamics of these blood rheology parameters revealed less improvement in the group of patients who had experienced IS. Parameters such as PTI and fibrinogen levels were particularly resistant to the effects of antiplatelet therapy. In our view, this is one of the factors determining the risk of developing IS after TIA. In the TIA group, the dynamics of rheological parameters significantly improved with treatment with acetylsalicylic acid (cardiomagnyl), highlighting the importance of prescribing this medication in the secondary prevention of ischemic strokes.

From the provided data, it is evident that our observations showed such disruptions in blood coagulogram as shortened blood clotting time, increased prothrombin index, elevated

fibrinogen, and alteration in thrombotest. This, in turn, justifies the prescription of antiplatelet therapy for these patients.

The improvement in blood rheological properties, in turn, influenced both the subjective complaints of the patients and the frequency of TIAs, and in some cases, the duration of transient cerebral ischemia. In this regard, to clarify the effect of treatment with acetylsalicylic acid (cardiomagnyl) on nitric oxide exchange indicators, we analyzed nitric oxide exchange indicators and the state of cerebral hemodynamics in patients from both groups who were taking this medication. It is worth noting that the studies were conducted twice, before treatment and at 6 months of medication intake, as according to literature data, the most persistent changes are observed during these periods. The analysis of the dynamics of nitric oxide exchange indicators did not reveal significant changes during antiplatelet therapy. From the presented table, it is clear that treatment with the antiplatelet agent acetylsalicylic acid (cardiomagnyl) had little impact on free radical oxidation indicators. The insignificant changes that occurred were observed across all nitric oxide exchange indicators. For example, the level of NO in the blood serum of patients in Group I decreased by only 3.7% after treatment, and in patients in Group II, it decreased by 7.3% compared to the initial data, with a significant difference from the control group. The activity of endothelial eNOS in Group I decreased by 10.1% during treatment, and in patients in Group II, it decreased by 2.9%, while the level of nitrate reductase (HP) decreased by 2.2% in Group I patients and by 2.02% in Group II patients. The decrease in ONOO" also had an insignificant character. While the dynamics of this indicator in Group I patients was 14.8%, in Group II patients, it was 7.6%.

Summarizing the dynamics of nitric oxide exchange indicators in patients with TIA and IS after TIA, it can be noted that there was no dynamic change in the indicators during treatment with acetylsalicylic acid (cardiomagnyl). The minor changes that occurred may have been due to the traditional therapy including neuro-metabolites, anti-hypoxants, and other medications, which to some extent affect nitric oxide exchange and the level of free radicals in the blood. However, based on our data, it can be stated that there was a slight influence of comprehensive therapy including acetylsalicylic acid (cardiomagnyl) on the course of TIA in terms of reducing attack duration and frequency.

Endothelial dysfunction is accompanied by vasospasm, resulting in insufficient blood supply to the brain. Therefore, to clarify the state of cerebral hemodynamics during treatment with acetylsalicylic acid (cardiomagnyl), we conducted research on cerebral hemodynamics using Doppler ultrasound.

The ABCD2 scale was used to assess the prognosis of stroke and the degree of vascular comorbidity. On average, over the course of a year of observation since TIA, 9 ischemic strokes

developed (19.6% of cases in the observation group). The majority of strokes occurred within the first month (first seven days) after TIA, and they occurred significantly more frequently ($p<0.001$) in patients at medium and high risk of stroke according to the ABCD2 scale than in patients at low risk of stroke according to this scale. Strokes occurred significantly more often ($p<0.01$) in patients who presented with unilateral limb weakness (mono- or hemiparesis) during the clinical presentation of TIA, as well as in patients with stenosis of the carotid artery of more than half the diameter.

Ischemic strokes occurred in patients who experienced TIA in both the carotid and vertebrobasilar basins. The difference in the frequency of strokes was not significant ($p>0.05$).

After discharge from the hospital, strokes occurred only in patients who refused to take the recommended medications regularly. None of the 23 patients who continued regular medication intake after TIA experienced a stroke. The differences in the frequency of stroke development between the group of patients regularly taking medication and the group of patients who refused regular intake were statistically significant ($p<0.001$).

CONCLUSIONS:

1. The research results revealed the longest duration of TIA episodes in patients with transient disturbances in the carotid basin (61.7%). It is worth noting that strokes occurring after TIA were predominantly observed in the carotid basin.

2. Vascular comorbidity factors (atherosclerosis 65%, hypertension 93.7%, diabetes mellitus 11.25%, ischemic heart disease 27.5%) contribute to endothelial dysfunction with an increase in nitric oxide levels, thereby promoting an increase in TIA episodes and duration. These comorbidities are accompanied by cognitive impairments, leading to decreased complexity.

3. The most pronounced disruption of cerebral blood flow was observed in the vertebrobasilar basin, confirming the vulnerability of this vascular basin to transient ischemia, which explains the predominance of dizziness syndrome or cerebellar-ataxic syndrome in the clinical picture of TIA.

4. Comprehensive examination and therapy according to stroke treatment standards in patients with TIA reduce the risk of stroke development in the first 6 months.

PRACTICAL RECOMMENDATIONS:

1. Identifying vascular comorbidity factors in patients with TIA will allow timely implementation of preventive measures to prevent the development of ischemic stroke.

2. Identifying the peculiarities of hemodynamic disorders in patients with TIA will enable the selection of the correct strategy for conservative treatment or recommendation for carotid endarterectomy.

3. Upon detection of TIA episodes, patients are recommended to undergo examination and therapy according to stroke treatment standards, which will help prevent further development of ischemic stroke.

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