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COMPLEX RADIATION DIAGNOSTICS OF NON-TRAUMATIC SUBARACHNOID HEMORRHAGE IN THE ACUTE PHASE AND DURING POSTOPERATIVE FOLLOW-UP

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CONTENT

INTRODUCTION

Research Rationale

Acute non-traumatic subarachnoid hemorrhage (non-traumatic SAH) is a potentially life-threatening condition with a mortality rate of 30 to 50% according to various authors [57]. Despite advances in the development of diagnostic radiology methods, there are cases in which this pathology is diagnosed late. It is also known that more than 15% of patients with non-traumatic SAH die before they have time to seek medical help, and many of the survivors often suffer from neurocognitive and psychological disorders that negatively affect their quality of life [144].

Modern medicine allows us to provide high-tech care for patients with ruptured intracranial aneurysms (IA), where accurate diagnosis prior to surgery based on visualization of the intracranial vessels is extremely important. At the same time, there are restrictions, such as the time limit, the equipment features, the qualifications of specialists, the referral of patients. Solutions that enable minimally invasive treatment follow-up are also in great demand.

With the increasing need for precise preoperative diagnostics in limited time due to medical-technical progress and the priority of minimally invasive treatment follow-up, the need to optimize the protocols of diagnostic radiology methods has increased.

In the modern context of the rapid development of diagnostic radiology, it is necessary to update the scientifically based concept of the organization of medical and diagnostic care for patients with intracranial aneurysms, which is based on multidisciplinary solutions. The use of artificial intelligence (AI) systems to analyze data in patients with non-traumatic SAH and determine their treatment appears promising. It remains important to define more precisely the indications for the use of modern methods of diagnostic radiology in this pathology and to combine the data obtained for the choice of treatment tactics and postoperative management of non-traumatic SAH in patients with IA ruptures.

This approach, based on the principles of evidence-based medicine and the benefits of modern diagnostic and information technologies, enables optimal referral triage patients with intracranial aneurysms and suspected intracranial aneurysms at every stage of medical care. The development of a new diagnostic strategy for the detection of non-traumatic SAH and intra/extracranial vascular diseases will help to further improve treatment outcomes and reduce the risk of early and late complications.

Extent of Previous Research

Ruptures of intracranial aneurysms are the cause of 80-90% of all intracranial hemorrhages. It has been reported that only 1% of existing IA ruptures result in non-traumatic SAH. However, the severity of the consequences of non-traumatic SAH and the high risk of adverse outcomes require immediate recognition of both the hemorrhage itself and the IA that caused it in order to choose the most appropriate treatment tactics and follow the dynamics [57]. Digital cerebral angiography (CA) is traditionally considered the gold standard for diagnosing the source of bleeding in non-traumatic SAH in the acute phase [57, 144]. However, some authors have expressed the opinion that computed tomography angiography (CTA) usually comes close in terms of accuracy, even in emergency diagnosis, and is more attractive from an organizational and economic point of view [36, 169].

Magnetic resonance angiography (MRA) is also becoming increasingly important for the diagnosis of IA and non-traumatic SAH. It has been reported that the sensitivity of CTA and MRA in detecting IA larger than 2-3 mm in diameter is 80-98% [140, 169]. At the same time, it is understood that the use of CA remains mandatory in the case of complex and multiple intracranial aneurysms when occlusion testing or concomitant endovascular surgery is required, but there is a lively controversy on this topic [81, 152].

An important problem is the postoperative follow-up of patients who have recovered from non-traumatic SAH in the early and late phases. In the early postoperative phase, it is necessary to ensure careful monitoring of postoperative changes and to rule out life-threatening complications. CTA is currently becoming a routine method for assessing the condition of IA after clipping [91]. To date, the ability of CTA to visualize IA after treatment by endovascular coiling is limited due to artifacts caused by metallic microcoils (e.g. platinum). In such cases, the methods of choice may be MRA (albeit with limitations) or CA[13].

Particular importance is currently attached to late postoperative control after IA treatment with CA, which is associated with the risk of complications. The inclusion of non-invasive radiation techniques such as CTA and MRA in the standard of postoperative care will allow patients to be monitored on an outpatient basis without the need for hospitalization. This also significantly reduces the amount of contrast medium used and the radiation exposure for patients.

Research Goals

Improving IA diagnostics to define case management for patients with acute non-traumatic SAH in the pre- and postoperative phases using comprehensive imaging data to improve outcomes and reduce the incidence of complications.

Research Tasks

1. Research the clinical characteristics and statistics of SAH, the scope of diagnostic medical care in the early hospital phase in the Krasnodar Territory.
2. Assessment of the diagnostic efficiency of computed tomography angiography of the brachiocephalic artery (CTA BCA) in emergency situations to identify the source of bleeding in the acute phase of non-traumatic SAH under emergency department conditions.
3. Research the need to include extracranial BCA segments in the CTA protocol and the impact of identified concomitant vascular pathology on treatment tactics in patients with acute non-traumatic SAH.
4. Evaluation of the influence of radiologists’ experience on the assessment of the CTA BCA results in patients with IA.

5. Evaluation of the capabilities of automatic image processing algorithms based on a prototype three-dimensional convolutional neural network in the identification of IA using CTA BCA data.

6. Validation of CTA BCA in the non-invasive follow-up of the results of surgical treatment of aneurysms.

7. Assessment of the diagnostic efficiency of dynamic MRA in the postoperative follow-up of IA.

8. Evaluation of the efficiency of the developed algorithm for the emergency diagnosis of acute non-traumatic SAH at an early hospital phase.

Scientific Novelty

The research has returned the following results:

1. The high diagnostic value of CTA BCA in patients with acute non-traumatic SAH in the early hospital stage is demonstrated both at the primary care level and in a multidisciplinary hospital.

2. The concept of the benefit of using an extended CTA protocol (with an analysis of the brachiocephalic artery condition) in patients with SAH in the emergency department of a multidisciplinary hospital is established. The impact of the developed approach, which is based on the principles of evidence-based medicine, on triage, patient referral and choice of treatment is examined.

3. An organizational model in the form of referral of patients with acute non-traumatic SAH in the Krasnodar Territory is presented.

4. An algorithm for examination of patients with acute non-traumatic SAH in the emergency department is developed.

5. A model for the use of modern non-invasive diagnostic radiology methods in the long-term postoperative follow-up of IA is shown.

6. A prototype convolutional network was developed to detect IA using CTA BCA data in the emergency department.

7. The use of the prototype convolutional neural network in the diagnosis of IA is tested and the feasibility of its use is demonstrated.

Research Theoretical and Practical Relevance

The scientific relevance of the work is to obtain evidence-based data on the high diagnostic performance of modern methods of diagnostic radiology in the detection of non-traumatic SAH, identification of its source and assessment of the patient's condition before and after surgical treatment, which significantly complements and expands the currently available ideas in this area. In turn, the results obtained can significantly improve the accuracy of diagnostics and reduce the time spent on it according to the needs of medical institutions of different categories (vascular surgery departments and regional vascular centers).

A comparative study of the diagnostic capabilities of different imaging modalities for IA and non-traumatic SAH (CT, MRI, CA) made it possible to optimize protocols for the treatment of patients with non-traumatic SAH, minimize the risks of CA and also increase the speed of medical decision-making based on reliable data.

The practical relevance of the work lies in the creation of an optimized model for the effective organization of the work of the emergency department, diagnostic radiology subdivisions of medical institutions and ambulance services providing emergency care for patients with non-traumatic SAH. The model presented made it possible to improve their interaction with specialized medical institutions that offer high-tech assistance to this group of patients. The application of the optimized model improved the diagnosis, triage and referral of patients with non-traumatic SAH and IA, which was confirmed by the absence of recurrent non-traumatic SAH in the studied patient group. An improved standard for the emergency diagnosis of non-traumatic SAH has been established, regardless of the severity of the patient's condition. based recommendations were developed to improve the medical care of patients with non-traumatic SAH at an early hospital phase.

The work covers all phases of care for patients with symptoms of non-traumatic SAH: from the triage and referral phase to treatment and postoperative follow-up, including long-term.

The use of an optimized model for the diagnosis of non-traumatic SAH and IA, introduced into the clinical practice of the medical service of one of the largest and most densely populated regions of the Russian Federation – the Krasnodar Territory, – has significantly reduced the examination time of patients with non-traumatic SAH in the emergency department without increasing the number of errors. Based on the data obtained, the principles of triage and referral of patients depending on the treatment method were developed, which have been shown to offer cost advantage.

A prototype of a three-dimensional convolutional neural network was developed for the use of AI to identify IA. Its testing showed a positive impact on CTA BCA outcomes in the emergency department and on tactical decisions in the treatment of patients with acute non-traumatic SAH.

Research Materials and Methods

This thesis research has been conducted in several stages.

1. The first stage covered a detailed analysis of publications on this problem.
2. The second stage was dedicated to analyzing the current triage and referral approaches for patients with acute non-traumatic SAH in the Krasnodar Territory.
3. The third stage was dedicated to the implementation of optimized protocols for the imaging examination of patients with acute non-traumatic SAH in the emergency department of the Krasnodar Regional Vascular Center (RVC).
4. At the fourth stage, a retrospective analysis of the medical history of patients with acute non-traumatic SAH who received diagnostic and medical evacuation measures according to the new unified regional protocol and underwent surgical intervention at the Regional Neurosurgical Center of the S.V. Ochakovskiy Regional Clinical Hospital No. 1, a Research Institute of the Ministry of Health of the Krasnodar Territory (Research

Institute / RCH No. 1) in the period from September 2017 to August 2020 (650 patients in total), was carried out.

5. The basis of the fifth stage was the selection of patients with non-traumatic SAH caused by the rupture of an intracranial aneurysm. The work also analyzed the diagnostic efficiency indicators used for diagnosis after imaging procedures. The comparative diagnostic value of CT, CTA, MRI, MRA and CA for assessing the condition of the brain, cerebral vasculature and brachiocephalic artery in patients before and after surgery, including the late phase, was determined.

6. The sixth stage consisted in analyzing the experience of implementing the optimized protocols proposed by the author for the examination of patients with acute non-traumatic SAH in the emergency department of Novorossiysk City Hospital No.1 (NCH No.1), a state budgetary institution of the Ministry of Health of the Krasnodar Territory, in 2019-2020.

7. Based on the analysis of the results obtained, recommendations were formulated for the optimal identification of sources of acute non-traumatic SAH in the emergency departments of various medical institutions, as well as algorithms for postoperative imaging monitoring of treated IAs that have caused non-traumatic SAH.

8. A separate innovative and independent part of the work was the development and testing of the prototype three-dimensional convolutional neural network for the identification of IA from CTA BCA and the evaluation of the impact of the computer analysis results on the speed of decision making in relation to the treatment of patients with acute non-traumatic SAH.

The research was conducted in accordance with the WMA Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects as amended in 2000 and the Rules of Clinical Practice in the Russian Federation approved by the Ministry of Health of the Russian Federation, Order No.266 dd. 19/06/2003.

The protocol of this thesis work, Complex Radiation Diagnostics of Non-Traumatic Subarachnoid Hemorrhage in the Acute Phase and During Postoperative Follow-Up, was approved by the Ethics Committee of the Kuban State Medical University of the Ministry of Health of the Russian Federation, Protocol No.58 dd. 11/12/2017.

Provisions to Be Defended

1. The diagnostic efficiency of CT and CTA offers a high degree of detection of non-traumatic SAH with determination of the source, while reducing diagnostic time, the number of techniques and invasive procedures used and the patient's exposure.
2. The CTA protocol for the examination of patients with non-traumatic SAH, which allows simultaneous assessment of the condition of the intracranial and extracranial BCA segments, increases the detection of concomitant vascular pathologies and influences the choice of treatment tactics.
3. The diagnostic efficiency of dynamic MRA and CTA of the brachiocephalic artery for monitoring the treated IA allows them to be used as a substitute for invasive techniques (CA) in the long-term postoperative phase in almost all cases.
4. Using the prototype three-dimensional convolutional neural network increases the accuracy of the diagnosis, which is important in emergency situations when qualified radiologists are not available.

Correspondence of Thesis Work with Specialization Certificate

The main scientific provisions of the thesis correspond to specialization certificate 3.1.25 Diagnostic Radiology.

Author’s Personal Contribution

The author directly has conducted all phases of this study, including formulating a research problem, conducting radiation studies, collecting and analyzing clinical and diagnostic material, statistically processing the material, discussing the results, and publishing them with subsequent implementation in clinical practice.

Degree of Credibility and Evaluation of Results

The degree of credibility of the research results is determined by the large number of patients involved in the work. The work has been completed, and the models developed on the basis of its results have been implemented in the health care system of one of the largest regions of the Russian Federation – the Krasnodar Territory, which proves the feasibility of their nationwide application.

Modern diagnostic equipment and techniques as well as professional image post-processing stations were used to carry out the research work.

The statistical analysis involved the appropriate and correct application of suitable methods using generally recognized software packages.

The conclusions of the research are fully consistent with the tasks set and the results obtained. Practical recommendations logically follow from the research results and can be transferred to other medical institutions in the country.

Links to Scientific Programs and Plans

The work has been carried out as part of the research program of the Department of Diagnostic Radiology No.2 of the Faculty of Continuing Education and Professional Development of the Kuban State Medical University.

The topic of the thesis was approved at a meeting of the Academic Council of the Kuban State Medical University (Minutes No.6 of 10/06/2021).

Implementation of Research Results

The results of the scientific research carried out (development of improved protocols for the diagnostic care of patients with non-traumatic SAH in the early hospital phase and in the postoperative phase) have been incorporated into the clinical practice of the Research Institute / RCH No.1 , the Primary Vascular Department (PVD) and the

Regional Vascular Center (RVC) of the Krasnodar Territory, as well as in the curriculum of the Department of Diagnostic Radiology No.2 of the Faculty of Continuing Education and Professional Development of the Kuban State Medical University in the form of methodological recommendations, lectures, practical courses, publications, abstracts and conference reports.

Peer-Reviewed Evaluation

The main results of the research have been presented in the form of verbal reports at the teleconference Modern standards of analysis of X-ray images and assessment principles (Online, 2020), at the Congress of the Russian Society of Radiology (Moscow, 2021), at the V All-Russian Scientific and Educational Congress Oncoradiology, Radiation Diagnostics and Therapy (Moscow, 2022), at the scientific and practical conference Neuroimaging (Krasnodar, 2022), at the All-Russian Congress Radiology-2022 (Moscow, 2022), at the round table Discussion Club of Radiologists (Online, 2022), at the regional scientific and practical conference Topical Issues of Diagnostic Radiology (Krasnodar, 2023), at the VI Congress of Neuroradiologists (Sochi, 2023).

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Publications

Fifteen printed works have been devoted to the topic of the thesis and published in journals recommended by the Higher Attestation Commission of the Ministry of Science and Higher Education of the Russian Federation, 14 articles are listed in Scopus; also published: a textbook, abstracts, guides for doctors and conference materials.

Scope and Structure

The thesis work comprises 210 typewritten pages and consists of an introduction, chapters, conclusions and a reference list. The work is illustrated with 29 tables and 44 figures. The reference list comprises 176 sources, including 36 local and 140 foreign authors.

CHAPTER I. CURRENT STATE OF THE PROBLEM OF INTRACRANIAL ANEURYSMS DIAGNOSIS AND TREATMENT (LITERATURE REVIEW)

1.1 Leading pathomorphological characteristics of acute ruptures of intracranial aneurysms and pathophysiological alterations caused by them

An intracranial aneurysm is an abnormal expansion of the cerebral artery lumen and its wall bulging. The main danger of having an aneurysm is the possibility of its rupture that leads to the outpouring of blood into the subarachnoid space. IA prevalence in the general population is about 2-5% [48]. The incidence of acute nTSH varies from 2.0 to 22.5 cases per 100000 people, mortality rate reaches 30-50% [57]. There is also evidence that the incidence of nTSH in low- and middle-income countries is almost 2 times high er than in countries with high income [72]. However, it is not possible to find out the exact figure, as about 12 - 15% of patients die before they have time to refer for medical assistance [144]. Despite the improvement of diagnostic and treatment variants, over the past four decades, the mortality rate from nTSH has not decreased [72]. It is worth mentioning that the incidence of nTSH increases with age: as a rule, this pathology develops in people over 50 years; in children, it is seen rarely (the frequency rate varies from 0.18 to 2.0 per 100 thousand people [66]). There is also evidence that women develop nTSH more often [146].

Among the risk factors for the development of IA, modifiable and unmodified are observed [20]. The main unmodifiable risk factors are genetic predisposition and the presence of certain diseases. Thus, autosomal dominant polycystic kidney disease (ADPKD) is a strong risk factor for the development of IA, despite the fact that ADPKD is the cause of pathology in only 1% of cases [78]. IA is found in 10-13% patients with ADPKD [125]. In this population, aneurysms are mostly associated with the middle cerebral artery and have a smaller size compared to aneurysms in patients without ADPKD [54]. However, studies show that the risk of aneurysm rupture in this category of patients does not exceed the general population, therefore, according to the current recommendations of the American Heart Association, routine screening for the presence of IA in patients with ADPKD is not indicated [42]. Also, risk factors for the development of IA include such a disease as Ehlers-Danlos syndrome type IV which is manifested by a hereditary violation of collagen synthesis associated with the development of saccular or fusiform aneurysms [124]. Invasive studies with intravascular administration of a contrast agent are not recommended for such patients due to the high risk of complications. It is noteworthy that two other genetic diseases, Marfan syndrome and neurofibromatosis show no association with IA formation [59, 60]. Other diseases predisposing to the development of this condition include sickle cell anemia, in which aneurysms are most often located in the posterior cerebral artery and are multiple, and aortic coarctation that is a risk factor for aneurysm rupture at a young age [47, 114].

The role of genetic factors for IA development is well known. About 10% of cases are familial, when the same pathology was noted in the patient's closest blood relatives [49]. At the same time, some differences between the phenotypes of sporadic and familial IA cases are described: familial aneurysms are more often multiple, more common in the middle cerebral artery and less common in the anterior connective artery [100]. IA ruptures in familial cases are observed at an earlier age compared to sporadic cases [100]. There is also evidence that familial aneurysms are larger in size [137]. The risk of developing nTSH in patients with familial cases of aneurysms is 3-7 times higher than in patients with sporadic aneurysms [50]. As for the prognosis after the breakup, more complications are registered among family cases than among sporadic ones [49]. Thus, the issue of careful study of the family history of a patient with IA has its relevance; it is also important to refer the patient's close relatives for examination, regardless of their age and the presence of symptoms, especially if they have risk factors.

The modifiable risk factors for IA formation include mainly smoking and hypertension [50]. According to a recent meta-analysis, atherosclerosis is not a significant risk factor for aneurysm development [30]. Similar risk factors determine the likelihood of developing NSAIDs: arterial hypertension, smoking, as well as the use of sympathomimetics. It is noted that alcohol consumption also increases the risk of nTSHs, while not affecting the risk of IA formation; perhaps this is due to a transient increase in blood pressure [164]. Large-sized IA giving clinical symptoms, are most often subjected to rupture. In addition, the presence of a previous nTSH, a family history of IA and some genetic diseases are of great importance [35, 46].

There are a number of patterns in the IA localization and the frequency of their rupture: IA is more often ruptured in the posterior connective artery or vertebrobasilar system. In patients with a burdened family history, aneurysms in the middle cerebral artery basin are more common, and such people are also more likely to develop nTSH at a young age. Ruptures of the anterior cerebral artery aneurysm are often found in patients older > 55 years, when ruptures of an aneurysm of the posterior cerebral artery are more often registered in men [103]. In patients who smoke and/or drink alcohol, the size of the aneurysm at the time of rupture is smaller than in patients without bad habits [71]. The probability of aneurysm rupture increases under stress; a strong risk factor for aneurysm rupture is when its size greater than 7 mm; the risk of aneurysm rupture does not increase during pregnancy [82, 96, 148].

IA rupture is the cause of 85% cases of nTSH. Clinical manifestations of this condition include sudden severe headache and it can be accompanied by loss of consciousness, nausea, vomiting, photophobia and neck pain [120]. Acute encephalopathy, convulsions, fainting and subsequent injuries caused by falling are also possible [32]. In 40% patients, intraocular hemorrhage is detected as a result of a transient increase in intracranial pressure (Terson syndrome) that correlates with an unfavorable prognosis. If intracranial pressure is maintained high for a long time, coma and death may occur. Surviving patients often have complications in the form of impaired cognitive functions (especially higher mental functions, as well as short-term memory), chronic headache, sleep disorders, which significantly reduces their life quality [23].

Mechanisms such as earlier brain damage and delayed cerebral ischemia, vascular spasm, microthrombosis, spreading cortical depolarization, and inflammation are very important play for the pathogenesis. There is still no unified theory that fully explains all pathological processes in SAH [2, 3, 7, 8, 14, 21, 26, 28, 36, 37, 68, 73, 80, 83, 86, 91, 94, 105, 139].

The literature recognizes the events associated with the aneurysm itself (repeated bleeding, delayed cerebral ischemia, hydrocephalus); factors associated with treatment (complications of surgical clipping or endovascular embolization), as well as complications from prolonged immobilization as factors of deterioration of the prognosis after SAH. SAH itself can cause stress hyperglycemia, cardiopulmonary complications, as well as hypercoagulation, which, regardless of other factors, worsens the patient prognosis [152].

Despite the successes achieved in understanding the pathogenetic mechanisms of nTSH and associated conditions, the question of the diagnostic medical care scope at the early hospital stage in the framework of regional health care currently remains open. One of the main problems is related to the insufficient provision of the population of the regions with teams and equipment to provide specialized neurosurgical care, as well as the lack of equipment for emergency non-invasive diagnostics of nTSH (CT, CT, MRI) and shortage of staffing. The solution of these problems is achieved through continuous improvement and operation of the emergency advisory department of emergency medical care that provides round-the-clock advisory assistance, based on the results when a decision is made to transfer the patient to a specialized hospital, continue conservative treatment or face-to-face consultation. The scope of diagnostic medical care in a multidisciplinary specialized hospital includes non-invasive methods (CT, CT, MRI, MRA) and invasive methods (CAG). Another problem is the lack of unambiguous generally accepted clinical practice for providing care in these cases.

1.2 Methods of non-invasive diagnosis of rupture of intracranial aneurysms as a cause of non-traumatic subarachnoid hemorrhage in the acute phase

Most IA remain asymptomatic throughout life, and often the first manifestation of the disease is a rupture, leading to acute nTSH. The treatment of this complication is largely determined by the choice and timely application of a particular diagnostic method. Of particular importance is the correct medical assistance during the acute period and the first two weeks after the rupture, since it is at the time when there are conditions for the development of complications: repeated bleeding, vasospasm, brain edema [17].

Invasive and non-invasive methods exist to diagnose nTSH and determine therapeutic tactics. The latter include native CT, CT angiography, as well as MRI and MRA [29]. Various aspects of their application will be discussed in detail below.

1.2.1 CT capabilities for identifying the source of acute nSAH

The first method of radiation diagnosis which is recommended to be used in case of clinical suspicion of nTSH, is native CT. In addition to the very fact of the presence of TSH, with this study it is possible to determine its source, assess the edema presence, hydrocephalus, dislocation of the median structures of the brain. Blood spilled into the subarachnoid space has an increased density relatively to normal brain tissue in the acute period of TSH. Considering the most typical location of IA, the proximal segment of the middle cerebral artery, at first blood enters the basal cisterns and the Sylvian sulcus, then into the subarachnoid space of the convexital surface of the large hemispheres. It is worth telling that it is not always possible to determine the exact localization of an aneurysm by the location of blood in the subarachnoid space, this is often associated with a certain degree of assumption. Sometimes there is an intraventricular hemorrhage (IVH) associated with TSH, for example, in the presence of aneurysms of the anterior connective artery, with blood breakthrough into the third ventricle through a terminal plate. If hemorrhage occurs repeatedly, then fresh blood is defined as a structure of increased density in the basal and convexital subarachnoid spaces [12].

During the first day after nTSH, the sensitivity of the native CT is approaching 100%, but already on the third day it decreases to 85%, and on the seventh – up to 50%. According to recent studies, CT sensitivity during the first 24 hours after nTSH is estimated at 93%, and during the first 12 hours – in the range 98-100% [118]. The decreased sensitivity occurs as a result of the regular changes observed during the clot retraction. Thus, it is recommended to use exclusively native CT to exclude the diagnosis of nTSH only in the first hours from the onset of symptoms. Nevertheless, it is believed that if a negative result of native CT is obtained in the first hours after the symptoms onset, a lumbar puncture should be performed in order to avoid underdiagnosis of a potentially life-threatening condition [69]. However, it should be remembered that lumbar puncture is an invasive procedure that can be associated with a number of complications, including post-operative headache (occurring in almost 40% patients), back pain, iatrogenic meningitis, nerve damage, epidural and subdural hematomas [135]. It is also worth considering that in about 20% cases during lumbar puncture, blood may enter the cerebrospinal fluid due to iatrogenic vascular damage. Native CT data also make it possible to assess the likelihood of symptomatic vasospasm after nTSH, which is an important pathophysiological link of further complications. To do this, it is justified to use the modified Fisher scale [75], in which four levels of risk are distinguished: 1 (minimum) – no TSH or minimum TSH without IVH; 2 – minimum TSH with IVH; 3 – diffuse or focal TSH without IVH; 4 (maximum) – diffuse or focal TSH with IVH. In clinical practice, along with CT data, it is worth considering some other factors that are also predictors of vasospasm in nTSH: arterial hypertension in the anamnesis and high blood pressure during the patient admission to a medical institution. All these data make it possible to present the clinical picture more clearly and prevent vasospasm, for example, by mechanical lysis of a blood clot in a cistern [75]. However, based on this scale, it is impossible to predict further clinical events, including ischemia.

The severity of IVH is assessed according to the Greb scale, while each ventricle is considered separately: for the lateral ventricles, 0 points correspond to the blood absence, 1 point – traces of blood or minor hemorrhage, 2 points – blood filling less than half of the ventricle, 3 points – blood filling more than half of the ventricle, 4 – filling and stretching of the ventricle. For the third and fourth ventricles, 0 points correspond to the absence of blood, 1 point – the presence of blood without ventricular enlargement, 2 points – filling and stretching of the ventricle [45].

Despite a number of advantages, the native CT method has several limitations, in addition to a gradual sensitivity decrease, which must be taken into account. If the patient has anemia (hematocrit less than 30%), the hematoma may have a given structure, which makes it indistinguishable from normal brain tissue. False negative results on CT can also be given by factors such as small-sized TSH and artifacts from the patient movement [70].

CTA is recommended for using primarily when receiving negative results of native CT, as a possible alternative or addition to lumbar puncture. The advantages of CT are patient convenience, safety and diagnostic accuracy. This noninvasive method makes it possible to diagnose IA with 98% sensitivity and 100% specificity [169]. Difficulties arise in the presence of aneurysms smaller than 3-4 mm. Nevertheless, clinical data indicate that IA larger than 5 mm are more likely to be ruptured. There is evidence in the literature that obtaining negative results with native CT and CTA gives grounds to assume a benign outcome for the patient: negative prognostic accuracy is estimated in more than 99% [111].

Headache is an important indicator of a possible IA rupture. Thus, if it is present, the risk of TSH is 8 times higher [133]. On the other hand, CTA has sufficient accuracy to detect even very small aneurysms, and the probability of an aneurysm rupture correlates, among other things, with its size: it is very unlikely that an aneurysm smaller than 3 mm will undergo rupture and cause nTSH.

Difficulties in interpreting CTA outcomes include the need for sufficient clinical experience of a radiologist or double data control, as well as some features of the aneurysm localization: IA at the base of the skull (pools of the internal carotid and posterior connective arteries) are often difficult to interpret due to numerous nearby bone structures, as well as complex vascular anatomy. Small aneurysms can cause diagnostic difficulties, since vascular "funnels" of the posterior connective or anterior choroidal arteries can be masked under them if it is impossible to trace the course of the vessel precisely. The features of the arterial structure in the form of the formation of loops can also resemble aneurysms. Thus, in the presence of small aneurysms, there is some probability of overdiagnosis [169]. On the other hand, false negative results are also possible, for example, in cases of the presence of artifacts from movement or incorrect timing of the delay in the administration of a bolus contrast agent. In addition, if a patient has systemic diseases associated with the formation of multiple aneurysms, including in the brain (for example, Moya-Moya disease and arteriovenous malformations), as well as with occlusive vascular lesions, aneurysms may be missed. It is also noted that diagnostic errors are possible in cases of arterial dissection without the formation of aneurysmal lumen expansion.

These problems are possible to be avoided by the technology of "subtracting" bone tissue from the image, which makes it possible to more clearly distinguish vessels and bone structures. Disadvantages of this method are as following: increased radiation load on the patient, as well as the possible occurrence of artifacts from reconstruction [64]. This can be avoided by applying the two-energy CT method, which allows obtaining additional information about tissue differentiation based on specific absorption of radiation from iodine at high and low energy levels with the construction of iodine distribution maps. For carrying out the study, one- or two-tube systems with different radiation sources or two-layer detectors are used. The main purpose of obtaining images with higher energy is to reduce the severity of artifacts, with low energy – to increase the contrast of images. Also, the method of dual-energy CT allows to perform subtraction of bone structures, which makes it possible to obtain a three-dimensional reconstruction and improve the aneurysm visualization in places that are difficult to diagnose, for example, in the area of the skull base. Spectral scanning makes it possible to detect not only a blood clot as a haemorrhage consequence, but also a fresh outflow of blood from IA, which is of great clinical importance. In addition to obtaining diagnostic information, this method makes it possible to plan tactics considering the IA morphological features and its environment: for example, the aneurysm wall calcification makes it difficult to clip it, which can be taken into account already at the preoperative stage [5]. There are data in the literature on the high sensitivity and specificity of the dual-energy CT method for the IA diagnosis [168]. According to various data, the sensitivity of this method is about 95%, and the specificity is 100%; it is also important to take into account that in this way a reduced radiation load is achieved by an average of 60% compared to CAG [113].

Considering the fact that the causes of nTSH can be different (IA rupture causes it in about 85% cases [107]), an important issue is the differential diagnosis of other conditions leading to nTSH. CTA in combination with native CT plays an important role in the detection of amyloidosis, vasculitis, perimesencephalic venous hemorrhages, as well as idiopathic hemorrhages of unknown origin. The high negative predictive power of CTA (about 98.6%) makes it possible to avoid CAG with nTSH of unclear genesis [119]. Also useful for clinical practice is the ability of CTA to differentiate ruptured and unexploded aneurysms by calculating the density of the contents of the aneurysmal sac (535 Hounsfield units are recognized as the boundary value).

Possible complications of CTA include contrast-induced kidney damage, adverse reactions to the drug, as well as radiation exposure [15, 104]. On average, to perform the study, the patient should be injected with 40-80 ml of an iodine–containing contrast agent at a rate of 3.5-5 ml / s. Modern tomographs allow to reduce this dose, as well as the radiation load on the patient due to a larger number of sections [12]. Nevertheless, in most cases, the disadvantages of CTA are compensated by wide availability, efficiency, non-invasiveness, as well as relative safety [8]. Modern detectors have good sensitivity for detecting aneurysms, including small ones, due to the high spatial resolution, 0.4–0.7 mm currently. With the advent of systems with 256 and 320 detectors, the spatial resolution and diagnostic accuracy of the CTA method continue to increase [112].

The success of providing care to a patient in the acute period of nTSH is largely determined by the choice and timely application of a certain diagnostic method, which allows providing the attending physician with the necessary information in sufficient volume. Based on the above, the priority direction in identifying the bleeding source during the acute period of nTSH is the emergency implementation of non-invasive methods of radiation diagnostics in the emergency room. Conducting a native CT in the first hours of the symptoms onset enables not only to determine the presence of blood in the subarachnoid spaces, but also to assume its source, evaluate the parenchyma and ventricular system of the brain; for visualization of vascular pathology, the protocol is supplemented with CTA.

Despite the theoretical advantages of these non-invasive methods, in some practical cases the information they provide is not enough. This can be caused by both objective (physical limitation of the method, anatomical features of IA, artifacts from bone tissue/metal/movement of the patient) and subjective (operator-dependent methods of radiation diagnostics, stressful conditions, lack of the possibility of expert evaluation of the images obtained in emergency and/or non-working hours) difficulties. There is also a need for clear criteria to determine cases when the addition of CAG to the examination is justified both from the point of view of possible complications of an invasive procedure and from the point of view of health care economics.

1.2.2 Importance of MRI and MRA in detection of ruptured intracranial aneurysms

As for native MRI, its sensitivity and specificity in the diagnosis of acute nTSH, in comparison with native CT, are somewhat limited. In the images obtained using Fluid attenuation inversion recovery (FLAIR), you can see blood in the subarachnoid space, but this signal in many cases is non-specific and is caused by various technical factors, hyperoxygenation, the introduction of anesthetics or other processes in the soft meninges. There are MRI sequences that are particularly sensitive to blood detection (Susceptibility weighted imaging (SWI); Susceptibility weighted angiography (SWAN)), however, they make it possible to detect hemorrhages at the acute, subacute and chronic stages, but not at the TSH onset when oxyhemoglobin has not yet undergone decomposition. Thus, after two or more weeks after nTSH, MRI sensitivity increases significantly [83].

MRA in Time-of-flight (TOF) mode is the most frequent method of IA assessment, which makes it possible to create maximum intensity projections (MIP) and 3D reconstructions for accurate visualization without the need for contrast preparation and without radiation exposure. Unlike CT and CAG methods, MRA is based on recording a signal from moving blood; this determines the main characteristics of the images obtained - the vessel wall is not displayed, the image depends on the intensity of blood flow. Factors that can impair visualization include vascular tortuosity, turbulent blood flow in the cavities of large aneurysms, as well as metal artifacts. MRA can be performed with intravenous administration of a contrast agent based on gadolinium salts: the image quality becomes better, but the time resolution of MRA is less than in the case of CAG: about a few seconds for the first compared to fractions of a second for the second.

According to a systematic review, MRA sensitivity in the IA diagnosis is 95%, and the specificity is 89%. Diagnostic errors were mainly associated with aneurysms located at the base of the skull, as well as in the middle cerebral artery [140]. It is shown that later processing and the creation of 3D reconstruction improve the quality of visualization compared to images in three standard planes. Images obtained on a magnetic tomograph with a magnetic field strength of 3 T demonstrated a statistically significant advantage over images obtained on a 1.5 T device [92]. In addition, it is important to take into account that the sensitivity of the method decreases when examining aneurysms < 5 mm.

Despite all MRA limitations, it has a number of important advantages over CT and CAG. MR-research is based on obtaining images involving radio frequency waves, therefore it is not associated with patient radiation load. In modern conditions, there are ways to reduce radiation exposure without impairing the quality of visualization, however, with long-term monitoring of the patient, it is necessary to carry out a number of studies, the cumulative effect of which may be significant. Contrast preparations for MRI contain gadolinium salts, so they can be used in patients with a history of adverse reactions to iodine. In addition, during the MR study, along with angiographic projections, T1- and T2-weighted sequences are performed, which give a complete picture of the associated states, for example, allow visualization of intraluminal thrombi [83].

MRA disadvantages include less widespread availability, especially in emergency situations, the presence of contraindications for the study (first of all, implanted metal devices), longer study time, the impossibility of conducting for patients in serious condition and a relatively higher cost [26].

Despite the fact that MRA is often used to diagnose IA, in the case of nTSH, its use is severely limited due to the long study time, possible artifacts from the movement of the patient and less accessibility, as well as due to the fact that the sensitivity and specificity of detecting IA using MRI, especially in the case of small-sized IA, is inferior to CTA and CAG techniques [57]. Only in some cases, MRA is the method of choice, for example, during pregnancy, when it is critically important to reduce radiation exposure. Thus, the MRS inclusion in the routine examination of patients with nTSH symptoms in the emergency room is not justified.

1.2.3 Diagnostic algorithm of patients with acute non-traumatic SAH

With regard to the diagnostic algorithm for nTSH, it is recognized that native CT and CTA are the first-line methods of choice, as MRA is time-consuming and often impossible in an emergency situation. In addition, it could be complicated to gather information about possible contraindications for MRI performance in a patient. Conducted by R. Jabbarli et al. (2013) an analysis of the economic aspects of the initial examination of patients in the acute period of SAH showed that CT application for this purpose is more preferable than CAG [86].

Concomitant congenital and acquired diseases of the extracranial parts of the BCA can affect the course of the acute and subacute periods of nSAC. Since it is often difficult to collect anamnesis in an emergency situation, and also due to the fact that the patient does not always know about the presence of such pathological conditions, clinicians face the question if it is necessary to exclude diseases of the extracranial parts of the BCA by expanding the scanning area during CTA to the level of the aortic arch. Nevertheless, this will lead to an increase in the radiation load on the patient, but it will not always affect the treatment tactics. The answer to the question whether it is worth simultaneously excluding diseases of the neck vessels in patients with the SAH status depends on several crucial, but not yet fully clarified circumstances: the influence of concomitant pathology of the cervical vessels on the likelihood of complications in patients with nTSH, on treatment tactics and its outcomes. Whether the radiation load increases significantly when the extracranial departments of BCA are included in the research area and to what extent this risk is proportional to the possible benefits – not enough research has been conducted on this topic yet. There is an obvious requirement to develop recommendations on the criteria to include extracranial departments of BCA in the examination of patients with suspected nTSH; notabely, it is desirable to clearly determine in which age-sex group of patients and in which clinical picture it will be justified both therapeutically and economically.

1.3 Role of cerebral angiography in the diagnosis of intracranial aneurysms

CAG is among the diagnostic methods most commonly used to detect both unruptured aneurysms and ruptured with an outcome in the nTSH. Good spatial and temporal resolution, as well as the availability of 3D reconstruction make this method useful for detailed characterization of the entire vascular system of the brain. CAG is a method that makes it possible to identify not only the geometry of the aneurysm, including the size and shape, but also the diameter of the hole, as well as the degree of involvement of the main vessel in the lesion and anatomical features. These data are needed to determine which tactics are mostly justified in a particular case: endovascular or surgical treatment.

The disadvantages of the CAG method include the inability to detect intravascular thrombi and calcification, which may adversely affect the decision-making process on tactics, as both intravascular thrombi and aneurysm neck calcification may significantly complicate microsurgical clipping and increase the risk of AVCC. In addition, due to the invasiveness of the method, there is a risk of neurological complications, the incidence of which is estimated at about 0.5% (there are both local complications in the form of hematomas and abscesses at the puncture site and global complications, such as ischemic-type AVCC); however, there are recent literature data on the risk reduction to about 0.04-0.3% in the conditions of using modern techniques and if there is sufficient experience present [73].

In this regard, the question arises about the possibility of replacing CAG with CTA. The advantages of the latter include its relatively low cost, speed and wider availability, especially in an emergency situation [169]. The noninvasiveness of CTA and the significantly lower number of complications than in CAG also play an important role. In general, the research data show that CTA sensitivity practically corresponds to the CAG sensitivity, with the exception of relatively rare situations of IA presence in hard-to-visualize places or small-size IA (less than 3 mm in diameter) [83]. CTA is also able to show the condition of vertebral, common, internal and external carotid arteries: their anatomical features, development options, the presence and degree of atherosclerotic lesion. Besides, extravasation of the contrast agent can be detected on the CTA, which indicates the presence of ongoing bleeding. All these data may be crucial for IA treatment planning.

Both methods have advantages and disadvantages, so it makes sense to combine them, and also, if possible, apply them together depending on the specific situation: the severity of the patient condition, the availability of time and opportunity, logistical circumstances, clinical features, and the patient's desire. In the European Recommendation Protocol for the Diagnosis and Treatment for IA and nTSH from 2013, all angiographic techniques (CAG, CTA and MRA) are assigned the same level of evidence (class II, level B) in identifying the source of hemorrhage in nTSH. CAG is recommended only if the source of hemorrhage could not be determined during CTA [7]. However, according to J. J. Heit et al. (2016) CAG comparing with CTA, provides an average of 13% more data, but IA is detected in only 5% of cases; in other cases, patients were diagnosed with arteriovenous malformations, vasculitis and other possible causes of nTSH [80]. In this regard, it is also worth noting the results of a retrospective analysis by A. A. Khan et al. (2013) as they found out even repeated use of CAG when receiving a negative result on CTA in the acute phase of nTSH in most cases does not add diagnostic information and therefore is not recommended for routine use [94].

On the other hand, there is evidence that in some situations it is still necessary to carry out CAG when receiving a negative result on CT; for example, it has been shown that if blood is localized in the sulci of the brain, CTA should be supplemented with CAG due to the fact that nTSH in this case may be caused by vasculitis [36]. Other authors show that small aneurysms are not well detected during CTA, and an invasive study should be performed, especially in cases when nTSH is accompanied by threatening clinical manifestations, for example, loss of consciousness [68].

Another important aspect is how effectively it is possible to determine the therapeutic strategy for a particular patient with the help of CTA and CAG. Relatively few studies have been devoted to this problem. It is most important to determine the ratio between the diameters of the neck and the widest part of the aneurysm, as well as the geometric relationship between the aneurysm and the main vessel, the inclusion of arterial branches in the aneurysmal neck. R. Agid et al. (2006) indicated that in 95.7% cases in female patients with IA, the appointment of CTA was reliable for making a decision on the joint use of treatment. The remaining 4.3% patients required CAG due to difficulties in determining the morphology of aneurysms. It is noted that sometimes CTA shows poor quality for technical reasons, which limits the ability of this method to detect small perforating arteries in the aneurysm immediate vicinity. In one of the large studies of patients who were referred for endovascular spiral embolization according to the CTA results, the operation was successful in 92.6%; in other cases, there were problems with operative access (most often due to vasospasm or excessive tortuosity of the cervical vessels). Thus, the CTA method has shown sufficient effectiveness in planning surgical treatment [36]. Nevertheless, the phenomena of partial volume averaging during CTA could visually expand the aneurysmal neck and lead to the incorrect conclusion that the aneurysm cannot be cured by endovascular embolization. This is due to the different technical characteristics of the tomographs themselves (the number of detectror rows), the thickness of the slice and post-processing algorithms. The best representation of morphology is provided by a combination of two- and three-dimensional CAG methods, that is often used when planning endovascular intervention.

The place of MRA in the diagnosis of IA and nTSH in clinical practice still remains a debatable issue. Despite the fact that CAG remains the standard of diagnosis, it is an invasive and time-consuming procedure; CTA is non-invasive, but also associated with radiation exposure and possible adverse reactions to an iodine-containing contrast agent. MRA does not have these disadvantages, so there was previously a need to compare the sensitivity of these techniques [21]. Comparison of MRA and CTA showed that the sensitivity of these methods is comparable, but the MRA specificity is slightly inferior to CTA [113]. It should be noted that in both methods, diagnostic errors were mainly associated with aneurysms located at the base of the skull, and if in the case of CTA the cause is the close location of bone structures, then in MRA errors are caused by the complex variable anatomy of vessels in this localization. In terms of accessibility, speed of implementation and cost-effectiveness, MRA is also inferior to CTA, therefore MRA being a first-line method is recommended only if the patient has a proven allergic history of iodine-containing contrast agents or severe renal dysfunction.

1.4 Artificial intelligence in diagnosis of intracranial aneurysm

A relatively new direction in the diagnosis of IA and nTSH is the introduction of artificial intelligence (AI) systems for processing CT and MRI outcomes. They can be useful assistants in matters of screening for the IA presence, assessing the probability of their rupture and outcome prediction. The first system described in the literature for detecting unruptured IA using AI was a program developed by N. Arimura et al. (2004), based on the use of a three-dimensional selective enhancement filter for gray range values [39]. The program showed 100% sensitivity, but there were also false positive results. In subsequent studies, the algorithm was improved, and the sensitivity continued being high; however, the algorithm was not fully automated and had limitations in detecting small-size or fusiform IA [81, 88]. Using CAG data as a reference, H. Yang et al. (2011) developed a more automated algorithm by combining two techniques: automatic segmentation of intracranial arteries and detection points of interest on segmented vessels [173]. The sensitivity reached 95%, but was still lower for IA being less than 5 mm, as well as for IA located in places of bends or bifurcations.

Recently, IA detection systems based on MRA using deep learning algorithms have been developed. T. Nakao et al. (2018) in a single-center study, used two-dimensional neural network to detect IA and reported sensitivity of more than 90% [121]. Another neural network using 2D MIP images also showed efficiency [153]. Convolutional neural networks developed in the late 1980s have also recently found application in the detection of IA according to CTA data [11]. Nevertheless, the improvement of these and other models requires further research, especially considering that in most published studies on this topic, CAG, as a reference method for detecting IA, is not involved.

The prospects of AI systems in the IA diagnosis have several main practical applications: an automated system for selecting high-risk patients, predicting outcomes depending on the patient condition, predicting the outcomes of various patient treatment strategies, detecting IA de novo or IA recurrences and predicting the risks of repeated ruptures [147]. The main problems of AI application are as following: insufficient validation of research results; it takes a long time to train an algorithm, especially one that works in several directions (IA size and shape, the probability of rupture, estimated outcomes), an assessment of economic efficiency, which can be influenced by parties concerned. It is necessary to continue research in different directions, expand patient samples to increase the amount of imaging data before it is possible to ensure more active implementation of AI systems in routine practice.

1.5 Surgical treatment of intracranial aneurysms, modern approaches

Essencially, the methods of IA operative correction are divided into two directions: surgical clipping and endovascular embolization. The evolution of IA treatment methods is conditionally divided into four time periods: pre-microsurgical (before 1960), early microsurgical (1960-1980), late microsurgical (1980-2000) and the era of innovation (2000–present). Surgical aneurysm clipping was first proposed in the 1930s and soon became the accepted standard of treatment. Innovations in this technology during the twentieth century included the improvement of clips, visualization methods, as well as the introduction of a surgery microscope into practice. After the 1980s, another treatment approach began to gain popularity - endovascular embolization, which allows achieving a good result and avoiding a number of complications associated with open surgery [7]. MRA appearance in 1986 and CTA in 1992 also occured to be a big step forward. New stents and liquid embolizing materials are currently being developed [105]. With the improving technologies, the criteria for determining the characteristics of an aneurysm and the patient condition for each treatment method undergo constant changes [117].

Considering the fact that the question of the preference of a particular method of treatment is still not resolved, in the course of many studies attempts have been made to determine the clinical characteristics of patients who are better treated with endovascular or surgical method. It has been shown in the literature that middle cerebral artery aneurysms are preferable to be treated by surgical clipping [64]. The evidence that endovascular treatment should be preferred in elderly patients is still contradictory [89]. Patients with a hematoma in the cerebral parenchyma with a volume of more than 50 ml have a high probability of an unfavorable outcome, but their prognosis improves significantly if the hematoma is evacuated within the first 3.5 hours, and in this case, clipping is the preferred method of treatment [134]. On the contrary, it is better to treat patients with vascular spasm with endovascular intervention, while considering the aneurysmal anatomy and its connection with spasmodic vessels. In a serious condition of the patient, especially the elderly, endovascular treatment is recommended, since in these cases the long-term prognosis is less significant than the short-term survival [130]. Nevertheless, it is extremely important that patients in serious condition have the opportunity to receive treatment in centers where both methods are available [2]. It is also worth noting that there are some features of the treatment for posterior cerebral artery aneurysms. Literature data suggest that it is preferable to treat such aneurysms endovascular, however, with spiral embolization of the basilar arteries, incomplete occlusion of the aneurysm and its subsequent re-filling may occur. The study of K. Uda et al. (2001) is significant in this regard as they reported complete or almost complete occlusion occurring immediately in 85% of the treated patients; with prolonged follow-up, they showed no signs of insolvency. As for cases of incomplete occlusion, 47% of patients underwent recanalization in dynamics, and some demonstrated repeated bleeding [159]. Based on this, careful monitoring of the patient condition after treatment should be carried out, especially if we are talking about spiral embolization of the basilar arteries and in cases where complete occlusion of the aneurysm cavity has not occurred.

Unruptured IA is conventionally classified into asymptomatic IA (random diagnostic finding), symptomatic IA and unruptured IA in patients with SAH (cases of multiple aneurysms) [14]. On the one hand, preventive treatment of such aneurysms by embolization or clipping should minimize the risk of rupture and SAH in future, on the other hand, the ratio of the rupture risks and postoperative complications is unknown, research in this area is still insufficient [3].

It should be noting, however, a major study by ISUIA (The International Study of Unruptured Intracranial Aneurysms), as a result of which it was found out that among patients with unruptured IA, it is justified to distinguish two categories: those who had a history of SAH, and those who did not have it, because it significantly affects the prognosis and, accordingly, the decision depends on the necessity and scope of possible treatment. Thus, the presence of SAH anamnesis should be regarded as a strong risk factor for a new SAH and treatment should be planned with this in mind [96].

When choosing a treatment method, it is necessary to consider the peculiarities of the patient condition, the availability of specialists and equipment; it is also important to monitor blood pressure [28, 33].

1.6 The role of non-invasive diagnostic methods in assessing the results of surgical treatment for intracranial aneurysm rupture in the long-term postoperative period

IA treatment is primarily aimed at preventing rupture (for an unruptured IA) or repeated SAH (for a ruptured IA). During the postoperative period, visualization of intracranial vessels is very important to assess the residual aneurysm and possible violation of the main vessel integrity [25].

Currently, clear recommendations on the frequency of imaging studies in patients after IA treatment have not been developed, therefore, an individual algorithm is selected for each case depending on the patient condition, life expectancy and aneurysm characteristics. Optimal regular monitoring benefits to prevent repeated nTSH, minimize costs and reduce patient anxiety.

After endovascular treatment, the first observation is usually planned after 3-6 months, depending on the patient condition, the characteristics of the aneurysm and the presence of conditions. Medium-term monitoring is usually carried out for 3-5 years. Most recurrences occur during the first year after treatment, which causes increased attention to the patient during this period. More frequent follow-up may be indicated in patients with risk factors for recurrent nTSH (incomplete postoperative occlusion, large aneurysm with a wide neck) [126]. However, some data suggest that even 3-5 years may not be enough for a number of patients: in one study, recurrences were detected in 12.4% of treated patients between medium-term (3-5 years) and long-term (more than 10 years) follow-up [98]. Among the risk factors for late relapse, the size of the aneurysm is more than 10 mm, the presence of a residual neck and requirement for repeated treatment that emerged during the first five years after embolization. Longer follow-up (more than 10 years) should be recommended for such patients [150].

1.6.1 CTA for intravranial aneurysms

Postoperative monitoring of IA status after CTA treatment is an increasingly used alternative to CAG in clinical practice, and it has traditionally been considered the method of choice in such a case.

R. T. Vieco et al. (1996) were among the first to propose the use of CTA for postoperative IA diagnosis which were clipped surgically. The authors presented the SSD (Single shot detector) and MIP algorithms, as well as a post-processing method in which the MIP model was electronically superimposed on the SSD model [163]. A little later, a study was conducted comparing the methods of CTA, MRA and CAG to assess the aneurysms postoperative state. The researchers noted that during MRA it is not possible to assess the dome and neck of IA due to artifacts from titanium clips, while CTA can be used to monitor the residual filling of the aneurysm and the patency of the main vessels, despite the presence of artifacts from the clips [162]. The diagnostic accuracy of CT to assess the residual aneurysm after clipping was estimated at 88.1%, which indicates the feasibility of using this method in routine clinical practice [100].

The small size of the aneurysm can cause both hyper- and "underdiagnosis". Due to the good resolution, CTA scan makes it possible to visualize irregularities of the vessel wall 1-2 mm in size, which often causes a diagnostic dilemma. Such areas are not always possible to visualize with CAG due to projection; the use of 3D reconstructions increases the accuracy. I. Van der Schaaf et al. (2006) mentioned that such sites were often regarded as false positive results [161].

A. R. Dehdashti et al. (2006) conducted a study comparing the effectiveness of CAG and CTA methods in the diagnosis of clipped aneurysms. Each of the 60 aneurysms was examined independently by two radiologists; the quality of visualization, the presence and severity of artifacts, the completeness of IA shutdown from the bloodstream, and the patency of the main vessel were evaluated. As a result, the sensitivity and specificity of CTA for detecting residual aneurysmal neck were 100%, and the sensitivity and specificity for assessing vascular patency were 80 and 100%, respectively [63]. In another study, however, it was found that with CT, there is a possibility of missing a residual neck and aneurysms of minimal size [43]; in case of doubt, CAG is recommended.

Recently, dual-energy CT has been increasingly used, which is a promising method of imaging treated IA and a potential replacement for CAG. A feature of this technology is the possibility of subsequent data processing and selection of the best energy values for visualization of residual aneurysms and patency of the main arteries [161].

Reducing the number of artifacts in CTA can currently be achieved in several ways, primarily by optimizing the scanning step (recommended value - 0.6 mm) and increasing the peak voltage. Also, the intensity of artifacts from clamps depends on the material: when using titanium clamps, fewer artifacts occur than in the case of clamps made of alloys with the addition of cobalt. In addition, the location of the clips perpendicular to the scanning plane also reduces the number of artifacts [162].

As for the possibility of CTA in the visualization of IA following endovqscular embolizqtion treatment, they are severely limited due to artifacts of to the platinum spiral. Thus, for such IA, the selection methods are MRA or CAG. Currently, there is not enough data on this topic for unambiguous judgments, so further studies are needed with the inclusion of a large number of patients, as well as with the possibility of comparing the methods of CTA, MRA and CAG [9].

Thus, regardless of the chosen surgical technique, IA requires further monitoring for early diagnosis of postoperative complications and relapses. Currently, CTA is increasingly recognized as the method of choice for postoperative aneurysm monitoring, which allows visualizing even small-size aneurysms, which may be a limitation for CAG. The main area of CT application is postoperative monitoring of clipped aneurysms, since aneurysms treated by endovascular embolization still remain insufficiently distinguishable for CT [150].

1.6.2 MRA for intracranial aneurysms

Currently, MRA popularity for monitoring the condition of IA after treatment is growing: both endovascular and surgical. This is a non-invasive method, contraindications to which are the presence of ferromagnetic metal implants and pacemakers. During MRA, a gadolinium-containing contrast agent can be administered to the patient or TOF mode can be used, application of this method is limited by slow or turbulent blood flow [145].

In the dynamic observation of IA after embolization, contrast-enhanced MRA is recognized as the preferred method due to the better ability to diagnose residual aneurysms and fewer artifacts. However, it is necessary to consider the probability of vasa vasorum contrasting with organized blood clots in order to avoid inaccurate results [76]. There is information in the literature about a relatively infrequent but severe side effect of gadolinium-containing contrast agents – nephrogenic systemic fibrosis [56].

MRA sensitivity and specificity for postoperative diagnosis of IA by embolization are evaluated differently in different studies - from 50 to 100% [145]. Many authors in recent years recommend using MRA instead of CAG, which is considered the "gold standard". It was shown that with long-term follow-up of patients using MRA, the survival rate and the number of years of working capacity were not lower than in the case of using CAG, and economic costs were reduced [99, 143].

There is some uncertainty regarding the use of MR tomographs with a magnetic field strength of 3 T versus 1.5 T. In a large analysis, L. Pierot et al. (2012) showed that studies in TOF mode on a 3T MR tomograph were preferable for assessing the completeness of aneurysm occlusion due to better image quality [126]. However, there is also evidence that when using tomographs of 3 T and 1.5 T, images of comparable diagnostic value are obtained [52].

Also, the question of the MRI preference in the TOF mode against MRI with contrast enhancement remains not fully clarified. Some authors do not consider it necessary to introduce a contrast agent, however, there are recommendations to perform both contrast-free series and series with contrast enhancement to increase the effectiveness of assessment [60, 151]. There is evidence that the sensitivity and specificity of contrast-enhanced MRI and TOF MRI are approximately 86.6 and 91.9% versus 83.3 and 90.6% (the difference does not reach statistical significance) [95].

Significantly fewer studies have been conducted on the use of MR angiography to monitor patients after surgical clipping. In 2020, S. Takubo et al. (2020) conducted a study on a phantom using a native sequence of ultrashort echo (Ultrashort echo, UTE); by scanning a phantom with embedded clips, the authors studied the characteristic features of the resulting artifacts. As a result of the study, the authors concluded that adding a sequence in the UTE mode to the standard scanning mode is a useful method of monitoring patients after clipping IA [154].

In their study, K. H. Ryu et al. (2020) used the so-called "silent scanning" (Silent MRA) as a control method and considered it a useful addition to the diagnosis of IA, increasing the accuracy of visualization [138].

It should be noted that in order to detect the re-growth of IA, it is important to evaluate not only the clipped aneurysm itself, but also the adjacent cerebral arteries, as well as postoperative cerebral vasospasm. In 2020, M. Katsuki et al. proposed to use 3 T MRI scanners in Silent UTE mode for this purpose. The obtained images allowed us to evaluate both the clipped IA itself and the nearby arteries, as well as the bringing cerebral vessels from the main trunk to the periphery: this helped to determine the presence of vasospasm [90].

Thus, MRA (with and without contrast enhancement) is increasingly being used today as a non-invasive diagnostic method for monitoring postoperative ruptured aneurysms. This method is more widely used in the case with embolized aneurysms. The addition of a contrast-free MRA with the introduction of a gadolinium-containing contrast agent, as a rule, increases the accuracy of diagnosis and in some cases avoids CAG. However, in ambiguous diagnostic cases, MRA is not yet fully able to replace CAG.

1.7 The Cerebral angiography in assessing results of surgical treatment in long-term postoperative phase

CAG is recognized as the "gold standard" for assessing the IAstate after endovascular treatment. Due to the high spatial resolution and the possibility of 3D reconstruction, this method allows us to assess the presence of recurrent flow in the aneurysm. Predictors of relapse include factors such as suboptimal results of surgery, large sizes of the rupture or the aneurysm itself, and a wide neck. The Raymond scale is widely used: class I means complete aneurysm occlusion, class II – the presence of a residual neck, class III – the presence of a residual aneurysm [132].

An important advantage of CAG is the absence of artifacts from implanted devices (mainly coils and various stents), which makes it possible to analyze the flow after any endoscopic interventions.

Nevertheless, the CAG invasiveness is the cause of the probable development of complications in patients such as thromboembolism of the cerebral arteries (from occlusion of small arteries to transient ischemic attacks and OCVA), adverse reactions to contrast agents, ionizing radiation and hematoma at the puncture site [150]. It is reported that the risk of neurological complications during CAG is about 0.34–1.3% [62].

As the technique improves, especially in the MRI field, the question arises more and more often whether MRA can become an adequate replacement for CAG. Z. Serafin et al. (2011) conducted an analysis of the literature sources on the topic of diagnostic accuracy of various methods and finding out the optimal timing of patient follow-up after endovascular IA treatment. The review, which included 35 studies from 1991 to 2021, showed that CAG using 3D reconstruction has a 100% sensitivity and a specificity of 58.3-94.7%, and a MRA sensitivity of 28.4–100% and a specificity of 50-100% [145]. In the period between the first six months after treatment and delayed visualization, the proportion of aneurysms with recanalization was 0-2.5%. The authors of the review concluded that MRA was the preferred method of visualization in the long term. In cases where CAG is needed, 3D reconstruction should be performed to increase diagnostic accuracy. Most patients may not need further follow-up six months after embolization.

The question of rational MR imaging for patients after stent implantation, however, remains difficult: artifacts from the stent material in combination with the Faraday cell effect significantly affect diagnostic accuracy, leading to a false conclusion about the presence of artery stenosis. In the course of some studies, a cautious assumption has been made that the administration of a contrast agent is preferable in this case, since it can improve the assessment of the main artery and aneurysm neck by reducing the number of artifacts [55]. The same applies to flow-modeling aneurysms consisting of braided strands of cobalt, chromium and platinum: J. Attali et al. (2016) found that even when using 3 T tomographs, MRA with contrast makes it possible to detect aneurysm recurrence with a sensitivity of 83% and a specificity of 100%, and MRA in TOF mode – with a sensitivity of no more than 50% and a specificity of 100% [40]. Both methods proved to be insufficiently effective for assessing the vessel lumen: an underestimation of the vessel diameter index and a lower quality of vascular reconstruction images compared to CAG were revealed. Thus, despite the MRA advantages, in clinical practice, most often at least one CAG is required for dynamic monitoring of patients after stenting.

As for the use of CAG in surgical clipping of aneurysms, it can begin already intraoperatively. G. Tang et al. (2002) in their review noted that the use of intraoperative CAG contributes to a change in operational tactics in 12.4% cases; mainly by adjusting the position of the clip [156]. Nevertheless, despite the data on complete or almost complete occlusion of the aneurysm during surgery, the IA recurrence rate after clipping may be higher than is commonly believed: for fully clipped aneurysms, it is less than 1% for the first year, and in the long term (up to 10 years) – up to 5%. Moreover, there is a probability of IA detection de novo, which varies from 3 to 10% [157]. These data indicate that even after intraoperative CAG in the long term, it is necessary to conduct imaging studies; noninvasive techniques are most often used for this, however, for patients who may need further treatment, CAG is the method of choice [83].

In their work S. Marbacher et al. (2020) compared the quality and diagnostic value of intraoperative and postoperative CAG and came to an interesting conclusion: when using three-dimensional intraoperative reconstruction, clinicians receive a sufficient amount of information, and it is possible to do without subsequent CAG in the long-term follow-up period [106].

Thus, despite the CAG existing advantages in the diagnosis of treated IA, in the long-term postoperative period, preference is increasingly given to non-invasive techniques. In particular, in the case of IA treatment by endovascular embolization, MRA can be used instead of CAG without significant loss of diagnostic accuracy. As for clipped aneurysms, as well as stent implantation, the issue of completely replacing invasive methods with non-invasive ones has not yet been resolved: CAG still has greater diagnostic accuracy due to the absence of metal artifacts.

Conclusion

Acute aneurysmal subarachnoid hemorrhage is a potentially life–threatening condition that is often diagnosed too late or not diagnosed at all.

A lot of publicationss by both domestic and foreign authors are devoted to the problems of diagnosis, treatment and postoperative control of IA. Specifically these problems have caused the development and implementation of the federal vascular program in the Russian Federation in the last decade. So, in the Krasnodar Territory in 2017, 6 RVCs and 12 PVUs were already functioning.

The opening of vascular centers posed a number of other tasks: the need to develop patient routing, examination algorithms, advanced training and solving the problem of the shortage of radiologists.

Now part of the problems associated with the diagnosis of non-traumatic subarachnoid hemorrhage (nTSH) caused by the rupture of IA also remains unresolved. The question of what should be the optimal tactics for managing patients with clinical suspicion of SAH at an early hospital stage is partly debatable. In addition, the diagnostic effectiveness of invasive and non-invasive techniques in the search for the source of nTSH in the emergency unit needs to be clarified. The problem of further development and improvement of the optimal diagnostic algorithm in a multidisciplinary hospital remains very relevant, which allows timely provision of the attending physician with sufficient information about the patient condition.

The question of the significance of concomitant congenital and/or acquired vascular pathology of the neck and its possible impact on the prognosis in nTSH also remains unclear. It is possible that this group of pathologies may influence treatment tactics, as well as worsen the prognosis in patients with nTSH, therefore, the question of including extracranial BCA departments in the CTA protocol remains open.

The problem of choosing the optimal method of postoperative control of aneurysms in the long-term period is also relevant due to the significant difference in the diagnostic capabilities of imaging techniques. Unfortunately, due to the individual characteristics of the switched-off aneurysm and the patient condition at large, as well as differences in the chosen tactics of surgical treatment, there is currently no single algorithm for postoperative control of discharged patients, as well as recommendations for choosing a method of radiation diagnostics for monitoring the patient at the outpatient stage.

CHAPTER II. RESEARCH MATERIALS AND METHODS

2.1. General Description of Materials

The work is based on the examination of patients with acute non-traumatic SAH using computed tomography angiography of the brachiocephalic artery (CTA BCA) in the emergency department of regional vascular centers of the Krasnodar Territory, followed by an analysis of the results obtained. Since 2016, 650 patients admitted to the RVC emergency department with a diagnosis of acute non-traumatic SAH have undergone a native CT scan. If non-traumatic SAH was revealed, patients underwent angiography, the results of which were used to select tactics for further treatment.

In 2017, a unified diagnostic protocol was introduced in the Krasnodar region, according to which all RVC patients with suspected acute non-traumatic SAH receive a native CT of the head and CTA BCA to verify non-traumatic SAH. Medical evacuation has been carried out based on the results of CTA BCA. After the introduction of the regional diagnostic protocol, 650 case histories of patients with non-traumatic SAH who were diagnosed, medically treated and operated on at the Regional Neurosurgical Center of the Research Institute / RCH No.1 in the period from September 2017 to August 2020, were evaluated according to a uniform regional protocol. The causes of acute non-traumatic SAH in these patients were as follows: Rupture of intracranial arterial aneurysms, vascular malformations, vascular malformations in combination with IA, cavernomas; in some patients, the cause of non-traumatic SAH was not recognized.

Research Inclusion Criteria:

- patients with acute subarachnoid hemorrhage, IA rupture is initially diagnosed using non-invasive methods (CT, CTA, MRI, MRA) – a total of 393 patients;
- age – 18 years and older;
- non-invasive methods (CT, CTA, MRI, MRA) were performed in the acute phase (no later than 3 days after the onset of clinical manifestations).

Research Exclusion Criteria:

- CTA performed more than three days after the onset of clinical manifestations of subarachnoid hemorrhage;
- IA initially diagnosed with cerebral angiography;
- Other causes of non-traumatic SAH revealed, apart from IA.

The patients in the study group were divided into two categories: The first included patients who underwent CTA or MRA in the emergency department of the Research Institute / RCH No.1 (CTA – 277 patients, MRA – 8 patients), the second included patients diagnosed with the same methods in other hospitals of the Krasnodar Territory (CT-CTA – 101 patients, MRI-MRA – patients).

Upon admission to the Research Institute / RCH No.1, patients were examined according to the protocol, which included general somatic, neurological, laboratory and imaging. Description of CTA BCA in the emergency department and the CTA review in the RVC Krasnodar were interpreted by radiologists with a professional experience of 1 year to 20 years.

The medical records of 650 patients of the Neurosurgical Department No. 2 of the Research Institute / RCH No.1 with a diagnosis of acute non-traumatic SAH were analyzed, all non-invasive and invasive examinations of 393 patients performed in this institution were reviewed.

Subsequently, the results of the implementation of the protocol in the Krasnodar RVC were analyzed based on the experience of Novorossiysk City Hospital No.1 in 2019-2020.

In the long-term postoperative phase, all patients treated at the Research Institute / RCH No.1 were invited to a consultation with a neurosurgeon, CA was performed. In 52 cases, cerebral angiography was supplemented by dynamic MR angiography, in 47 cases – by CT angiography of the brachiocephalic artery. See Figure 1 for the Research Concept.

STAGE 1	
Analysis of publications literature on the issues of diagnosing the source of non-traumatic SAH	Russian and foreign publications
STAGE 2	
Analysis of routing and transportation of patients with non-traumatic SAH in the Krasnodar Territory	Local and federal orders, reports of local specialists
STAGE 3	
Implementation of the protocol for the examination of patients with acute non-traumatic SAH	RVC of the Krasnodar Territory
STAGE 4	
Analysis of medical records, neurosurgery department No.3, Research Institute / RCH No.1	Medical records of 650 patients with acute non-traumatic SAH, 09/2017 – 08/2020
STAGE 5	
Selection of patients with SAH caused by IA rupture (393 patients)	Analysis of the methods of radiation diagnostics to verify the source of non-traumatic SAH (CT, MRI), comparison of CTA BCA with the verification methods. Revision of CTA BCA, carried out at the Research Institute / RCH No.1, analysis of the primary description.
STAGE 6	
Analysis of experience with the introduction of CTA BCA in the emergency department for patients with non-traumatic SAH in the RVCs	Novorossiysk City Hospital No.1 **(122 patients) for the period 2019-2020.**
STAGE 7	
Postoperative follow-up of treated aneurysms	CTA BCA and MRI-MRA (52 patients) in performed in addition to standard CA
STAGE 8	
Development of recommendations to identify the source of acute non-traumatic SAH in the emergency department	Development of recommendations for the postoperative follow-up of treated aneurysms
STAGE 9	
Development of a prototype three-dimensional convolutional neural network to determine the probability of intracranial aneurysms using CTA BCA data (451 CTAs)	Testing the prototype three-dimensional convolutional neural network that determines the probability of IA presence using CTA BCA data

Figure 1 – Research Concept

Based on the results obtained, recommendations are proposed to identify intracranial aneurysms as a source of bleeding in patients with acute non-traumatic SAH in the RVC emergency department and to monitor the treatment of aneurysms in the long-term postoperative phase.

Among patients with ruptured aneurysms, women (n = 237) were most commonly represented (in 60% of cases), while a smaller group (40%) were men (n = 156). The age of the men ranged from 23 to 85 years (average – 51 years). The age of the women ranged from 18 to 90 years (average – 56 years). The mean age of all patients was 54.2 ± 12.5 years. The age details and gender distribution of the patients are shown in Figure 2.

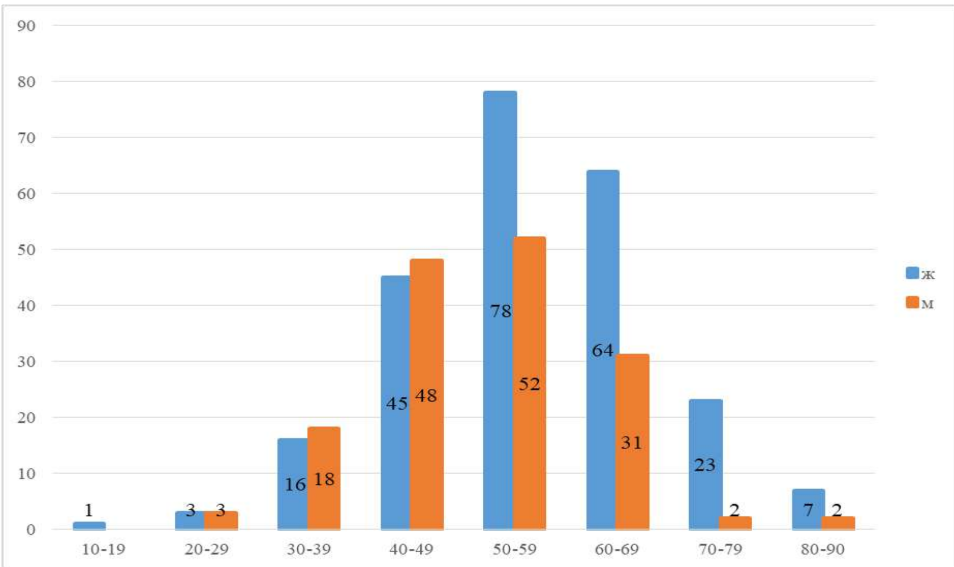


Figure 2 – Distribution of patients with ruptured IA in terms of gender and age. Axis X – age, years; Axis Y – number of patients

2.2 General Somatic, Neurological Examination and Imaging

Due to the severity of the disease, it was difficult to obtain a medical history from most patients on admission. According to the available emergency department records and medical history, non-traumatic SAH manifested itself in all patients in the form of headaches of varying intensity. The Hunt-Hess scale (HH) with a possible score of 0 to 5 was used to assess the severity of condition:

– grade 0: unruptured aneurysm;

– grade 1: asymptomatic or minimal headache and slight neck stiffness (meningeal symptoms and signs);

– grade 2: moderate to severe headache, neck stiffness (meningeal symptoms and signs), no neurologic deficit except cranial nerve palsy;

– grade 3: drowsy; minimal neurologic deficit;

– grade 4: stuporous, moderate to severe hemiparesis, possibly early decerebrate rigidity and vegetative disturbances;

– grade 5: deep coma, akinetic mutism, decerebrate rigidity.

Patients admitted with grade 1, 2 and 3 of the HH scale were classified as compensated, with grade 4 and 5 – as decompensated.

On admission to the emergency department, all patients were consulted by a group of specialists: a neurologist, a neurosurgeon, a general practitioner, an anesthesiologist and an intensive care physician. If the medical history or clinical data indicated somatic diseases that could complicate the course of a cerebral aneurysm, cardiologists, pulmonologists, endocrinologists, nephrologists, cardiovascular surgeons and general surgeons took part in the examination; other specialists were also consulted if necessary. All patients underwent a chest X-ray (chest CT in unconscious patients), electrocardiography (ECG), general clinical blood and urine tests, biochemical blood tests, a coagulation test, a blood serology test to determine blood group and rhesus factor, human immunodeficiency virus (HIV), syphilis and hepatitis. Additional ultrasound examinations and function tests of the internal organ, as well as other laboratory tests were carried out on the instructions of the specialists.

When seeking medical care against a background of clinical symptoms of non-traumatic SAH, the vast majority of patients were found to have high blood pressure – 98% (n = 385), of whom 83% of patients (n = 327) also had high blood pressure when assessed in the emergency department.

According to the medical history, some patients had concomitant pathology, mainly diseases of the cardiovascular system: arterial hypertension (n = 336; 85%), signs of chronic heart failure (n = 262; 67%), angina pectoris (n = 26; 7%), previous myocardial infarction (n = 26; 7%), cardiac arrhythmia (n = 6; 1.5%), pathology of the heart valves (n = 11; 2.8%), cardiomyopathy (n = 5; 1.3%). In addition, diseases of other organs and systems were also identified. All types of concomitant pathology are listed in Table 1.

Table 1 – Concomitant pathology in patients with non-traumatic SAH

Concomitant Pathology	Male Patients	Female Patients	Total
High Blood Pressure	128 (19.6%)	208 (32.0%)	336 (51.7%)
Chronic Heart Failure	96 (14.8%)	165 (25.4%)	261 (40.2%)
Angina Pectoris	10 (1.5%)	16 (2.4%)	26 (4.0%)
Previous Myocardial Infarction	10 (1.5%)	16 (2.4%)	26 (4.0%)
Concomitant Pathology	Male Patients	Female Patients	Total
Pathology of the Heart Valves	1 (0.2%)	10 (1.5%)	11 (1.7%)
Cardiac Arrhythmia	15 (2.3%)	22 (3.4%)	37 (5.7%)
Cardiomyopathy	3 (0.5%)	2 (0.3%)	5 (0.8%)
Chronic Hepatitis Infection	15 (2.3%)	19 (2.9%)	34 (5.2%)
Diabetes Mellitus	4 (0.6%)	13 (2.0%)	17 (2.6%)
Neoplasms	4 (0.6%)	4 (0.6%)	8 (1.2%)
Obesity	1 (0.2%)	6 (0.9%)	7 (1.1%)
Polycystic Kidney Disease	5 (0.8%)	2 (0.3%)	7 (1.1%)
COPD	3 (0.5%)	1 (0.2%)	4 (0.6%)
Gastroduodenal Ulcer	3 (0.5%)	–	3 (0.5%)
Hypothyroidism	–	2 (0.3%)	2 (0.3%)
Human Immunodeficiency Virus	2 (0.3%)	–	2 (0.3%)
Iron Deficiency Anemia	1 (0.2%)	1 (0.2%)	2 (0.3%)
Neurofibromatosis	1 (0.2%)	–	1 (0.2%)
Brain Arteriovenous Malformation	1 (0.2%)	1 (0.2%)	2 (0.3%)

2.3 Preoperative Imaging Modality

Patients had to fill out a consent form before undergoing diagnostic radiological imaging. If a patient was unconscious or in a very unstable condition, the examination was performed by a neurosurgeon and an emergency physician based on the vital signs noted in the medical documentation. In 390 patients from the study group, a native CT was performed in the emergency room. If acute non-traumatic SAH was detected, CTA BCA was subsequently performed to determine the source of the hemorrhage. Sixteen patients underwent MRI and MRA.

Subsequent native imaging on admission to the Research Institute / RCH No.1 was performed if the patient's clinical condition deteriorated from the time of transportation from the place of initial examination to the Research Institute / RCH No.1 and did not match the data of the previously performed examinations, as well as in the absence of imaging data (X-ray film, CD/DVD). In 284 patients who had undergone CT and CTA and in all 16 patients after MRI-MRA, which was not performed in RCH No.1, a subsequent native examination was required. Subsequent CTA BCA in the preoperative phase was performed in 7 patients. All imaging modalities performed in patients with non-traumatic SAH at different stages of hospitalization and evacuation are listed in Table 2.

Table 2 – Imaging modalities performed in patients with non-traumatic SAH at different stages of hospitalization and evacuation

Imaging Modality / Institution	Research Institute / RCH No.1	District and City Hospitals	Subsequent Examination at Research Institute / RCH No.1 after District and City Hospitals
Native CT	337 (51.8%)	330 (50.8%)	283 (43.5%)
CT Angiography of	278 (42.8%)	101 (15.5%)	7 (1.1%)

Brachiocephalic Artery			
MRI	8 (1.2%)	16 (2.5%)	–
CA	94 (14.5%)	–	–

Verification of pathology was performed using CA, microsurgical and autopsy data. Detailed information about the verification can be found in the following chapters.

2.3.1 Native Brain CT and CT Angiography of Brachiocephalic Artery

The native brain CT at the Research Institute / RCH No.1 was performed with a 32-slice Siemens CT scanner using the spiral scanning method. To avoid artifacts caused by movement, a triangular soft cushion was used under the knees to ensure patient comfort. To avoid artifacts caused by metal, hairpins and other metal objects were removed beforehand. In case of unconsciousness, soft wedge-shaped pads in the headrest on both sides of the patient’s head and flexible clamps on the tomography table were used to immobilize the patients. The native scan was performed in the traditional way: Patients were placed on their back and their head was positioned in a gantry. After creating the lateral topography, scanning was planned without inclination along the supra-orbital-meatal line connecting the external auditory canal and the upper edge of the orbit. The examination area included the head from the level of the greater occipital foramen to the vertex, including the skin. The slice thickness was 2 mm. The reconstructions were performed in two modes: Bone window and brain.

The following features were considered in the description of the native scan:

- the state of the subdural, convexital, subarachnoid spaces and basal cisterns;
- the severity of SAH as per formalized scales (Fischer scale);
- the state of the brain parenchyma;
- the extent of displacement of the median structures of the brain;
- the state of the ventricular system of the brain;
- the severity of the IVH (Graeb scale);

- the indication to a possible source of hemorrhage;
- the assessment of the bone structures contained within the scan area.

If a non-traumatic SAH was detected on the native CT, the patient underwent CTA BCA on a Siemens 256-slice dual source CT.

The examination protocol for the cerebral arteries included scans of the head and neck to visualize the intracranial arteries and the extracranial segments of the internal carotid artery and vertebral artery, as well as the external arteries. The position of the patient and the laser marking were selected in the same way as for the native scan.

The patient was fitted with a peripheral venous catheter (size 18G) connected to an Ulrich automatic syringe injector. The rate of administration of the contrast agent was 4-5 ml/s (depending on the condition of the patient's peripheral veins and the size of the catheter installed), and the volume of contrast agent administered was 50-70 ml. The iodine concentration in the nonionic contrast agent was 350 mg/ml.

The study area was planned with two digital topographies, direct and lateral, from the aortic arch to the vertex. The scan direction was caudocranial. The scan was performed with bolus tracking (search for the target density in the vessel) at the level of the aortic arch. The premonitoring was set on the ascending aorta, the target density was 100 HU. The slice thickness was 0.75 mm, the distance was 0.6 mm.

The imaging was created with high and low energy – 100 kV and 140 kV. In addition, multiplanar imaging was performed.

The following was taken into account when carrying out the CT angiography:

- location of arterial aneurysms, arteriovenous malformations as probable causes of non-traumatic SAH;
- determination of the number, location, size and shape of the IA; in multiple aneurysms, the most likely source of hemorrhage was determined based on the location of the blood, the aneurysm’s size and shape;
- evaluation of the individual anatomical features of the cerebral arterial ring and the developmental anomalies;

- relationship of the aneurysm to the bone structures and the tentorium cerebelli;
- assessment of the carotid and vertebral arteries.

For each of the aneurysms found on CTA BCA, the standard protocol also included the size of the aneurysm neck, the ratio between the diameter of the dome and the diameter of the neck, the angle of the aneurysm in relation to the carrier vessel (for lateral aneurysms), the relationship between the maximum size of the dome and the diameter of the carrier vessel, the size of the IA in three planes, the presence of calcifications in the wall of the IA, the presence of blood clots in the lumen of the IA, signs of rupture of the IA.

Characteristics of development (anomalies and developmental variants) and acquired pathology (pathological tortuosity, thrombosis, condition of the vessel wall) were evaluated in extracranial vessels.

The NASCET scale (North American Symptomatic Carotid Endarterectomy Trial) was used to calculate the degree of arterial stenosis [140]. The patients were divided into subgroups according to the severity of the stenosis: Stenosis up to 50%, stenosis from 51 to 70%, stenosis from 71 to 99% and occlusive thrombosis 99-100%.

CA was performed in 24% of patients (n = 67) to clarify CT angiography data, to search for sources of bleeding or to perform surgical treatment. The results of the CT and CT angiography determined the further treatment tactics of the patients (embolization or clipping of the IA).

2.3.2 Brain MRI

The MRI was performed with MR Signa Excite 1.5 Tc General Electric, MR Signa Excite 3.0 Tc General Electric. This method was used selectively for the differential diagnosis of the intracranial pathology present in the patient. In three patients with intolerance to iodinated contrast media, the localization of the ruptured IA was determined using MRA data.

The MRI protocol included the following pulse sequences: T1-weighted images (WI), T2-WI, Fluid Attenuation Inversion Recovery (FLAIR), diffusion-weighted imaging (DWI), 3D-Time-of-Flight (TOF), Spoiled Gradient Recalled (SPGR) (the latter -with contrast).

When multiple IA aneurysms were present after non-invasive techniques and a X-ray surgical method to close them was suspected, as well as in complex and controversial cases, a cerebral angiography was performed.

2.3.3 Cerebral Angiography

Cerebral angiography (CA) was performed with General Electric Innova 3000, Siemens Axiom Artis DTC. Native and subtraction examinations of the extra- and intracranial areas of all sections of all brachiocephalic arteries were performed. An additional rotational examination was performed if pathologies were detected in the vascular basin. The CA data were also used to determine the location, size and characteristics of the patient's individual aneurysm anatomy and supporting arteries. In addition, the presence, severity and prevalence of cerebral arteriospasm were assessed according to the classification of V.V. Krylov. The degree of IA from the blood circulation was determined according to the Raymond-Roy occlusion classification.

In contrast to CTA, CA could solve additional tasks:

- localization and type of existing vasospasm (the severity of the arterial constriction and the prevalence of the spasm in the segments);
- performing occlusion tests when planning surgeries;
- determining the characteristics of collateral circulation.

In cases where the patients' condition was severe and/or unstable and the localization of the hemorrhage detected on native CT matched the source of hemorrhage identified on CTA, the patients underwent surgery based on the CTA data; the remaining patients underwent CA. A total of 94 patients underwent cerebral angiography, four of them – twice. The treatment tactics for the patients were determined on the basis of the results of the clinical and radiological examination.

2.3.4 Subsequent CT and CT Angiography

All native CT scans and CT angiographies of the brachiocephalic artery performed in patients with non-traumatic SAH at the Research Institute / RCH No.1 in the preoperative phase were extracted from the image archive and retrospectively reviewed (n = 278). The condition of the intracranial and extracranial arteries was analyzed in all patients. The data obtained were compared with the primary description, the intraoperative data and the CA results. When comparing data from CA and CTA BCA, the entire arterial circle of Willis was analyzed and the sensitivity and specificity of CTA BCA were calculated. When comparing CTA BCA and the surgical data during clipping, only the surgical part was analyzed and the sensitivity of the CT angiography was evaluated.

The description of CTA BCA in the emergency department was performed by an on-duty radiologist with at least 0 years of professional experience or more (immediately after internship, residency, and primary specialization). The second review of this CTA was performed by an experienced radiologist (n = 275).

Primary CT angiographies of the brachiocephalic artery performed in district and city hospitals were not analyzed because there were no corresponding data in the local archive.

To determine the criteria of an experienced radiologist for neuroimaging in this research, the average annual number of CT scans of the head and CT angiographies of the brachiocephalic artery in the radiology departments of the PVDs and RVCs of the Krasnodar Territory was determined using the example of the Emergency Hospital, the Research Institute / RCH No.1 and the Research Institute / RCH No.2 according to the annual reports for 2017-2022.

Most head CT scans and CT angiographies of the brachiocephalic artery were performed at the Research Institute / RCH No.1, namely 31,268 and 4,033 examinations, respectively, due to the organized flow of outpatients from all over the region (up to 800,000 visits per year), many hospital beds (1,958) and emergency care on admission (up to 110,000-120,000 calls from patients per year) and neurosurgical activity.

In the Emergency Hospital where the PVD is organized, up to 29,777 CT scans of the head and 448 CT angiographies of the brachiocephalic artery are performed every year. This medical facility provides emergency medical care to the patients of Krasnodar (up to 115,000 patients per year). The number of hospital beds is 839, outpatient care is not offered, patients with cerebral aneurysms from the Emergency Hospital are transferred to the Research Institute / RCH No.1.

Up to 12,131 CT scans of the head and up to 2,000 CT angiographies of the brachiocephalic artery are performed at the RVC of the Research Institute / RCH No. 2. The hospital has 1,402 beds, offers outpatient care (up to 800,000 patients) and emergency admissions. Patients with IA are referred to the Research Institute / RCH No.1 for treatment.

The average number of examinations reviewed by one radiologist per year was also calculated using data from the Radiology Department of the Research Institute / RCH No.1. Seventeen radiologists work in the CT rooms every day. Each of the radiologists describes 1,839 CT scans of the brain and 237 CT angiographies of the brachiocephalic artery per year. In five years – 9,195 CT scans of the head and at least 1,185 CT angiographies of the brachiocephalic artery.

According to the results of the calculations, in this research a neuroimaging expert is considered to be a specialist with more than five years of experience, who has described at least 7,000 CT scans of the head and at least 1,000 CT angiographies of the brachiocephalic artery. At the same time, a neuroimaging specialist must work in a medical facility that has the following departments:

– Department of Neurosurgery/Vascular Surgery/Neurology, intensive care unit for neurological/neurosurgical/vascular surgery patients;

– CT, MRI and ultrasound equipment operating around the clock.

The expert participated in the analysis of fatal cases and complications, consultations and clinical conferences in the specialties of neurosurgery, neurology and vascular surgery.

2.4 Surgical Intervention

Microsurgical interventions were performed by employees of the Neurosurgical Department No.3 of the Research Institute / RCH No.1 (Head of the Department – Dr. V.V. Tkachev MD). Rigid head fixation systems from Mayfield and Aesculap, Stryker and Codman power equipment were used for the microsurgical procedures. Surgical microscopes were used to perform surgeries: Leika 500 ultra from Leika Camera AG, OPMI Neuro NC 4 and OPMI Pentero from Carl Zeiss with 8-16x magnification and microsurgical instruments from Aesculap, Codman. Clips from Aesculap, Mizuho and Codman were used to clip the aneurysms. All surgical procedures were performed according to generally recognized modern methods. Microconductors, microcatheters, microcoils, intracranial stents and cylinders for temporary occlusion from various manufacturers were used in surgeries. Intravascular interventions were performed by the staff of the Department of Radiosurgical Diagnostics and Treatment of the Research Institute / RCH No.1 (Head of the Department – Dr. A.N. Fedorchenko MD).

According to the results of a comprehensive clinical and radiological examination, 376 intracranial aneurysms were clipped microsurgically (95.7%), 12 IAs – embolized (3%), embolization with clipping was required in three cases (0.8%), and two patients did not undergo surgery (0.5%). Fifty-six patients (14.2%) died as a result of the treatment, one of whom did not undergo surgery. All discharged patients are recommended to see a neurosurgeon in the long-term postoperative phase and have the treated aneurysms checked.

2.5 Postoperative Follow-Up

All discharged patients were advised to see a neurosurgeon again in the long-term postoperative phase and to monitor the IA healing. Thirty-seven patients attended in the follow-up examinations; the time after the surgery ranged from 3 to 49 months. (Table 3). All 37 patients were hospitalized in the Department of General Neurology and in the Neurosurgical Department No. 2 of the Research Institute / RCH No.1. Their postoperative follow-up included CA, CTA BCA, MRI, MR angiography, dynamic MR angiography (TRICKS).

Table 3 – Terms of long-term postoperative phase

Term	Number of Patients
Up to 6 months	6
6 months – 1 year	8
1 year – 2 years	11
3 years and more	12
Total	37

2.5.1 Non-Invasive Imaging Modalities in Long-Term Postoperative Phase

A non-contrast CT scan was performed according to the same protocol as in the preoperative phase.

After creating the lateral topography, scanning was planned without inclination along the supra-orbital-meatal line. The examination area included the head from the level of the greater occipital foramen to the vertex, including the skin. The slice thickness was 2 mm. The reconstructions were performed in two modes: Bone window and brain.

The following features were considered in the description of the native scan:

- the state of the subdural, convexital, subarachnoid spaces and basal cisterns;
- the state of the brain parenchyma;
- the extent of displacement of the median structures of the brain;

- the state of the ventricular system of the brain;
- the assessment of the bone structures.

A CT angiography of the brachiocephalic artery was performed with a 256-slice dual-source CT from Siemens. Post-processing was performed with Siemens VIA workstations, Osirix and Horos applications for MAC. The CT angiographies were analyzed using multiplane reconstructions, with and without exclusion of bone structures.

The IA examination protocol included scanning of the head and neck to visualize the IA itself and the extracranial segments of the internal carotid artery, vertebral artery, and external carotid artery using the Carotid angio protocol without the dual-energy mode. The position of the patient and the laser marking direction were selected in the same way as for the native scan.

The patient was fitted with a peripheral venous catheter (size 18G) connected to an Ulrich automatic syringe injector. The rate of administration of the contrast agent was 4–5 ml/s (depending on the condition of the patient's peripheral veins and the size of the catheter installed), and the volume of contrast agent administered was 50-70 ml. The iodine concentration in the nonionic contrast agent was 350 mg/ml.

The study area was planned with two digital topographies, direct and lateral, from the aortic arch to the vertex. The scan direction was caudocranial. The scan was performed with bolus tracking (search for the target density in the vessel) at the level of the aortic arch. The premonitoring was set on the ascending aorta, the target density was 100 HU. The slice thickness was 0.75 mm, the distance was 0.6 mm.

The imaging was created with high and low energy – 100 kV and 140 kV. In addition, multiplanar imaging was performed.

The following was taken into account when carrying out the CT angiography:

- treated aneurysms (extent of aneurysm closure, presence of the aneurysm neck);
- location of arterial aneurysms, arteriovenous malformations;
- assessment of the carotid and vertebral arteries.

The first stage of brachiocephalic artery evaluation was the analysis of image quality: contrast and the presence of artifacts due to clips, emboli and stents.

For each of the IA treated by microsurgical clipping on CTA BCA, the standard protocol reflected the presence and size of the aneurysm neck and near-neck segment. In the resected and stented aneurysms, arterial patency, absence of thrombosis and residual blood flow were considered controls for healing.

Characteristics of development (anomalies and developmental variants) and acquired pathology (pathological tortuosity, thrombosis, condition of the vessel wall) were evaluated in extracranial vessels.

The radiation exposure during CTA BCA was compared with the radiation exposure during CA.

A total of 35 out of 37 patients underwent CT and CTA in the long-term postoperative phase; two patients refused the examination.

2.5.2 MRI and MR Angiography in Postoperative Phase

In the long-term postoperative phase, 3 to 49 months after microsurgical clipping of the IA aneurysm with fixed YASARGIL clips from Esculap, patients were invited for a follow-up examination to assess the remaining aneurysm and possible damage to the main vessel. According to the instructions for use for the YASARGIL aneurysm clip made of titanium and Phynox alloy, there is no additional risk for the patient when performing a 1.5 and 3T MRI; however, moderate MR artifacts may occur. However, the extent of the artifacts may vary depending on the MRI pulse frequency.

There were no clinical manifestations of repeated non-traumatic SAH in the patients.

The MRI and MR angiography were performed with a MR Optima Mr450w 1.5T from General Electric.

The examination protocol included the following pulse sequences: T1-WI, T2-WI, FLAIR, DWI, SWAN, 3D TOF, Trics, SPGR (Trics, SPGR – contrast-enhanced).

The non-contract examination evaluated: the state of the brain parenchyma and its ventricular system; the state of the subdural, convexital, subarachnoid spaces and basal cisterns. Imaging parameters: **T1 WI** (TR:352, TE: 11), **T2 WI** (TR: 4944–5133, TE 102-104), **FLAIR** (TR: 8800, TE: 123), **3DTOF** (TR: 28, TE:3,2) **SPGR** (TR: 4,4, TE: 1,4).

TRICKS-MR angiography parameters: FOV:24×19, NEX = 0.5 slices – 168, short, TR / TE (3,4/1,3), slice thickness 2.2 mm.

In TRICS, a gadolinium-containing contrast agent, 0.1 mmol/kg, was injected at a rate of 1.5 ml/sec with a bolus syringe.

During the bolus injection of the contrast agent, three-dimensional MRA images of the affected area were taken repeatedly (up to 16 times). The frame rate was approximately 2 seconds per sequence. The images were taken in the axial plane to make an initial assessment of the lesion. If necessary, a second scan was performed in the selected orthogonal, sagittal or coronal planes.

After completion of TRICS, SPGR was performed without additional administration of a contrast agent. The TRICS and SPGR images were viewed in 3D using a maximum intensity projection of the three-dimensional data volume.

All MRI examinations were performed using GE and MAC workstations with Osirix and Horos applications. The MR angiographies were analyzed using multiplane reconstructions.

In the MRA evaluation, particular attention was paid to clipped aneurysms (extent of aneurysm occlusion, presence of aneurysm neck), the location of arterial aneurysms and arteriovenous malformations.

During the MRA evaluation, attention was also paid to treated aneurysms (extent of aneurysm occlusion, presence of aneurysm neck), the location of arterial aneurysms and arteriovenous malformations. A total of 34 patients underwent MRI and MRA in the postoperative phase; three patients refused the examination.

2.5.3 Cerebral Angiography in Postoperative Phase

The examination was performed with General Electric Innova 3000, Siemens Axiom Artis DTC. Native and subtraction examinations of the BCA extra- and intracranial segments were performed. An additional rotational examination was performed if pathology was detected in the vascular basin. The CA data were also used to determine the location, size and characteristics of the patient's individual aneurysm anatomy and supporting arteries. The degree of IA from the blood circulation was determined according to the Raymond-Roy occlusion classification.

A total of 33 patients underwent CA in the postoperative phase. Of the patients who did not undergo CA, two patients refused the examination, one contracted coronavirus and was transferred to a specialized hospital, and one patient had an allergic reaction to a contrast agent after CTA BCA, which led to refusal of CA.

2.5.4 Definition of Diagnostic Accuracy of Non-Invasive Methods in Long-Term Postoperative Phase

Diagnostic accuracy was determined by comparing the obtained CTA and MRA data with CA using statistical methods.

The statistical data analysis has been carried out using the standard functions of Statistica 6.0. (Version 6.0) from StatSoft Inc., USA; using descriptive statistics. The links between the features were analyzed using Spearman's rank correlation coefficient – R. The correlation was classified as weak at $R \leq 0.25$ and moderate at $R < 0.05$.

2.6 Developing and Defining the Role of a Prototype Convolutional Neural Network in the Search for IA in Acute Non-Traumatic SAH

2.6.1 Methodology for Determining the Diagnostic Value of Artificial Intelligence in the Search for IA using CT Angiography Data of the Brachiocephalic Artery

On the basis of the Kuban State Medical College in Krasnodar, a prototype of a three-dimensional convolutional neural network has been created, the main function of which was to determine the probability of the presence of IA based on CTA BCA. The CT angiographies of the brachiocephalic artery in DICOM format performed in the Radiology Department of the Research Institute / RCH No. 1 were used to create and test the prototype. (n = 456).

Inclusion criteria:

- patients aged over 18 years;
- patients with acute non-traumatic SAH caused by IA rupture;
- patients with IA in the pre-hemorrhagic phase;
- patients with IA in the preoperative phase.

Exclusion criteria:

- patients younger than 18 years;
- patients with a previously operated IA (clipping, stenting, embolization);
- patients with IA due to arteriovenous malformations or Moyamoya disease.

The research concept is presented in the form of a diagram (Figure 3).

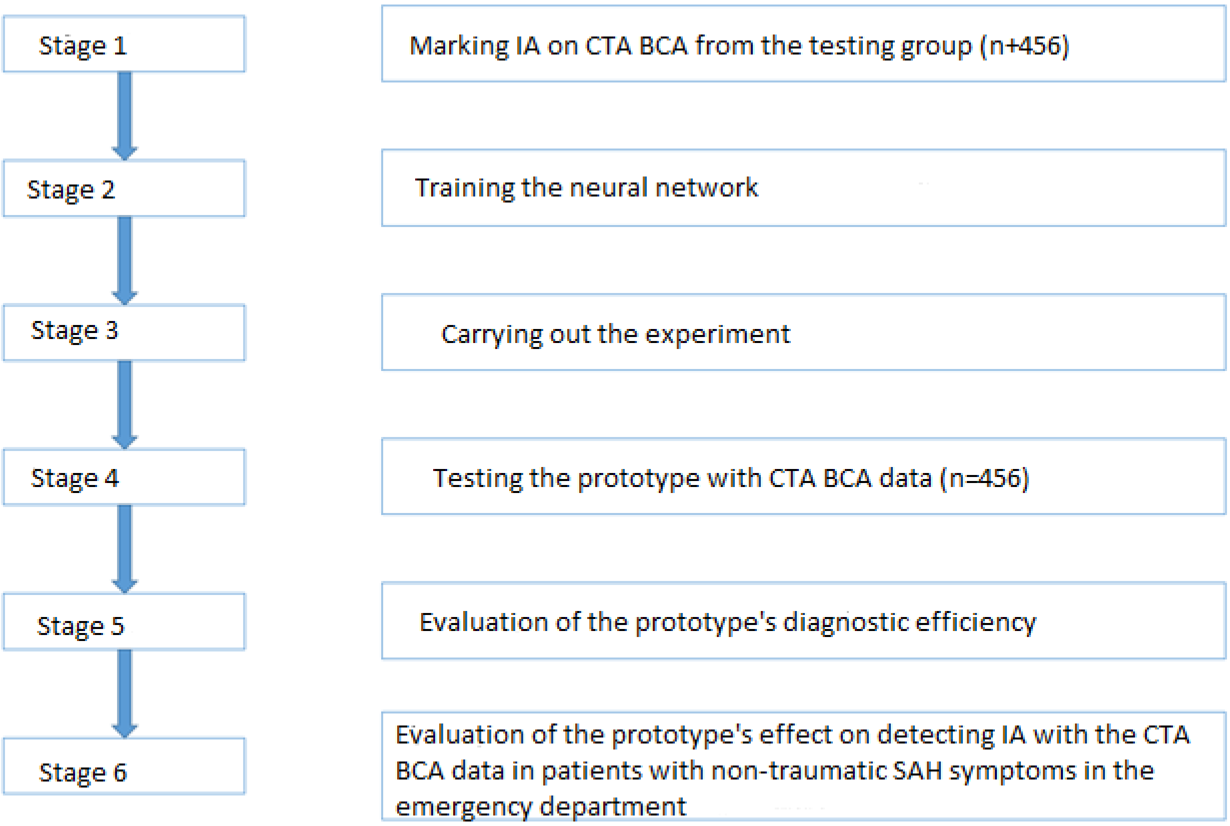


Figure 3 – Concept of an Experiment to Train a Three-Dimensional Convolutional Neural Network for the Detection of IA based on CT Angiography Data of the Brachiocephalic Artery

CT angiographies of the brachiocephalic artery were performed on Siemens and GE scanners according to the same protocols. The head and neck were scanned to visualize the intracranial arteries and the extracranial segments of the carotid and vertebral arteries. A contrast agent with iodine concentration of 350 mg/ml was injected via a peripheral venous catheter (size 18G) with an Ulrich syringe injector at a rate of 5 ml/s and a volume of 50-70 ml. The slice thickness when scanning with a Siemens device was 0.75 mm, the distance was 0.7 mm; with a GE device – 1.25 mm and 1.25 mm, respectively.

The research was conducted with three-dimensional convolutional neural networks of artificial intelligence, i.e. with machine learning algorithms [6]. In the compilation and tagging phase, a dataset of 206 CT angiographies of the brachiocephalic artery of patients with IA confirmed by CA data or intraoperatively was created. Regions of interest with aneurysms were marked with ovals in the OsiriX DICOM Viewer program. In addition, 250 CT angiographies of the brachiocephalic artery from patients without IA were used to train the prototype. The original dataset therefore consisted of 456 examinations in DICOM format.

In the data preparation phase, the original set of CT angiographies was converted into the Nifti format using the dicom2nifti library in order to be used by the machine learning algorithms. To extract information about the marked regions of interest with IA, a program was written in C++ using the libraries Qt6 and DCMTK (OFFIS DCM Tool Kit). As a result, a text file was created with the coordinates of the marked IAs.

Each CT scan in the examinations contains an unprocessed voxel intensity between -1000 HU and over 2000 HU. Bones with different densities correspond to 400 HU or more, so this value was used as an upper limit. To normalize the CT scans, an interval of -1000 HU to 400 HU was selected. The data was subjected to the following preprocessing: The orientation of the volumes was fixed by a 90-degree rotation; HU values from 0 to 1 in the selected interval were scaled; the dimension of the data was reduced to the width, height, and depth of 128, 128, and 64 voxels, respectively. For each iteration of the training, 100 trials were randomly selected from 456 trials. The dataset was divided into a training group and a verification group in a ratio of 70 to 30.

The training dataset was expanded to increase the number of training samples. Additional data was generated from the original data by rotating it by a random angle of -20, -10, -5, 5, 10 or 20 degrees.

In the development and training phase of the neural network, a model of a three-dimensional convolutional neural network with a dimension of 128×128×64 was developed. The Keras and Tensorflow libraries, the Python programming language, were used for the implementation. The neural network model consisted of four convolutional layers and a kernel of dimension 3, a maximum pooling function and a ReLU activation function. A fully connected layer with 512 outputs, a ReLU activation function and a dropout of 0.3 was used for the classification. Subsequently, a fully connected layer with one output and a sigmoid activation function was used.

In the experimental phase, training was performed in 100 epochs (iterations). Validation was carried out at the end of each training iteration. The network weights obtained during training were stored in a binary file to obtain predictions. At the end of the training, the Precision and Recall metrics of the classification were calculated.

$$\text{Precision} = TP / (TP + FP)$$
$$\text{Recall} = TP / (TP + FN), \text{ where} \tag{1}$$

TP – true-positive solutions;

FP – false-positive solutions;

FN – false-negative solutions.

The prototype indicated the possible presence of at least one aneurysm according to CTA BCA as a percentage from 0 to 100. Responses were categorized into three groups according to probability: high (71-100%), medium (51-70%) and low (1-50%).

The solution was considered true-positive if the neural network predicted a probability of 71% or more for an examination with IA; false-positive if the neural network predicted a probability of 71% or more for an examination without IA; false-negative if the neural network predicted a probability of less than 70% for an examination with IA.

The response of the prototype was compared with imaging data (CTA BCA and CA) and intraoperative data obtained during IA microsurgical clipping) Sensitivity, specificity and diagnostic accuracy were determined based on the prototype's response in a group of patients with and without single intracranial aneurysms.

2.6.2 Testing a Prototype Convolutional Network in the Emergency Department to Evaluate its Impact on the Detection of IA after Brachiocephalic Artery CT Angiography in Patients with Acute Non-Traumatic SAH in the Emergency Department

At Kuban State University in Krasnodar, a prototype of a three-dimensional convolutional neural network was developed, a laptop was installed and a hardware and software complex was created for use by medical professionals. To obtain a solution for the prototype, CT angiographies of the brachiocephalic artery were loaded into the hardware and software complex, and as a result of the processing the radiologists obtained the probability of IA in percent.

To test the prototype, the clinicians selected a group of 50 patients with IA (who were examined in the emergency department of the Research Institute / RCH No.1 and diagnosed with acute non-traumatic SAH) and 13 patients without IA (who were examined in the outpatient clinic of the Research Institute / RCH No. 1 and diagnosed with brachiocephalic artery atherosclerosis). Six clinicians took part in the test: four radiologists, one neurosurgeon and one first-year resident at the Department of Diagnostic Radiology No.2 of the Faculty of Continuing Education and Professional Development of Kuban State Medical College. Each of the participants viewed all CT angiographies (n = 63) both with and without the help of AI data in randomized order and at different times. The specialists had no knowledge of the initial data, the medical history or the results of subsequent imaging.

The specialists were randomly divided into two groups. Within each group, the examinations were randomized for the first half of the group and performed in reverse order – for the other half. The first group began with examinations without AI, the second group – with examinations with AI. After seven days, the sorting of the data was changed so that the first group reviewed the examinations with AI data and the second – without AI. This process is shown schematically in Figure 4.

MEDICAL SPECIALISTS		
2 radiologists	**2 radiologists**	**1 neurosurgeon** **1 resident**
• 63 CTA BCA without prototype data • ***2 weeks break*** • 63 CTA BCA with prototype data	• 63 CTA BCA with prototype data • ***2 weeks break*** • 63 CTA BCA without prototype data	• 63 CTA BCA without prototype data • ***2 weeks break*** • 63 CTA BCA with prototype data

Figure 4 – Schematic representation of an experiment to analyze CT angiographies of the brachiocephalic artery by three groups of clinicians with and without AI data

The reference standard for all examinations in the test group was established by a radiologist with 20 years of experience who determined the presence of IA based on CTA BCA and case histories in which the presence of IA was confirmed with CA data (if available), intraoperative and autopsy data.

The results of the specialists were formalized in the form of a table; the discovered IA was highlighted as a region of interest (ROI). The patient's examination result was considered positive if at least one IA was detected.

The conclusions drawn from the AI were communicated to the specialists in the form of a probability for the presence of IA, which ranged from 0 to 100%; the specialists could use or ignore this data when analyzing the images.

The CT angiography data provided by the specialists with or without the help of AI were used to determine sensitivity, specificity and accuracy. Sensitivity was the number of true-positive results in relation to the total number of cases with a positive result for the presence of IA, specificity was the number of true-negative results in relation to the total number of cases without IA and accuracy – the number of true-positive and true-negative results for all tests.

The average of these data for all participants was also calculated by measuring each statistical indicator in relation to the total number of true-positive, false-negative and false-positive results. To assess whether they achieved a significant improvement in their performance through the use of AI, a one-sided t-criterion was calculated for the differences in sensitivity, specificity and accuracy. To determine the reliability of the results and their possible dependence on the inclusion of a neurosurgeon and a clinical resident in the group, a sensitivity analysis was performed by calculating the t-criterion for the differences in sensitivity, specificity and accuracy among radiologists only.

2.7 Statistical Data Analysis

The statistical data analysis has been carried out using the standard functions of Statistica 6.0. (Version 6.0) from StatSoft Inc., USA, using descriptive statistics. The links between the features were analyzed using Spearman's rank correlation coefficient – R. The correlation was classified as weak at $R \leq 0.25$ and moderate at $R < 0.05$.

CHAPTER III. EVALUATION OF THE DIAGNOSTIC VALUE OF COMPUTED TOMOGRAPHIC ANGIOGRAPHY OF THE BRACHIOCEPHALIC ARTERIES IN THE ACUTE PERIOD OF NON-TRAUMATIC SUBARACHNOID HEMORRHAGE WITH INTRACRANIAL ANEURYSM RUPTURE

All patients included in the study, at admission to the emergency room of the regional vascular centers of the Krasnodar Region, had an urgent native CT scan of the brain to confirm nTSH and CTA of BCA to identify the source of hemorrhage. If patients were allergic to iodine-containing contrast agents (according to informed consent data), an MRI-MRA was performed.

3.1 Side effects and iatrogenic damage while performing radiological research methods

As a consequence of CTA of the BCA performed at the Research Institute – RCH No. 1, one vessel was damaged by a catheter in one case. This event resulted in hematoma development and contrast agent outpoured into the soft tissues of the elbow area. This complication required the resetting of a venous catheter to another limb.

In one patient in the procedure room of the CT department, after the administration of an iodine-containing contrast agent, an allergic reaction was observed in the form of unbearable itching and rash by the type of urticaria, meanwhile in the informed consent signed by the patient, an allergy to iodine was excluded. The patient received emergency care in a procedure unit, and further treatment was determined based on the CTA results.

Two patients, according to informed consent, had a history of adverse reactions to iodine, so we avoided CTA and replaced it by MRI-MRA.

There was no information in the case histories about complications that occurred in the regional vascular centers.

3.2 The quality of the performed CT examinations

The quality of the CTA of the BCA performed in the district hospitals was relatively low due to contrast errors in four cases, in two cases there were no image copies on the carriers during transportation of patients. These studies were re-done in the reception office of the Research Institute – RCH No. 1.

Poor image quality in the Research Institute – RCH No. 1 was observed in three cases: in one – due to the patient's motor artifacts, in two - due to contrast defects. CAG data were used to find the source of hemorrhage in these patients. The minimum radiation load during CT was 0.0615 mSv, the maximum was 0.99 mSv, and the average was 0.717 mSv.

3.3 Clinical and radiologic features of patients with IA rupture

In total, the data of 393 patients with nTSH were analyzed, and its cause was an IA rupture. Of those 81% patients had single aneurysms (n = 318) and 19% had multiple aneurysms (n = 75).

According to the case histories, all patients had headache as a clinical manifestation of SAH. The severity of clinical manifestations in patients was assessed according to the H H scale. The largest number of patients (n = 156; 39.7%) were admitted to the emergency ward in a state of somnolentia with moderate neurological deficit, a smaller group consisted of patients with moderate headache (n = 130; 33.1%), some patients were in sopor with moderate or severe hemiparesis (n = 72; 18.3%), some patients were in a deep coma (n = 26; 6.6%), as well as with mild and moderate headache (n = 9; 2.3%)

The distribution of patients according to clinical symptoms at admission to the admission ward is shown in Figure 5.

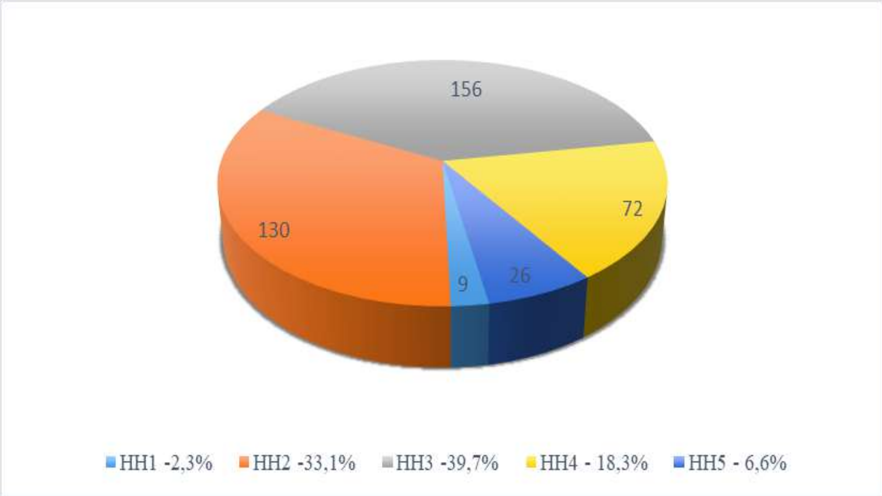


Figure 5 – Characteristics of patients regarding SAH severity according to the H H scale. The numbers on the diagram correspond to the number of patients in each group

The men-women ratio in assessing the severity was in this way: among patients with NN-1 and NN-4, women were more commonly observed, and among patients with NN-2, NN-3 and NN-5 there were predominantly men. A more detailed description of patients by sex and severity of the state, according to the H H scale, is shown in Figure 6.

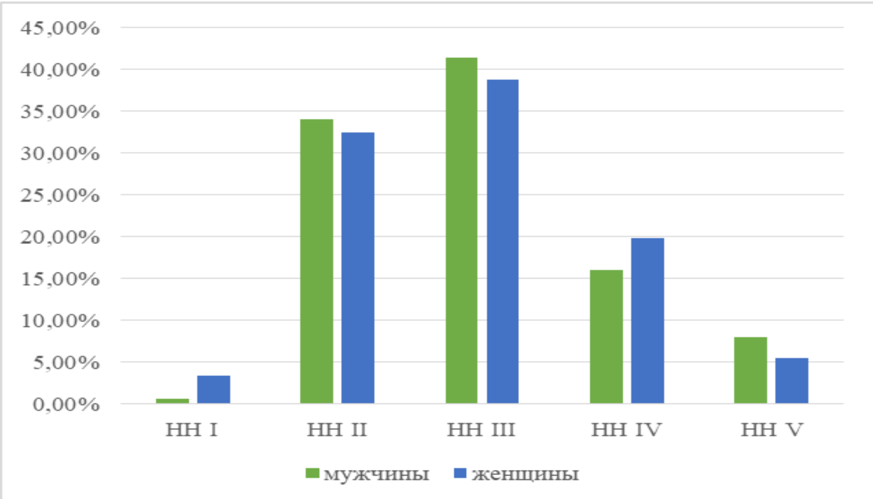


Figure 6 – Characteristics of patients by sex and state severity according to the H H scale. The x–axis is points on the NN scale, the y–axis is the relative (in %) number of patients)

The SAH severity was assessed according to the Fisher scale (Table 4).

Table 4 – Modified CT scale of basal SAH according to Fisher scale

Fisher 1	Fisher 2	Fisher 3	Fisher 4
No SAh, or minimum SAH, no IVH	Minimum SAH with IVH	Diffuse or focal SAH without IVH	Diffuse or focal SAH with IVH

According to the Fisher scale, severity of SAH in patients was distributed as follows: 1 degree – 22 patients (6%), 2 degree – 67 patients (17%), 3 degree – 98 patients (25%), 4 degree – 206 patients (52%) (Figure 7).

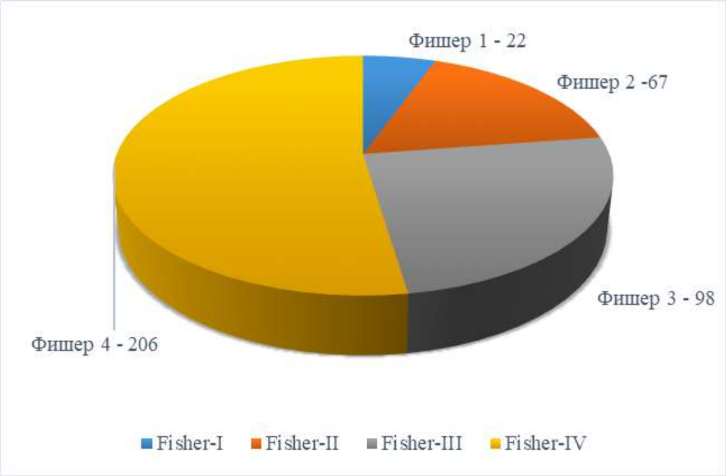


Figure 7 – Characteristics of patients according to the SAH severity according to the Fisher scale

There were no significant differences in the 3 and 4 degrees of SAH severity between men and women. According to the Fisher scale, 4 degree was determined in 52% men (n = 81) and 52.7% women (n = 125), stage 3 – in 24.3% men (n = 38) and 25.3% women (n = 60). Women were more likely to have the first degree of severity – 7.2% (n = 17), while men accounted for 3.2% (n = 5). In the case of 2 degree, men accounted for 20.5% (n = 32), women – 14.8% (n = 35), this is presented in Figure 8.

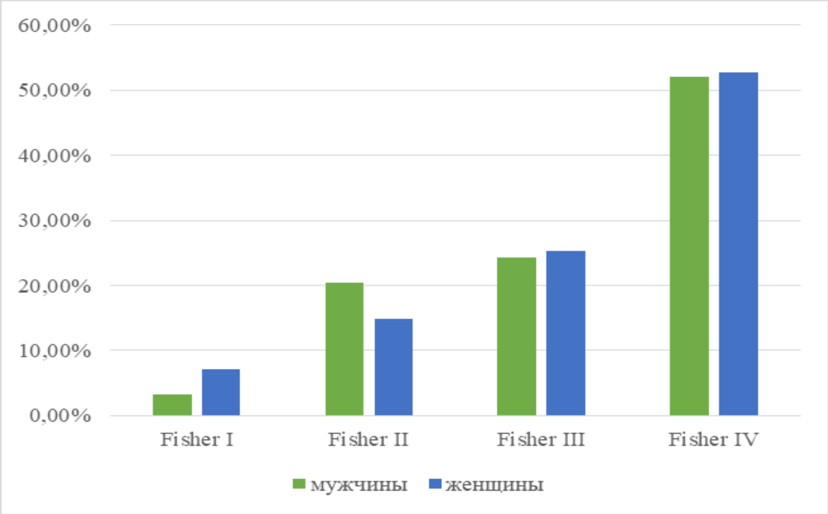


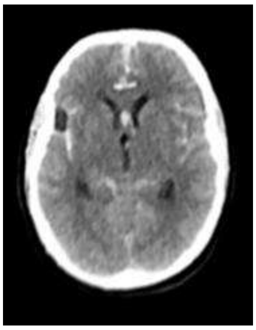
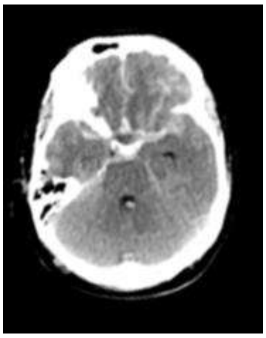
Figure 8 – Comparison of SAH severity by sex, according to the Fisher scale. The x–axis presents points on the Fisher scale; the y–axis is a relative (in%) number of patients

In 23% patients (n = 92), aneurysm rupture was accompanied by intracerebral hematomas. Intracerebral hematomas were commonly observed in the frontal (n = 52) and temporal lobes (n = 50), less often – in the parietal lobes (n = 14) and subcortical areas (n = 13); in isolated cases, hematomas were found in the corpus callosum (n = 3) and occipital lobe (n = 1). The frequency and localization of parenchymal hematomas are shown in Figure 9.

Figure 9 – Frequency and localization of associated parenchymal hematomas in patients with IA rupture (n = 92)

In 45% of patients, IA rupture was accompanied by IVH, the severity of which was assessed according to the Graeb scale (Table 5).

Table 5 – IVH sevirity according to Graeb scale: 1-4 points – light IVH, 5-8 points – medium-heavy IVH, 9-12 points – heavy IVH

<table>
<tr><td colspan="4">Lateral ventricles</td></tr>
<tr><td>Blood admixture or a slight hemorrhage</td><td>< half of the ventricle is filled with blood</td><td>> half of the ventricle is filled with blood</td><td>Ventricle is completely filled with blood and dilated</td></tr>
<tr><td>1 point</td><td>2 points</td><td>3 points</td><td>4 points</td></tr>
<tr><td></td><td></td><td></td><td></td></tr>
<tr><td colspan="4">Third and fourth ventricles</td></tr>
<tr><td colspan="2">Blood is in the ventricle, but its size is normal</td><td colspan="2">Ventricle is completely filled with blood and dilated</td></tr>
<tr><td colspan="2">1 point</td><td colspan="2">2 points</td></tr>
<tr><td></td><td></td><td></td><td></td></tr>
</table>

In most cases, IVH with minimum severity was observed: Graeb 1 (n = 45), Graeb 2 (n = 43) and Graeb 3 (n = 38); less often there were IVHs of 4 degree of severity (n =

17), the others – in isolated cases. More detailed information on the severity of associated IVH is presented in Figure 10.

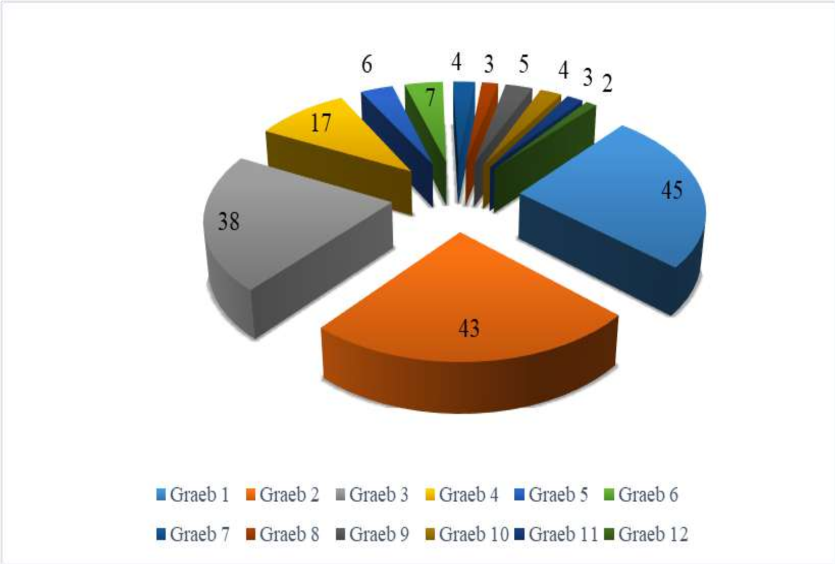


Figure 10 – Severity of associated IVH in patients with ruptured intracranial aneurysms

The probable source of the hemorrhage was assumed by blood distribution on the native CT scans with a certain error. Thus, rupture of an anterior connective artery aneurysm was supposed with hemorrhage into the cisterns of the terminal plate, the interhemispheric fissure, the area of the transparent septum, the anterior horn of the lateral ventricle, in some cases – into the third and fourth ventricles and with the presence of intracerebral hematoma in the mediobasal part of the frontal lobe. Ruptured aneurysms of the communicant segment of the internal carotid artery was assumed if blood was detected in the cisterns of the same hemisphere, in the inferior horn of the lateral ventricle and if there was an intracerebral hematoma in the basal ganglia and medial temporal lobe. Rupture of the middle cerebral artery aneurysm was supposed when the hemorrhage spread into the Sylvian fissure, the inferior horn of the lateral ventricle, and rupture of the posterior connective artery aneurysm – in the presence of blood in the suprasellar cistern. If there was blood in the posterior cranial fossa, the intervertebral and circumferential cisterns, the posterior part of the interhemispheric sulcus, as well as in the presence of intracerebral hematoma in the midbrain and hypothalamus, a rupture of the aneurysm of the main artery bifurcation was expected.

3.4 Effects of radiation diagnostic methods in patients with IA rupture in the emergency room

According to the case histories, 492 aneurysms were detected in 393 patients using radiation diagnostics methods (CT, MRI, CAG). The primary study was performed both in the district vascular centers and in the emergency room of the Research Institute – RCH No. 1. In general, 275 CTA were performed in the Research Institute – RCH No. 1, 104 CTA were performed in the district centers, 6 angiographs were performed repeatedly in the Research Institute – RCH No. 1. Repeated CTA were carried out in cases when patients did not have images with them during hospitalization or these images were of poor quality.

Of 393 patients, CTA of the BCA showed single IA in 81.3% (n = 320), 11.2% patients (n = 44) had two IAs, 1.5% (n = 6) had three IAs, 0.5% (n = 2) had four IAs, 0.3% (n = 1) had eight IAs, 3.4% (n = 13) had no IA according to CTA results. The remaining IAs (1.8%; n = 7) were detected by MRI.

Since the number of performed MRI and MRA was small, these data were not subjected to a separate analysis.

If, according to the CTA outcomes, SAH source was not found, or results of the examination were questionable, CAG was performed. The minimum radiation load during CAG was 8.75 mSv, the maximum was 16.362 mSv, and the average was 12.96 mSv.

Of the 485 aneurysms detected by CTA and CAG, the maximum number (37%; n = 179) was located in the anterior connective artery, 33.6% (n = 163) was in the middle cerebral artery, 16.3% (n = 79) – in the internal carotid artery. The frequency of aneurysm detection is showed in Table 6.

Table 6 – Site of IA distribution according to CT angiography and CAG data

IA	Number (n)	Incidence (%)
ACA	179	37
MCA	163	33,6
ICA	79	16,3
MA	15	3
PCA	13	2,7
PCA	11	2,4
ACA	8	1,6
SCA	6	1,2
PCA	5	1
STA	3	0,6
PICA	2	0,4
CMA	1	0,2

3.5 Results of a retrospective analysis of CTA of the BCA

As a result of CTA BCA revision, the source of bleeding was found in three patients – single IAs that were missed during the initial examination. In 11 patients with single IA, one more intact IA was additionally found, two patients with three aneurysms had one intact IA each. Thus, the initial description of 275 patients, showed 317 IAs, and 334 intracranial aneurysms were detected after revision (17 more). Among the additionally found IA, 3 were the source of bleeding, the remaining 14 were intact.

Data on the number of IA detected during the initial description and during further revision are shown in Figure 11.

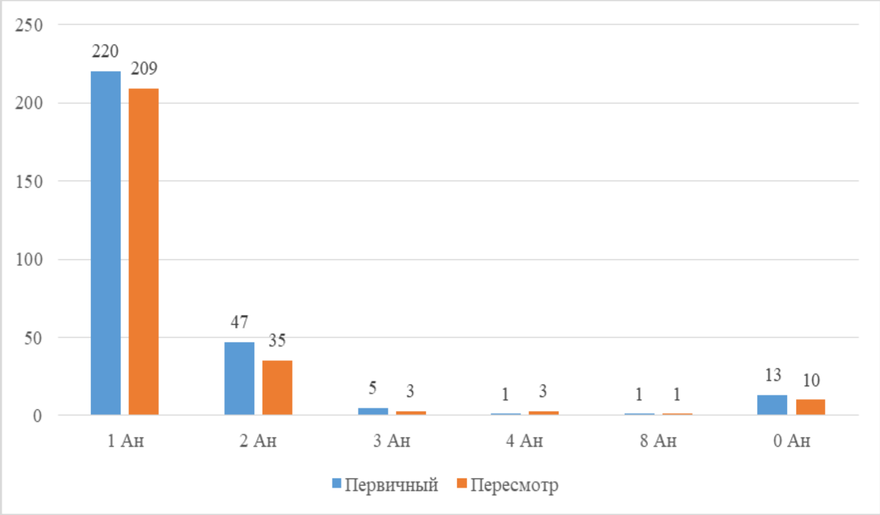


Figure 11 – Data on the number of aneurysms during the primary presentation and revision. X-axis is the number of aneurysms, Y–axis is the number of patients.

The reasons for missed IA, which were the source of bleeding, it was vasospasm in two cases, and in one case – dynamic blurring associated with the patient motion activity. The reasons for missing intact IAs in most cases (n = 10) were the size of the aneurysm < than 3 mm, in other cases (n = 3) – vasospasm.

3.6 Diagnostic value of CTA of the BCA comparing to CAG data

3.6.1 Comparison of the routine emergency description of the CTA BCA (example of the Central District Hospital) and the expert description the example of the Research Institute – RCH No. 1) with the data of the CAG performed in a specialized hospital

Of 393 patients, 26.5% (n = 104) underwent CAG. CTA data considering the number and localization of aneurysms noted in the case histories were compared with the CAG data. Among those 104 patients, 68 CTA were performed at the Research Institute – RCH No. 1, the remaining 36 patients were examined in district centers.

According to the analysis, in 4 cases, in none of the examinations conducted in the emergency room in presence of nTSH on the native CT, the source of bleeding was not detected. In one case, CTA BCA data were negative, the CAG data were controvercial; this patient underwent CTA BCA and CAG in a delayed period.

According to CTA BCA data, 64% patients (n = 67) had single aneurysms, in 36% (n = 37) there were multiple aneurysms; the total number of aneurysms was 106. CAG data demonstrated that 69% patients (n = 72) had single aneurysms, 31% (n = 32) – multiple; the total number of aneurysms was 126. The diagnostic consideration value of the CTA emergency description in comparison with CAG is shown in Table 7.

Table 7 – Diagnostic value of the urgent presentation of CTA BCA comparing to CAG

Sensitivity (%)	Specificity (%)	Overall accuracy	Positive prognostic value	Negative prognostic value
78,36 CI 71–84%	60,00 CI 23–88%	78 CI 70–84%	98,13	9,38

3.6.2 CTA BCA and CAG performed in a specialized hospital: comparing the outcomes of the second revision

Separately, CTA BCA and CAG were revised, and they were performed at the Research Institute – RCH No. 1; there were totally 68 patients.

According to the analysis, in three cases, in none of the examinations carried out in the emergency room in the nTSH presence on the native CT, the source of bleeding was not detected. In one of the patients, the CTA BCA data were negative, CAG data were suspicious; this patient underwent CTA of the brachiocephalic artery and CAG in a delayed period.

CTA outcomes demonstrated that 66% patients (n = 45) had single aneurysms, 19% (n = 13) had multiple aneurysms, in 15% (n = 10) there were no aneurysms; the total number of aneurysms was 76. According to CAG data, 69% patients (n = 47) had single aneurysms, 25% (n = 17) had multiple aneurysms, and in 4.5% (n = 3) no aneurysms were found, in one patient (1.5%) the result was uncertain; the total number of aneurysms was

87. The diagnostic consideration calculation of the revised CTA BCA compared to the CAG is shown in Table 8.

Table 8 – Diagnostic value of the revised CTA of the BCA compared to the CAG

Sensitivity (%)	Specificity (%)	Overall accuracy	Positive prognostic value	Negative prognostic value
84,95 CI 76–91%	50,00 CI 15–85%	84 CI 75–90%	97,53	12,5

3.7 CTA BCA diagnostic value comparint with intraoperative findings

3.7.1 Comparison of the primary urgent of CTA BCA performed in district centers and Research Institute – RCH No. 1 with intraoperative findings

The results obtained using CTA of the BCA were compared with intraoperative data, and the side of the Willis circle where theintervention took place was analyzed. The study group included protocols describing CTA performed in district centers and in the admission ward of the Research Institute – RCH No. 1, the total number of patients was 379. The calculation of the diagnostic consieration of the CTA primary description performed in district centers and Research Institute – RCH No. 1, compared with intraoperative findings, is shown in Table 9.

Table 9 – Diagnostic value of the primary presentation of CTA of BCA performed in district hospitals and Research Institute – RCH №1 compared with intraoperative data

Sensitivity, %	Overall accuracy, %	Positive prognostic value, %
96,56 CI 94–98%	97 CI 94–98%	100

The types of surgical interventions are summarized in Table 10.

Table 10 – Types of surgical interventions performed in selected patients

Surgery	Number of patients
Microsurgical clipping of IA	376
Embolization	12
Embolization + clipping	3
No surgery	2

In total, treatment resulted in 56 lethal cases, of those in one case no operation was performed.

3.8 Analysis of the routing SAH patients in the Krasnodar Region and the stages of the algorithm implementation

The organization of emergency care in cities with a multi-million population and within the regional health care framework differs significantly. In the conditions of the region, using the example of the Krasnodar Region with an area of 75,500 km2, with a population over 5,687,378 people, with a population density of 75.5 people /km2, it is complicated to organize medical evacuation measures in such a way that the aneurysm exlusion would be performed within the optimal 72 hours from the onset of the disease, and this is due to the impossibility of primary hospitalization of all patients at once in the Regional Vascular Center, late patient referral for medical care and time costs associated with the transportation of patients to the regional center. For these reasons, in regions with a large geographical extent and climate fluctuations, physicians face difficulties in following this standard and experince financial losses, since this item is taken out as a quality evaluation criteria.

The main consultant specialists of the Health Care Ministry of the Krasnodar Region developed a unified regional regulation for emergency care rendering to patients with IA ruptures, according to which all key diagnostic, therapeutic and evacuation measures were carried out in a region with an adult population of over 4 million people to the specified cohort of patients.

In accordance with the developed protocol, patients with suspected rupture of IA were evacuated to a regional neurosurgical center as soon as possible after diagnosis in the hospitals of primary hospitalization to verify the source of hemorrhage and surgical treatment. These organizational measures fully corresponded to the recommendation protocol of the Russian Association of Neurosurgeons, 2007, the recommendations of the American Stroke Association, 1994, 2009, 2012. [18, 42, 57, 109].

The main methods of diagnosing nTSH were CT of the brain, and in case of negative CT results or if it was impossible to conduct this study, lumbar puncture was performed. To verify the aneurysm itself as a source of SAH, CAG was used, which was performed in a majority of patients.

Until 2007, there was one principal vascular center to perform a native CT scan of the brain around the clock to verify nTSH, and to verify its source, CAG was performed in all patients. At the same time, most patients were transferred within 24 hours and urgently operated with microsurgical or intravascular method only in the main RVC (Research Institute – RCH No. 1), regardless of age, severity of the condition and the timing of diagnosis.

Since 2011, by virtue of the vascular program (Regional Order No. 4591, 11/30/2011), 4 RVCs and 3 DVSs equipped with CT and C-arc machines were organized in the Krasnodar Region, where native CT and CAG were performed.

After 2017, continuing the work of the vascular program (Regional Order No. 6091, December 27, 2017), 6 RVCs and 12 DVSs were already functioning in the Krasnodar Region, where already in the RVC, the CTA of the BCA was performed in cases with nTSH.

Today, DVSs are re-equipped with CT scanners and the introduction of a telemedicine consultation system, the verification of nTSH is already performed in the primary hospitals, and not in the principal RVC, as it was in 2007, when the vascular program just started. Now non-invasive verification of IA has become possibel due to the introduction of the protocol of urgent CTA in the emergency room. In simplified form the stages of the diagnostic algorithm implementation in the Krasnodar Region in different years is shown in Figure 12.

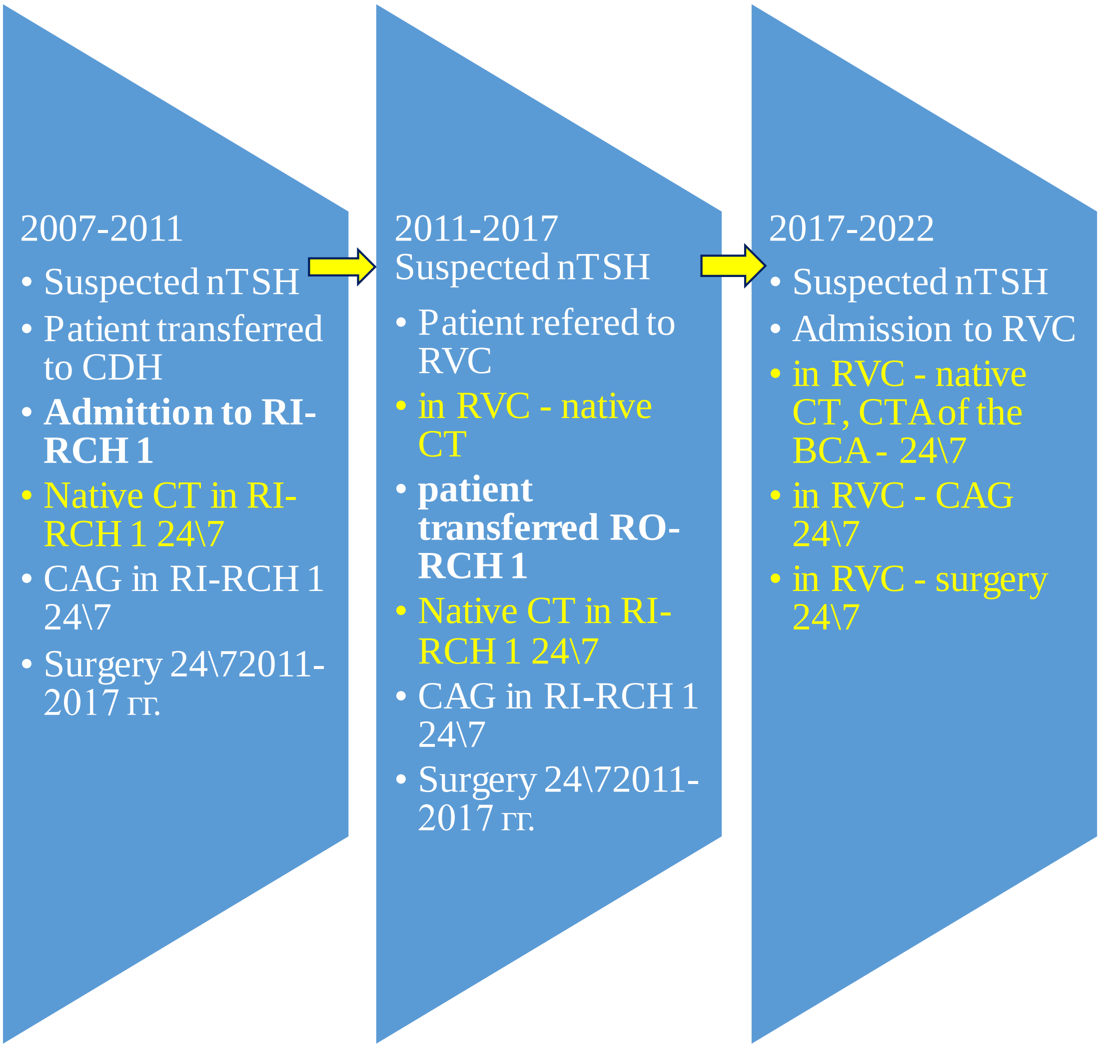


Figure 12 – Scheme of changes in the diagnostic algorithm and routing of nTSH patients from 2017 to 2022

With such a procedure for providing diagnostic care in the admission ward, early operations (during the first 3 days from the moment of aneurysmal rupture) are 66%, early delayed – 30%, and late operations are 4%. At the same time, every second operation is performed in NSD No. 1, Research Institute – RCH No. 1 in the evening and at night shifts. The frequency of repeated ruptures during the waiting period decreased to 2%.

3.8.1 Cost-effectiveness analysis of the proposed protocol

To calculate the economic efficiency, the marginal maximum prices for CAG and CTA BCA were taken from the price list of the Research Institute – RCH No. 1.

The cost of medical services was calculated according to the order of the Health Care Ministry of the Krasnodar Region (04.04.2019, No. 2022/1) on approval of the procedure for determining prices (rates) for medical services provided by state budgetary medical institutions under the jurisdiction of the Health Care Ministry of the Krasnodar Region, provided by them in excess of the established state task, as well as in cases determined by laws, within the established state tasks.

The calculation of the medical service costs included direct and indirect expenses. Direct charges included the costs directly related to the medical service and consumed in the process of its provision. Direct expenses included:

- remuneration of the main medical staff;
- payment accruals for the remuneration of basic medical personnel;
- material expenses consumed in the process of providing medical services (medicines, dressings, medical instruments, expendable materials, disposable medical supplies, food, etc.);
- deterioration of soft inventory by main divisions;
- depreciation of fixed assets (property) used in the medical and diagnostic process for providing paid medical services;
- other expenses.

Indirect expenses included the costs of the institution related to the management and maintenance of the process for providing paid medical services, which are not directly attributed to their cost.

Indirect costs included:

- remuneration of general administrative staff with accruals;
- general-purpose soft inventory deterioration;
- depreciation of fixed assets (property);
- repair of fixed assets (property);

- household expenses (costs of materials and items for current economic purposes, stationery, inventory and payment for services, including maintenance costs, etc.);
- other expenses (representation expenses, advertising).

The listed indirect costs were considered in the cost of medical services through a estimated coefficient.

CAG as a medical service consisted of angiography of brain arteries with examination of collateral blood flow and consultation of an X-ray endovascular surgeon with recorded invasive interventions on a digital storage medium (including the cost of a disk), the total cost was 18,848 rubles.

CTA of the BCA as a medical service consisted of CT with intravenous bolus contrast and subsequent three-dimensional mathematical processing of the obtained image on the workstation (examination of the aorta and its branches) and consultation with a radiologist with recording study data on a CD (including the cost of the disc), the total cost was 11,997 rubles.

The difference in the cost of CAG and CTA of the BCA was calculated, and then the number of patients who underwent only CTA of the BCA without CAG application was determined. The cost savings were calculated using the formula: economic benefit = number of patients with CTA BCA only × the difference in CAG and CTA rates.

The data were calculated for the entire study period and for each year.

It was revealed that the use of CTA of the BCA only (without CAG) allows saving 6,851 rubles for each patient with nTSH.

In the present study, using CTA only in 292 patients as the main technique for the diagnosis of aneurysmal SAH permitted to save 2,000,492 rubles.

Thus, the average annual economy amounted to about 666,831 rubles. And this is without taking into consideration the savings from not having to repeat examinations in another institution.

3.8.2 Analysis of the results following practical application of the proposed protocol for examination of patients with nTSH symptoms

As an example of the practical application of the protocol for examination in patients with nTSH symptoms, including CTA, we could offer an analysis of the experience in the Novorossiysk City Hospital No. 1 of the Health Care Ministry, Krasnodar Region, 2019-2020.

For two years 122 patients with acute nTSH symptoms have been examined using the developed and implemented protocol. As a result, 50 patients were found to have IA. During the first day from the moment of diagnosed IA, 45 patients were treated by surgical clipping in the neurosurgical department of CH No. 1. Only 5 patients were referred for treatment at the Research Institute – RCH No. 1, Krasnodar, where further CAG was performed as part of the follow-up examination.

Extensive data on the patient distribution arranged by years are presented in Table 11.

Table 11 – Surgical treatment experience in CH No. 1 for 2019-2020: patients with diagnosed nTSH

	2019	2020
Number of identified nTSHs	70	52
Number of IA	24	26
Treated in GB No. 1	21	24
Refered to the Research Institute – RCH No. 1	3	2

As it is seen from the presented data, the majority of patients after the detection of IA, that resulted in nTSH development, were treated in the same institution at the regional level, without contacting the head institution. Thus, conditions are created to accelerate the treating patients and optimize their management tactics, thereby improving the prognosis.

In addition, an important aspect of the protocol application with mandatory CTA is the undeniable reduction of radiation exposure due to selective CAG only in controversial diagnostic cases when CTA detects no IA, as well as the absence of the need to repeat CTA in another medical institution.

It is also worth pointing out the obvious economic benefits of the protocol application. Hence, the results of the analysis showed that the reduction in the cost of diagnostic procedures was significant. When calculating the funds spent in CH No. 1 for the diagnosis of aneurysmal SAH for the period 2017-2019, carrying out only CTA of the BCA (without CAG) allowed saving 1,979,939 rubles (16,500 rubles of savings for one case of SAH).

Thus, the average annual economy amounted to about 660,000 rubles, and this is without considering the savings from avoiding the necessity to repeat examinations in another institution. Application of the protocol also made it possible to significantly reduce the total radiation load to which patients were subjected: the minimum radiation load during CTA was 0.0615 mSv, the maximum was 0.99 mSv, the average was 0.717 mSv; the minimum radiation load during CAG was 8.75 mSv, the maximum was 16.362 mSv, the average was 12.96 mSv (on average 18 times more).

Conclusion

Hence, a staged introduction of a new algorithm for providing emergency care to patients with nTSH in Krasnodar Region enables achieving optimal indicators of timely diagnosis for this dangerous pathology and aiding patients. The results of the calculations carried out during the study allow us to recognize the devised nTSH diagnostic protocol as cost-effective.

The use of CTA of the BCA in the conditions of the RVC emergency unit creates conditions that allow in the nTSH acute period to confirm the presence of nTSH timely, identify its source, as well as accelerate emergency medical care to the patient and optimize management tactics. It is important to perform these manipulations in the same institution at the regional level, without contacting a federal institution. When one decides on the use of a new diagnostic protocol, it is also crucial to consider such important components as reducing a patinet's radiation load, as well as cost-effectiveness.

A study should be performed according to strict regulations; if possible, its results should be evaluated by an experienced radiologist or there should be the possibility of a second revision. The study showed that compliance with the CTA

protocol and interpretation of the data obtained by an experienced radiologist increase the sensitivity of the technique compared to CAG data from 78.36 to 84.95%, and the sensitivity in comparison with intraoperative data reaches 95.56%. These data suggest that IA detection with CTA of the BCA allows in 97% cases to avoid conducting invasive research methods.

The absence of vascular pathology according to CTA data in the presence of massive basal SAH, as well as the detection of "complex" aneurysms in BCA are still indications for CAG.

CHAPTER IV. RADIOLOGICAL CONTROL OF SINGLE ANEURYSMS

Of the 393 patients with nTSH, 318 patients had single IA. Of these, 215 patients underwent CTA in the Research Institute – RCH No. 1, the others – in regional centers. The studies performed at the Research Institute – RCH No. 1 were subsequently retrospectively revised.

4.1 General characteristics of patients

Among the patients with single IA, women were slightly more common – 59% (n = 184), men were 41% (n = 134). The average age of women was 55 years (mean range 25 - 80 years), the average age of men was 51 years (mean range 29 - 85 years). According to the HH scale, patients more often admitted (in 39.1% cases, n = 124) to the emergency room in a state of somnolentia with moderate neurological deficit (HH-3), a smaller group consisted of patients with severe headache (HH-2) (35.8%; n = 114), part of the patients was in sopor with moderate or severe hemiparesis (NN-4) (18.2%; n = 58), in a deep coma (HH-5) (4.7%; n = 15), with mild to moderate headache (HH-1) (2.2%; n = 7). The ratio of patients by severity is shown in Figure 13.

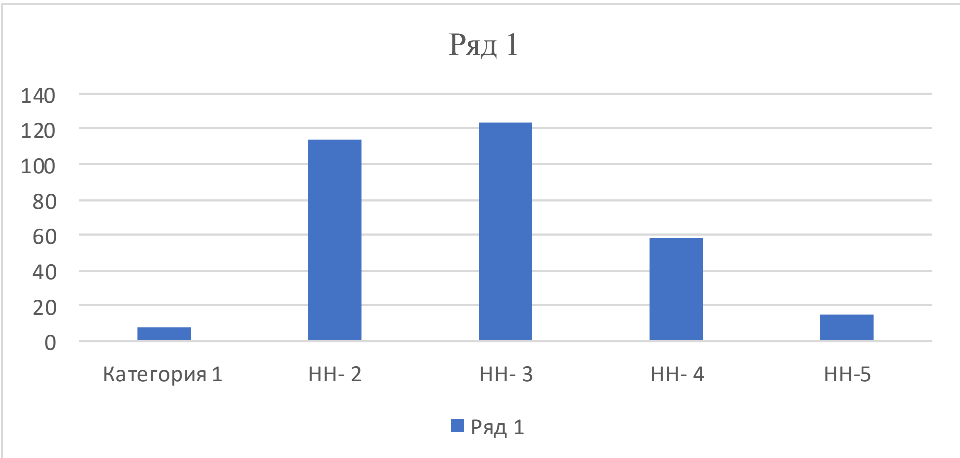


Figure 13 – Characteristics of patients with rupture of single IA by severity degree (Hunt-Hess scale). The x axis is the scores on the HH scale, the y axis is the number of patients

According to the Fisher scale, the patients were distributed according to the severity of SAH as follows: 4 degree – 167 patients (52.2%), 3 degree - 75 patients (23.5%), 2 degree – 54 patients (18%), 1 degree – 20 patients (6.3%), and this is presented in Figure 14.

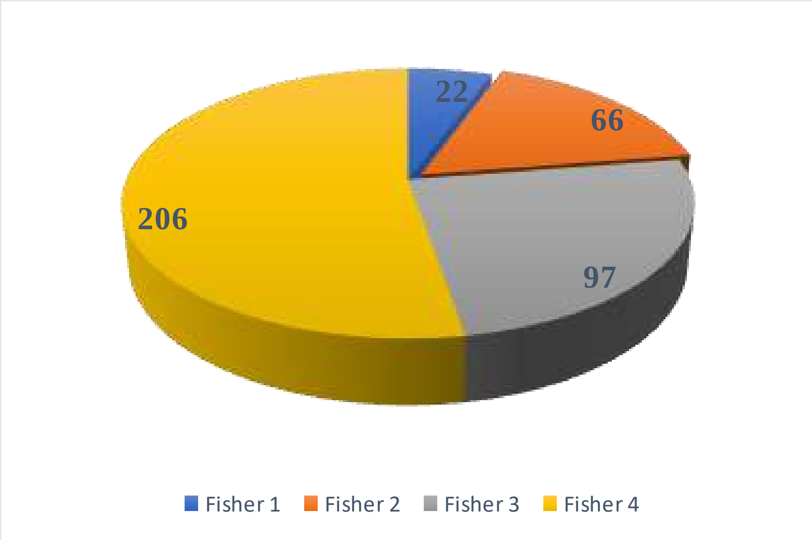


Figure 14 – Characteristics of patients with rupture of single IA according to the SAH severity (Fischer scale)

In 47% patients (n = 153), IA rupture was accompanied by IVH, its severity was assessed according Graeb scale. In most cases, patients had a minimal degree of IVH severity: 1 degree according to Graeb (n = 41), 2 degree (n = 36), 3 degree (n = 33); patients with 4 degree of severity (n = 15) were less common, the others - in isolated cases (from 2 to 6). Information on the severity of associated IVH is shown in Figure 15.

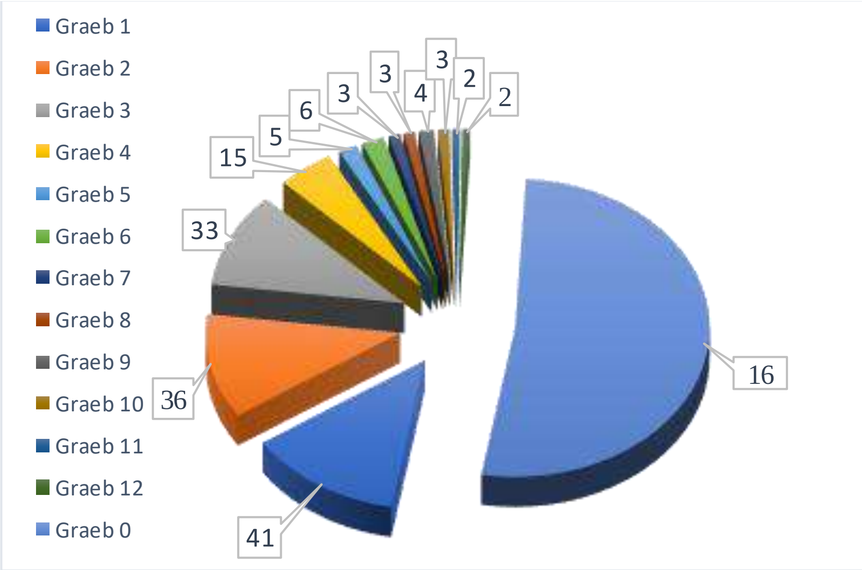


Figure 15 – Severity of associated IVH in patients with ruptured single IA

In 52 patients (24%), IA rupture was accompanied by intracerebral hematomas. They were most often observed in the temporal (n = 41) and frontal lobes (n = 47), less often in the subcortical (n = 11) and parietal lobes (n = 14), single hematomas were in the corpus callosum (n = 2). The localization and frequency of parenchymal hematomas are shown in Figure 16.

Figure 16 – Localization of associated parenchymal hemorrhages in patients with single IA

The general characteristics of patients with single intracranial aneurysms are presented in Table 12.

Table 12 – General characteristics of patients with single IAs

Number of patients	318
Sex: – female – male	 184 134
Age: – among female patients – among male patients	 58 (41–83) 50 (29–65)
IA dimensions (maximum diameter in mm) according to CTA data	Medium 6 mm (from 2 to 12 mm)
SAH severity according to native CT: – Fisher I – Fisher II – Fisher III – Fisher IV	 20 (6,3%) 54 (18%) 75 (23,5%) 167 (52,2%)
Associated IVH and parenchymal hemorrhage: – parenchymal hemorrhage only – IVH only	8 5 22
Number of patients	318
Parenchymal hemorrhage: – frontal lobes – temporal lobes – parietal lobes – occipital lobes – corpus callosum – subcortical areas	116 47 41 14 1 2 11
Distribution according to the Hunt-Hess scale: – 1 – 2 – 3 – 4 – 5	 7 (2,2%) 114 (35,8%) 124 (39,1%) 58 (18,2%) 15 (4,7%)
Type of treatment: – embolization – clipping	 9 (2,7%) 306 (97%)

– embolization + clipping	1 (0,3%)
Number of patients with vasospasm	99 (31%)
Outcome: –lethal – recovery	 49 (15,4%) 269 (84,6%)

4.2 Evaluation of aneurysm quantity, comparison of methods

4.2.1 Urgent assessment of CTA of the BCA – primary presentation

According to the data of the conducted examinations, in 318 of 393 patients, the found aneurysms were single.

Patients without any aneurysms during the primary CTA description underwent CAG.

4.2.2 Revision CTA of the BCA

All CTA examinations of the brachiocephalic arteries performed at the Research Institute – RCH No. 1 were retrospectively revised; the second review of the CTA was performed by a skilled radiologist with more than 10 years of experience.

Patients in whom the source of hemorrhage was not detected by CTA (n = 12), had CAG. According to the hospital charts, aneurysms up to 3 mm in diameter were found in 9 of 12 patients with hypertension, and the source of nTSH was not detected in three of those. The reasons for the lack of visualization of aneurysms on angiographic studies were: in one case – vasospasm (signs were noted on CTA and CAG), one aneurysm was completely thrombosed, and one patient had a miliary aneurysm (Figure 17).

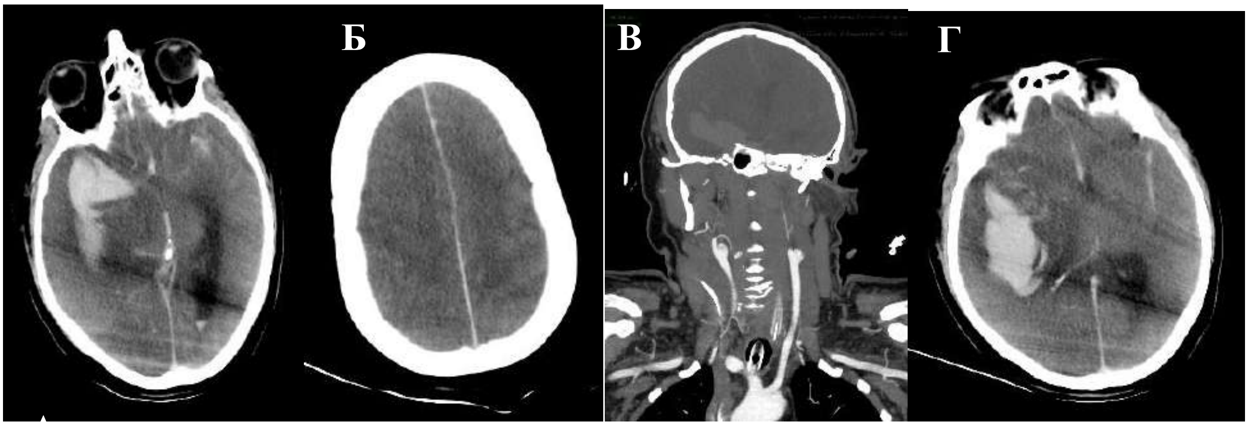


Figure 17 – A female patient, 43 years old, acute aneurysmal intracranial hemorrhage. Examination in the emergency unit A, B – native CT, C-G – CTA of the BCA. On native CT (A, B), an intracerebral hematoma in the right temporal lobe, diffuse subarachnoid hemorrhage and blood in the ventricles, cerebral edema are detected. On CTA of the BCA (B, D) with underlying cerebral edema, there is no contrast of the intracranial arteries – significant vasospasm. The patient has not been operated on, lethal outcome. According to the autopsy results: the cause of the hemorrhage is a rupture of the MCA aneurysm

4.2.3 Comparison of CTA and intraoperative data

The results obtained using CTA of the BCA were compared with intraoperative data. Thus, according to the CTA data, of 215 patients with single aneurysms, the source of nTSH was found in 203 patients during the primary presentation and in 206 patients in course of the retrospective review. The ratio of the aneurysms detected by CTA (primary presentation, retrospective review) and intraoperatively is shown in Table 13.

Table 13 – The radio of IA detected on CTA and intraoperatively

	Number of patients according to CTA BCA (primary presentation)	Number of patients according to CTA of BCA (retrospective review)	Number of patients (intraoperative CAG data + clipping)
No IA	12	9	0
Sin. IA	203	206	215

According to the obtained data, IA was most commonly observed in the anterior connective, middle cerebral and internal carotid arteries.

Single IA ruptures were also more often marked in the anterior connective arteries – in 49.4% cases (n = 157), less often – in the middle cerebral arteries (27.7%; n = 88), in the internal carotid arteries (12.3%; n = 39); in other arteries, IA ruptures were found in isolated cases (from 1 to 8). More detailed information about the frequency of aneurysm ruptures is shown in Figure 18.

ACA	MCA	ICA	BA	PCA	PA	ACA	SCA	PCA	STA	PICA
157	88	39	8	5	6	6	4	1	2	2

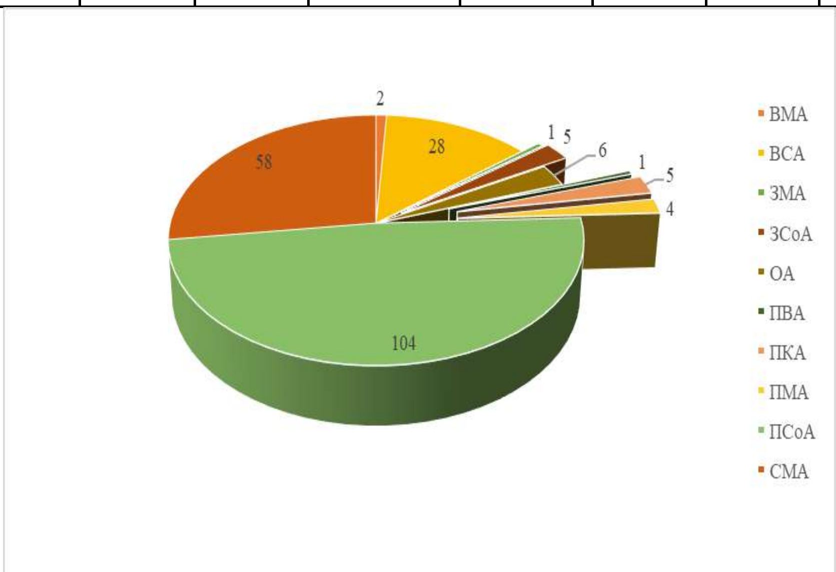


Figure 18 – Frequency of single IA ruptures

While assessing the diagnostic value of CTA BCA, the following data were observed: the sensitivity of the technique was 96.6%, the overall accuracy was 97%, the prognostic value of a positive result was 100%. The data are in Table 14.

Table 14 – Diagnostic significance of CTA of the BCA for the detection of single IA in patients during the SAH acute period comparing with intraoperative data

	Sensitivity, %	Overall accuracy, %	Predictive value of a positive test result, %
CTA (primary presentation)	94,4 CI 90–97%	94,0 CI 90–97%	100,0
CTA (retrospective review)	95,8 CI 92–98%	96,0 CI 92–98%	100,0

According to the results of the examinations, endovascular embolization of 9 single IAs and microsurgical clipping of 306 IAs were performed, one patient was not operated. A clinical case is shown in Figure 19.

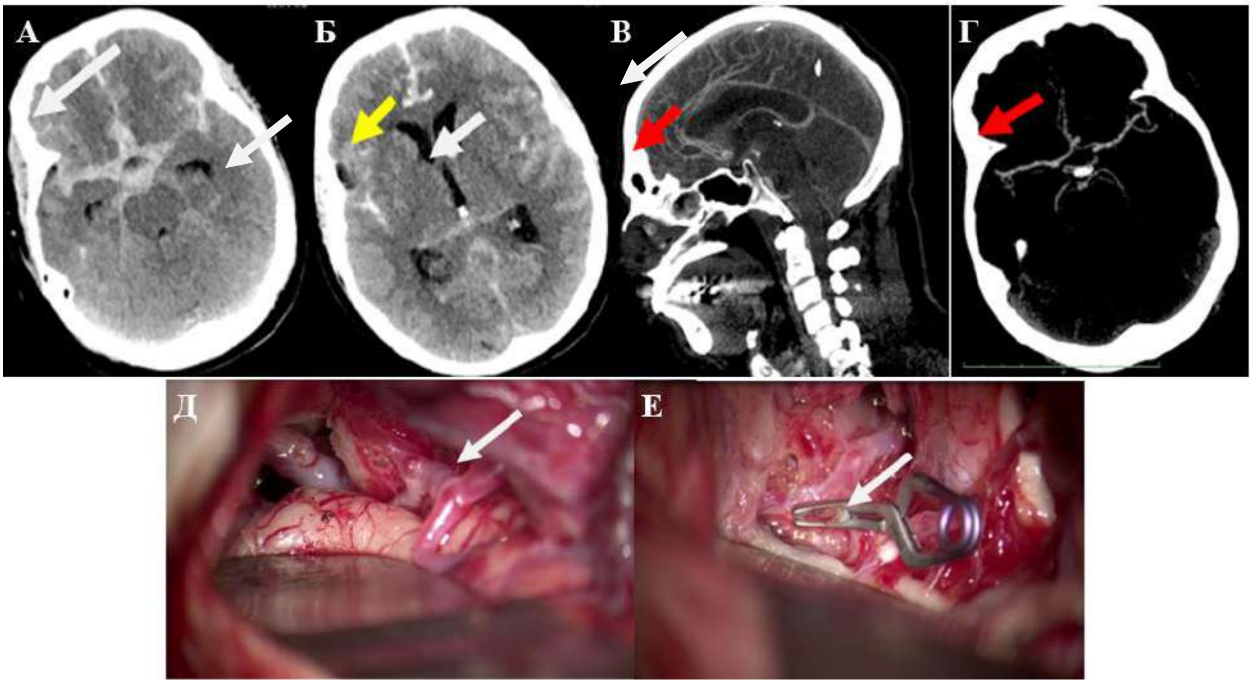


Figure 19 – Clinical case 1: a man, 41 y.o.; delivered by an ambulance team to the emergency unit with a preliminary diagnosis of nTSH
On the native CT (Figures A, B), a diffuse SAH (white arrows) associated with IVH (yellow arrow) is diagnosed. On the CTA of the BCA (Figures B, D), the IA of the anterior connective artery is seen (red arrows). Figures D, E – clipping of an anterior connective artery aneurysm (white arrows)

As a result of the treatment, 269 patients were discharged, 49 patients died. During the hospital stay repeated hemorrhages from single IA were not observed.

Conclusion

The outcomes showed that CTA is a reliable technique for diagnosing single aneurysms during the acute period of SAH. High sensitivity (95.8%) and overall accuracy (96%) make it possible to use this technique while planning further treatment. To obtain an accurate result, the study should be performed according to the protocol. In cases where, according to the CTA of the brachiocephalic artery, the source of the nTSH cannot be detected, a second viewing of the images is necessary, if the second analysis is negative, a CAG should be performed. CAG makes it possible to detect single aneurysms in sites which are difficult to be reached by non-invasive imaging, or small-size aneurysms (< 3 mm in diameter).

CHAPTER V. RADIOLOGICAL CONTROL OF MULTIPLE ANEURYSMS

Of the total number of the studied patients (n = 393), 19% (n = 75) had multiple IAs. All these patients initially underwent native CT to diagnosis the nTSH presence. Then, according to the protocol, CTA of the BCA was performed, so the cause of the SAH was found out. In the presence of multiple aneurysms, those that had signs of rupture were marked. Native CT and CTA of the BCA in nTSH acute period were performed both in the primary vascular centers of the Krasnodar Region (n = 16) and in the Research Institute – RCH No. 1 (n = 59). Repeated native scanning in a neurosurgical unit was performed only in patients with worsened condition during transportation. There were no repeated CTA of the BCA in the preoperative period.

In cases where the patient condition was severe and/or unstable, and the localization of the detected hemorrhage according to native CT corresponded to the identified source on CTA, they were operated according to CTA data (n = 42); the others (n = 33) had CAG.

In the group of patients with multiple aneurysms, the sensitivity and specificity of CTA for detecting aneurysms that were the source of SAH, comparing with CAG, were evaluated; the entire Willis circle was evaluated. The sensitivity of CTA was also determined in comparison with intraoperative data, while the part of the Willis circle where we performed the surgical intervention, was a subject to evaluation. It was not possible to evaluate the specificity of the technique in comparison with intraoperative data, since a negative result of CTA of the BCA was not a surgical indication.

Besides, the number and prevalence of IA in the arteries of the Willis circle, relationship of the number of IA with the age and sex of the patients were analyzed. The analysis of aneurysms missed on CTA was subject to a separate additional assessment. CTA of the BCA performed on the basis of RI – RCH No. 1 (n = 59) by a skilled radiologist with a 10-year experience of work were retrospectively reviewed.

Of particular interest was the comparison of IA detectability when performing CTA in the vascular centers of the region and in the neurosurgical center.

Considering the fact that the scanning area included the vessels of the neck from the aortic arch to the skull base, all of them were subjected to a mandatory analysis. Based on the obtained results, the significance of the information received about various vascular findings, their impact on patient management tactics and subsequent prognosis were evaluated. Detailed information and analysis of vascular findings are described in a separate chapter.

5.1 General characteristics of patients

According to sex and age, the patients were distributed as follows: most common there were women (n = 53) aged 41 to 83 years (average age 58 years), the age of men (n = 22) ranged from 29 to 65 years (average age 50 years). It was complicated to interview patients for collecting their anamnesis due to the severe condition at admission.

In all patients with multiple aneurysms, according to the case histories, SAH was clinically manifested in the form of headaches of varying intensity. The largest number of patients (42.7%; n = 32) were admitted to the emergency room in a state of somnolentia with moderate neurological deficit, a smaller group consisted of patients with severe headache (21.3%; n = 16); there were also patients in sopor with moderate or severe hemiparesis (18.7%; n = 14), in deep coma (14.7%; n = 11) and with mild to moderate headache (2.6%; n = 2) (Figure 20).

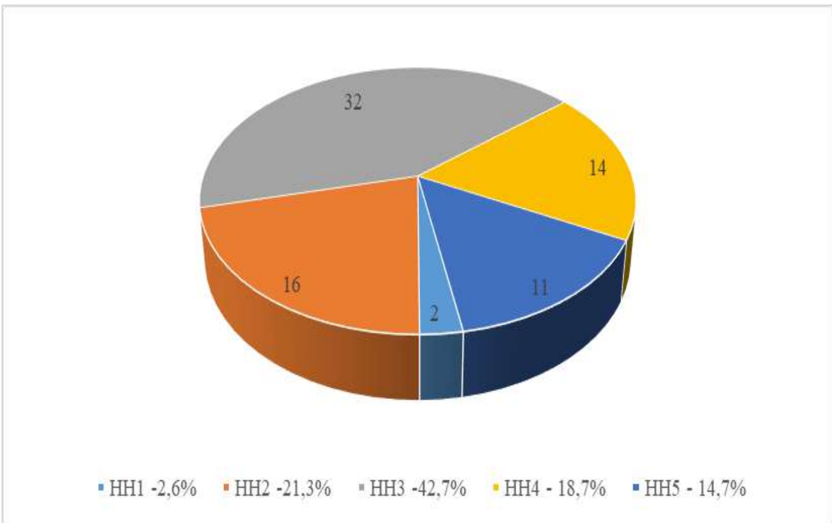


Figure 20 – Characteristics of patients in severe condition according to HH scale

Regarding the SAH severity (according to the Fisher scale), patients were distributed in a certain way: 4 degree – 39 patients (52%), 3 degree – 22 patients (29.3%), 2 degree – 12 patients (16%), 1 degree – 2 patients (2.7%) (Figure 21).

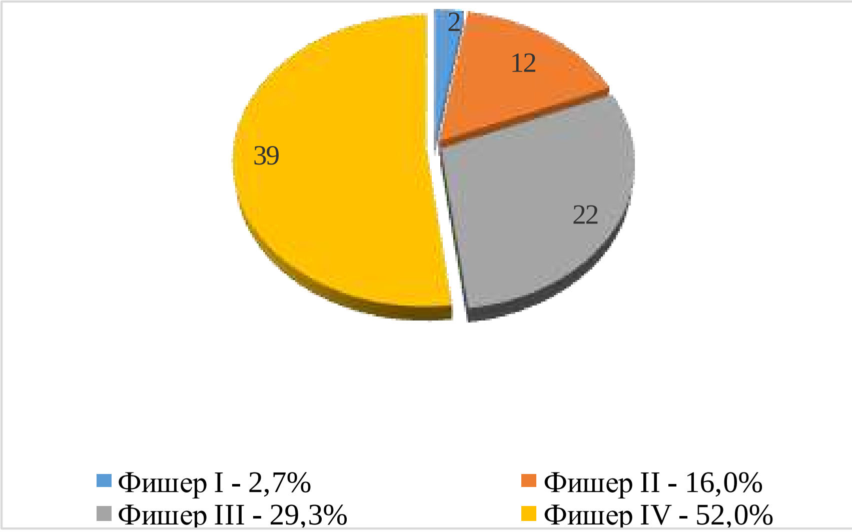


Figure 21 – Characteristics of patients according to the SAH severity regarding the Fisher scale

41% patients (n = 31) had associated IVH, 17% (n = 13) had parenchymal hemorrhage. The general characteristics of patients are in Table 15.

Table 15 – General characteristics of patients with multiple IAs

Number of patients	75
Number of IA	60
Sex: – female – male	 53 22
Age: – among women – among men	 58 (41-83) 50 (29-65)
IA dimensions (maximum diameter in m) according to CTA data	Medium – 6 mm (from 2 to 12 mm)
SAH severity according to native CT: – Fischer I – Fischer II – Fischer III – Fischer IV	 2 (2,7%) 12 (16,0%) 22 (29,3%) 39 (52,0%)

Associated IVH and parenchymal hemorrhage: – parenchymal hemorrhage only – IVH only	8 5 22
Parenchymal hemorrhage: – frontal lobes – temporal lobes – parietal lobes – occipital lobes – corpus callosum – subcortical areas	16 5 9 0 0 1 2
Distribution according to the Hunt-Hess scale: – 1 – 2 – 3 – 4 – 5	2 (2,6%) 16 (21,3%) 32 (42,7%) 14 (18,7%) 11 (14,7%)
Type of treatment: – embolization – clipping – embolization + clipping	3 (4%) 70 (93,3%) 2 (2,7%)
Outcome: – lethal – recovery	13 (17,3%) 62 (82,7%)

At admission, most patients had high blood pressure (n = 67), while 71 patients had hypertension. There was a history of nTSH in one case (a female patient, 59 years old).

5.2 Assessment of the number of aneurysms, comparison of techniques

5.2.1 Emergency assessment of CTA of the BCA – primary presentation

According to CTA of the BCA and SAG, as well as intraoperative data, a total of 169 aneurysms were detected in 75 patients.

According to the urgent CTA (primary description) we detected 114 aneurysms in the neurosurgical hospital and 25 – in the vascular centers of the region, in three patients, according to CTA data, no aneurysms were detected in the presence of nTSH. Thus, a the initial emergency description, 30 aneurysms were missed (subsequently detected intraoperatively or with CAG). Moreover, 27 of the missed aneurysms were intact, 3 had signs of rupture.

Patients who showed no aneurysms detected during the initial presentation, had CAG, following which aneurysms were detected. According to intraoperative data, one intact aneurysm described on CT was excluded in one patient.

5.2.2 CTA of the BCA revision

All CTA performed in a neurosurgical hospital (n = 59) were reviewed by a highly experienced radiologist. The quality of the conducted studies was overwhelmingly satisfactory, allowing us to evaluate both extracranial and intracranial BCA. In one case, the images were somewhat distorted by motion artifacts, in another case an aneurysm was missed due to vasospasm.

As a result of the revision according to the CTA, 129 aneurysms were detected (15 more aneurysms than at the initial presentation, including three IAs with rupture signs). Six aneurysms were not detected during the revision, of those 4 aneurysms were miliary (up to 3 mm in size), 2 aneurysms were not visualized on CTA (due to vasospasm and dynamic blurring).

All missed aneurysms were intact, and they were treated by clipping or embolization. The localization, size and methods of treatment of missed intact aneurysms are presented in Table 16.

Table 16 – Characteristics of IAs during revision

Site of missed aneurysms	Sizes of missed aneurysms, operative data (mm)	Reason of missed aneurysms	How IA was found, the method of treatment
Anterior choroid artery	2,5×4	Dynamic blurring	CAG, clipping

Middle cerebral artery	2,5×3×2	Small aneurysm	Clipping
Pericallous artery	2,5×2×3	Small aneurysm	CAG, embolization
Posterior communicating artery	2×2×2,5	Small aneurysm	CAG, clipping
Anterior communicating artery	2×3×2	Small aneurysm	Not found on CAG, detected during an open operation, clipping
Superior cerebellar artery	2×2,8×4	Vasospasm	CAG, embolization

5.2.3 CTA compared to intraoperative data

Separately, we compared the data of CTA and CAG in patients who had both methods performed in the preoperative period. As a result of the comparison, the following data were obtained: in total, CAG was performed in 35 patients, 80 aneurysms were found; according to CTA, 5 aneurysms were missed in the neurosurgical center, 3 aneurysms were excluded by CAG. All aneurysms missed during CTA and found on CAG were intact.

A comparison of the number of the found aneurysms during the urgent presentation of the CTA of the BCA CT in the Research Institute – RCH No. 1 and the subsequent revision are shown in Figure 22.

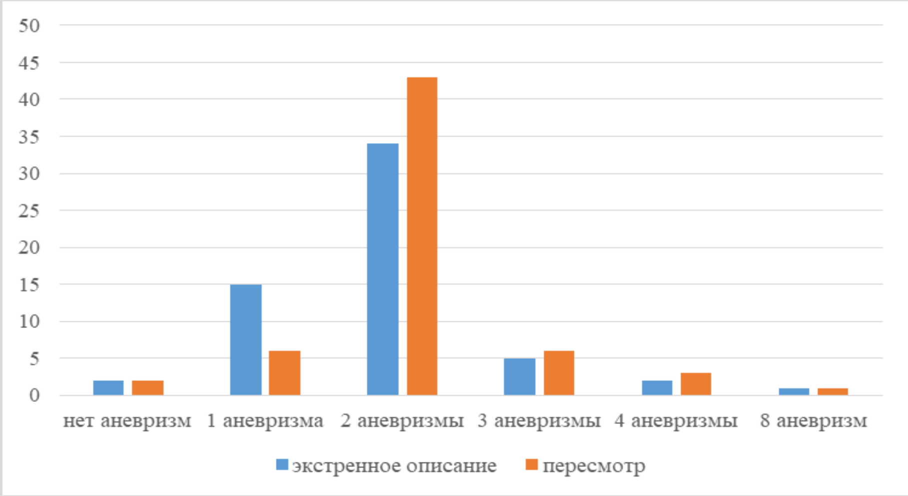


Figure 22 – Comparison of the number of aneurysms found on CTA BCA during urgent presentation and during retrospective analysis

Patients who underwent CAG (n = 33) in a neurosurgical hospital were selected to determine the sensitivity and specificity of urgent CTA of the BCA comparing to CAG. This group included patients who had initial CTA performed in district hospitals (n = 9) and in a specialized hospital (n = 24). At that, the overall sensitivity of urgent CTA in comparison with CAG was 85% and specificity – 80%. The results are presented in Table 17.

Table 17 – Diagnostic value of the urgent CTA comparing to CAG

Site of CTA	Sensitivity, %	Specificity, %	Positive predictive value, %	Negative predictive value, %
Specialized hospital	90,9 CI 80–96	66,7 CI 21–94	98,0	28,6
Vascular centers and specialized hospital	85,0 CI 75–91	80,0 CI 38–96	98,4	26,7

For determining the sensitivity of the ugent CTA compared with the operational data, we analysed information about the part of the Willis circle whrer the surgical intervention was performed. The specificity study was not carried out, since the absence of both IA and SAH was not an indication for surgical intervention. The sensitivity was evaluated according to the data of urgent CTA performed both in a specialized hospital and in the SC. The results are presented in Table 18.

Table 18 – Evaluation of the diagnostic value of emergent CTA of the BCA compared with intraoperative data (on the side of the performed operation)

Site of CTA	Sensitivity, %	Positive predictive value, %	Total accuracy, %
Specialized hospital	100,0 CI 94–100	98,3	98,0
Vascular centers and specialized hospital	94,5 CI 89–97%	98,3	93

5.3 Aneurysm localization, signs of rupture

According to the information of radialogical diagnostic methods and intraoperative data, aneurysms were divided by localization: in the internal carotid artery – 23.7% (n = 40), in the middle cerebral artery – 37.9% (n = 64), in the anterior connective artery – 20.7% (n = 35), in the main artery – 3.6% (n = 6), in the anterior cerebral artery – 4.1% (n = 7), in the posterior connective artery – 4.1% (n = 7), in the posterior cerebral artery – 1.2% (n = 2), in the superficial temporal artery – 1.2% (n = 2), in pericallous arteries – 1.2% (n = 2), in the superior hypophysial artery – 0.6% (n = 1), in the upper cerebellar artery – 1.7% (n = 3). Data are presented in Figure 23.

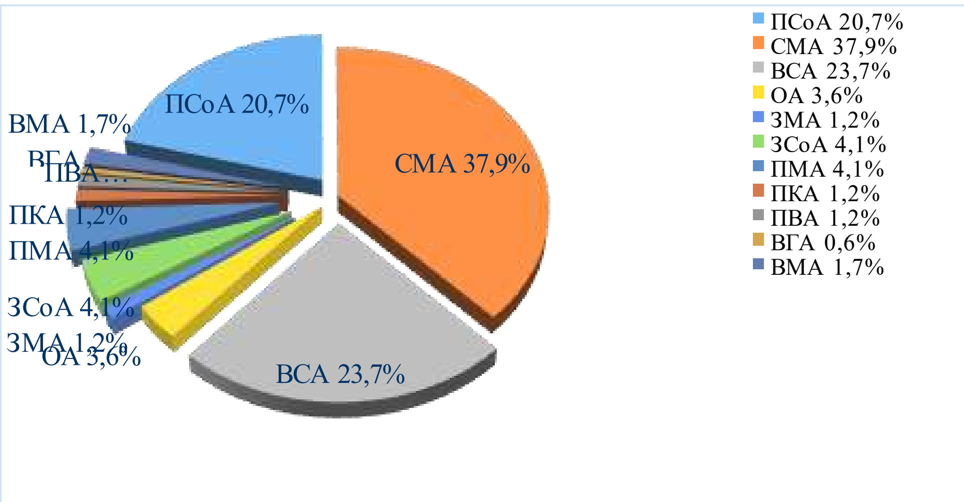


Figure 23 – Sites of multiple aneurysms regarding CTA data

5.4 Identification of unruptured aneurysms

According to CT and CT scans, the main signs of aneurysm rupture were considered to be the size of the aneurysm and the prevalence of SAC; large aneurysms were most often ruptured (n = 46), in two cases large size was combined with irregular shape and uneven contours, in seven cases the maximum size of the aneurysm was combined with widespread SAH.

In 19 cases, the leading sign of an aneurysm rupture was the prevalence of SAH: of those, one patient had vasospasm of the main artery, one of the patients had a ruptured aneurysm that was not the largest of the available ones, but of irregular shape with uneven contours.

In one case, 2 aneurysms of the same size were located on the same artery (left middle cerebral artery) with a typical distribution of blood in the subarachnoid space, so it was not possible to determine a ruptured aneurysm according to CT data. However, this had no impact on the choice of tactics and approach during surgery.

Blood in the subarachnoid space was always detected on the native CT scan of the head; blood spreading corresponded to the sites of aneurysms.

Thus, when a ruptured aneurysm was localized in the main artery (n = 4), blood was distributed into the cisterns of the brain base (n = 4), interhemispherically (n = 2), according to the tentorium of cerebellum (n = 3), in one case, blood was determined in the cerebrospinal space of the temporal lobe. In 3 cases, the blood was in the lateral ventricles, in 3 cases - in the fourth ventricle. Parenchymal hemorrhages during the rupture of the main artery aneurysms were not observed.

With ruptures of aneurysms located in the internal carotid artery (n = 14), blood was most often observed in the cisterns of the base (n = 12), IVH (n = 6) was most often found in the cavity of the lateral ventricles (n = 4), in the third ventricle (n = 3), less common in the fourth ventricle (n = 2). In all cases with rupture of the internal carotid artery aneurysm, a diffuse type of SAH was observed, in two cases there was associated parenchymal hemorrhage in the temporal lobes.

In case of ruptures of the posterior connective artery aneurysm (n = 2), blood was detected in the basal cisterns, in the Sylvian fissures (on the side of the rupture), in one case the blood spread intermispherically to the tentorium of cerebellum.

In cases of ruptures of the middle cerebral artery aneurysms (n = 25), 7 cases with associated IVH were observed (both in one ventricle and in several): 5 cases with IVH – in the fourth ventricle, 3 – in the third ventricle and 6 – in the lateral ventricles. In five cases, parenchymal hemorrhages occurred in the temporal lobes (on the side of the aneurysm rupture). In the subarachnoid space, blood was distributed extentionally on the side of the lesion (Sylvian fissure, cerebrospinal fluid spaces of the hemisphere), in half of the cases (n = 13) – interhemispherically and along the tentorium of the cerebellum.

Aneurysmal ruptures in the anterior connective artery (n = 23) in five cases resulted in associated parenchymal hemorrhage (4 cases – in the frontal lobes, 1 case – in the corpus callosum, 2 cases – in the temporal lobes, 1 case – in the subcortical region). In 14 cases, IVH was observed (11 cases – in the lateral ventricles, 8 – in the third and fourth ventricles). The type of nTSH was diffuse in all cases.

When we observed aneurysmal ruptures in the anterior cerebral artery (n = 2), blood was determined in the basal cisterns, interhemispherically, in the Sylvian fissure (on the side of the rupture), in one case there was associated IVH (in the lateral and fourth ventricles).

Ruptures of pericallous artery aneurysms (n = 2) were accompanied in one case by associated parenchymal intraventricular hemorrhage (frontal lobe and lateral ventricles). In both cases, the blood spread into the basal cisterns, through the cerebrospinal liquid spaces of the hemispheres, into the Sylvian fissure and along the tentorium.

According to the results of the study, there were 70 microsurgical interventions performed with aneurysm clipping, 3 embolizations, one clipping with embolization, one patient had an aneurysm embolization with further clipping. CT-CTA data on the localization of ruptured aneurysms completely coincided with intraoperative data.

The most frequent ruptures were observed in the middle cerebral artery (n = 25) and the anterior connective artery (n = 23), followed by the internal carotid arteries (n =

14). Futher details regarding the frequency of ruptured and unruptured aneurysm occurrence is presented in Table 19.

Table 19 – Localization of ruptured and unruptured multiple aneurysms of the intracranial arteries

Site	Ruptured aneurysms	Unruptured aneurysms	Total
ACA	23	12	35
MCA	25	39	64
ICA	14	26	40
MA	4	2	6
Site	Ruptured aneurysms	Unruptured aneurysms	Total
PCA	1	1	2
PCA	2	5	7
ACA	3	4	7
PCA	2	0	2
SHA	1	0	1
SCA	0	3	3

Clinical case

A man, 57 years old; associated with an increase in blood pressure to 150/100 mm Hg, he felt an unbearably severe headache, was refered to the emergency room of the Research Institute – RCH No. 1. The diagnosis upon admission is nTSH. When performing native CT, blood was found in the subarachnoid space, in the main cisterns, in the third and lateral ventricles (Figure 24A).

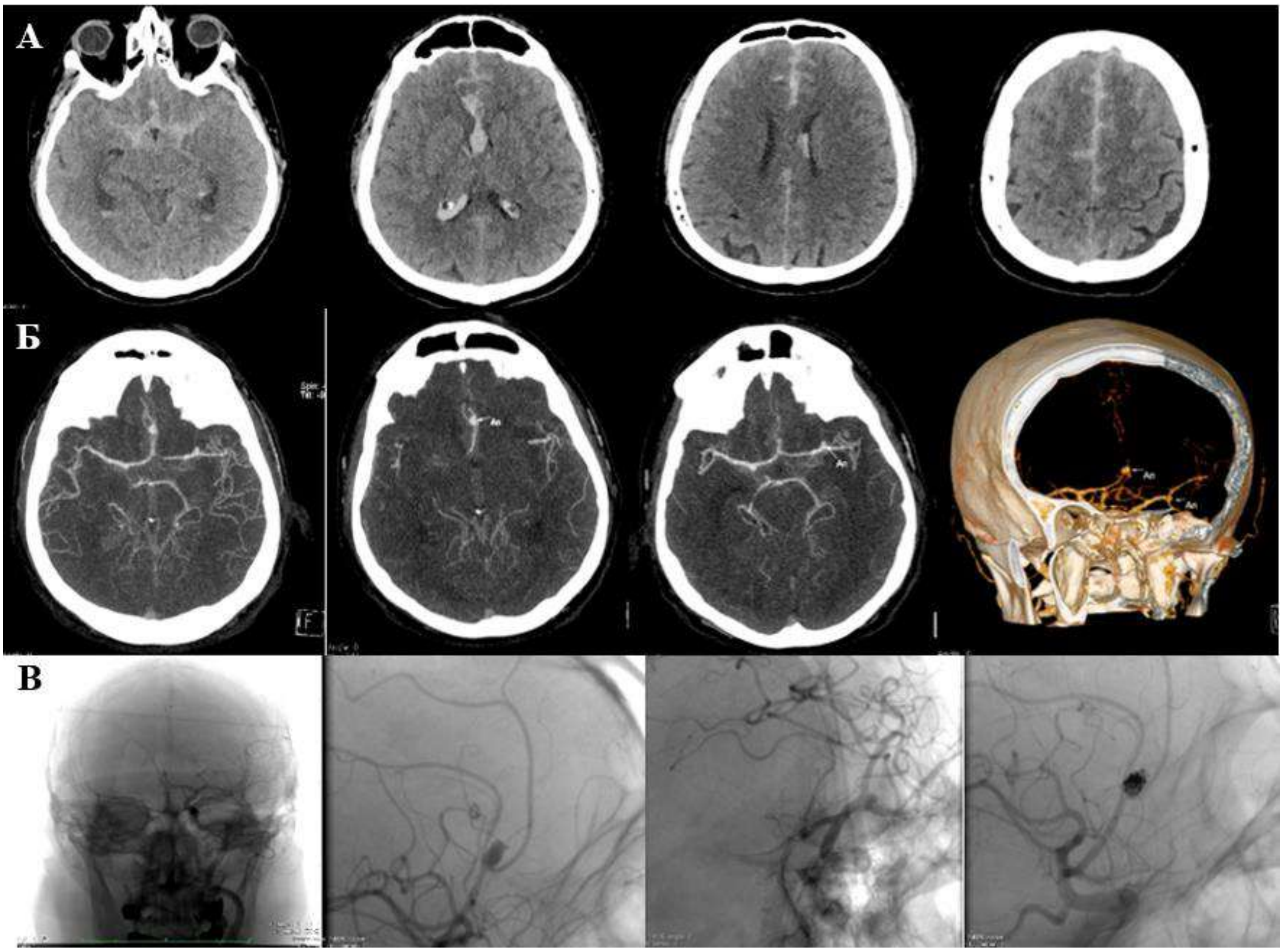


Figure 24 – Patient D., 57 years old. The diagnosis is nTSH. A – native CT: blood is detected in the subarachnoid space, in the main cisterns and in ventricles. B – CTA of the BCA: aneurysms of the pericallous artery (5.5 mm in size) and the left middle cerebral artery (3 mm in size) are determined. B – CAG: aneurysms of the pericallous artery (on the left and in the center), branches of the left middle cerebral artery (right); condition after embolization of the large pericallous artery aneurysm

While performing the CTA of the BCA, aneurysms of the pericallous artery (with a maximum diameter of 3×5.5×2 mm) and the left middle cerebral artery (with a diameter of 3 mm) were determined (Figure 24B). The irregular shape of the aneurysm and the almost symmetrical distribution of blood in the main cisterns, interhemispherically and in the fissures of the frontal lobes made it possible to indicate a rupture of the pericalous artery aneurysm.

The patient's condition was stable, which allowed him to be transported to the X-ray surgery department for CAG, and 3 aneurysms were detected: an aneurysm 3×6×3 mm in the pericallous artery and a miliary aneurysm 2 mm in diameter, and the last one (3 mm) was in the middle cerebral artery. A large aneurysm of the pericallous artery was embolized (Figure 24 B). The patient was discharged in a satisfactory condition.

Clinical case

Patient G., 72 years old, suffers from hypertension. Due to increased blood pressure to 165/100 mm Hg, she felt a severe headache and lost consciousness. Accompanied by relatives, she was taken by ambulance to the emergency room in the Research Institute – RCH No. 1 with a diagnosis of nTSH. When performing native CT, the presence of nTSH was confirmed. The greatest accumulation of blood was observed in the left Sylvian fissure, the blood also spread interhemispherically, along the tentorium of cerebellum and cisterns of the base. There was also associated IVH (third, fourth and lateral ventricles) (Figure 25A, B). When performing CTA of the BCA, 8 intracranial aneurysms were detected in a patient: in both internal carotid arteries, in the left posterior cerebral artery, in the main artery (Figure 25B, D).

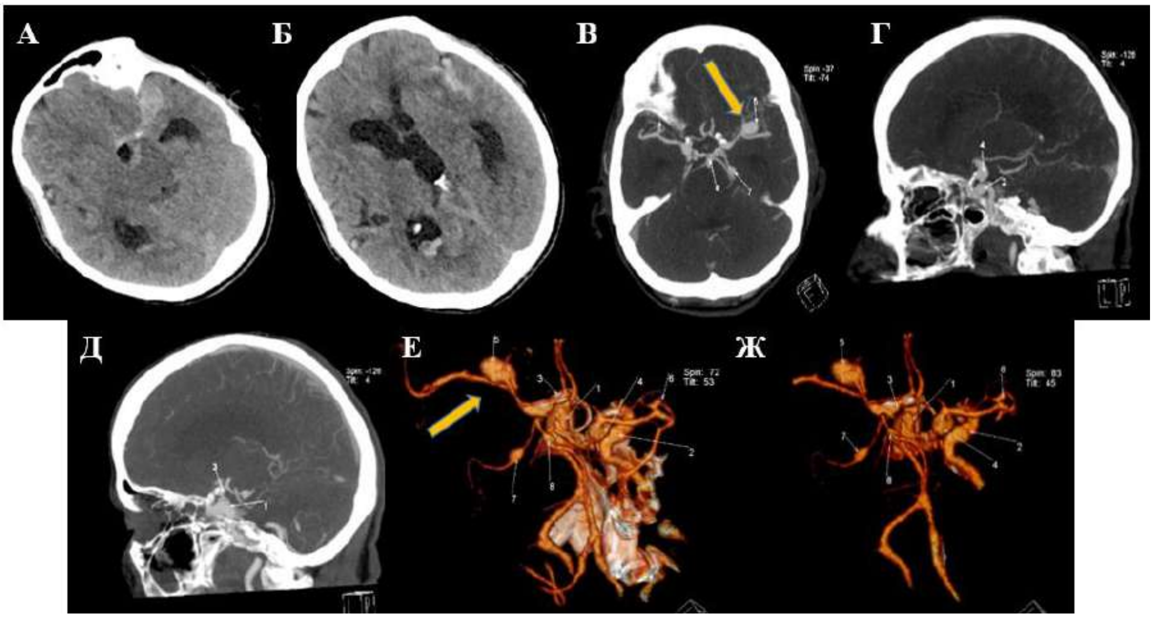


Figure 25 – a female patient, 72 years old, diagnosed with nTSH. The maximum accumulation of blood according to native CT (A, B) is determined in the left Sylvian

fissure. According to the CTA of the BCA (B-D), multiple aneurysms are determined (n = 8). The largest aneurysm (size 12×10×9 mm) – in the left MCA (yellow arrow) – was the source of nTSH and this was confirmed intraoperatively (E, F)

According to the maximum distribution of blood and the largest size of the aneurysm (12×10×9 mm), the probable source of SAH was a rupture of the left internal carotid artery aneurysm (Figure 26B). Intraoperatively, the source was confirmed and the aneurysm was clipped (Figure 26E-G).

After surgical treatment, the patient was discharged from a specialized hospital in a satisfactory condition.

Conclusion

Thus, the CTA of the BCA, compared with intraoperative data, showed high sensitivity and overall accuracy (100 and 98%, respectively) in detecting multiple aneurysms in the acute period of nTSH. Therefore, according to the native CT, there is nTSH, and the CTA results correspond to the localization of the hemorrhage, then there is enough evidence to consider the possibility of direct surgical intervention without obtaining preoperative CAG. This is especially important in cases with patients in a serious and unstable condition. In patients with multiple aneurysms, CAG application is recommended in controversial and complex cases, provided that IA is stable.

CHAPTER VI. THE SIGNIFICANCE OF CONCOMITANT VASCULAR PATHOLOGY IN THE ACUTE PERIOD OF SAH

6.1 General characteristics of patients with nSAH and concomitant extracranial vascular pathology

According to the concomitant extracranial vascular pathology nature detected by CT, the patients were divided into 5 groups:

– Group 1: atherosclerotic lesion of the carotid arteries;

– Group 2: atherosclerotic lesion of vertebral arteries;

– Group 3: pathological tortuosity of the carotid arteries;

– Group 4: pathological tortuosity of the vertebral arteries;

– Group 5: hypoplasia of the vertebral arteries.

In group 1, 34.5% of patients (n = 95) showed signs of the internal carotid arteries (ICA) atherosclerosis in the form of calcified, mixed and soft plaques, causing their significant and insignificant stenoses.

Atherosclerosis of extracranial segments of ICA was more often observed in women (n = 63) aged 31 to 83 years (mean age 62 years), in men (n = 32) atherosclerotic plaques were more often detected at the age of 33-85 years (average age 55 years).

In the 2 group with vertebral artery stenosis (from 70 to 90%), according to CT, 3 patients (1%) were identified.

In group 3, pathological tortuosity of ICA was found in 74 patients (26.9% of the total number of IA patients).

In group 4, pathological tortuosity of the vertebral arteries was observed in 38 (13.8%) patients.

In group 5, hypoplasia of the vertebral arteries was detected in 59 patients (21.5%).

6.2 Impact of concomitant extracranial vascular pathology on the management tactics in patients during the acute period of nSAH

In 22 patients, ICA stenoses (from 50 to 70%) were detected in combination with IA (8% of the total number of patients included in the study), 4 of them additionally had CAG. Aneurysm clipping was performed in 21 patients from this subgroup, one patient was not operated according to the severity of the condition. An example of ICA stenosis detected in this group according to CT data is shown in Figure 26.

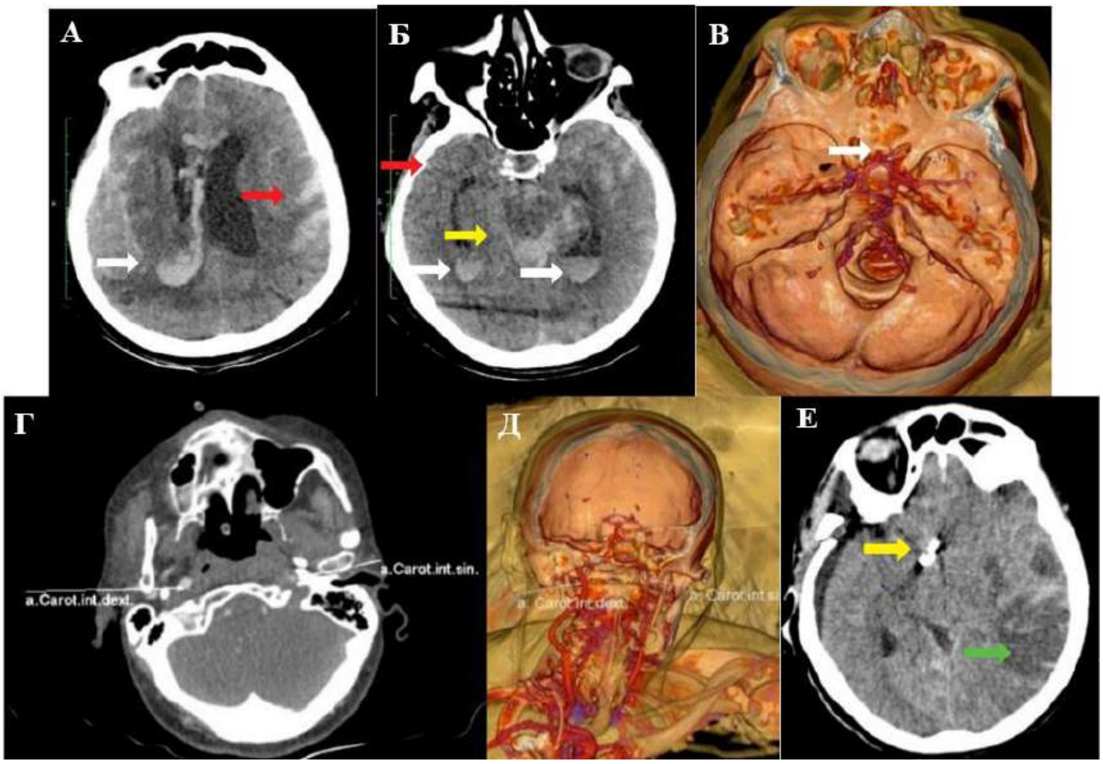


Figure 26 – Patient with nTSH, 67 years old. A, B – native CT. There is blood in the lateral ventricles of the brain (white arrows), in the cisterns (yellow arrow), in the fissures of both hemispheres (red arrows). B-D – CTA of ICA, IA of the anterior connective artery (white arrow), occlusion of the left ICA.
E – postoperative native CT, clipped aneurysm of the anterior connective artery (yellow arrow), signs of cerebral ischemia in the left carotid basin (green arrow)

ICA stenoses from 71 to 90% were found in 6 patients (2.2%) from group 1. Emergency embolization was performed in one of them in order to treat IA (the degree of ICA stenosis was 80%), the rest (n = 5) underwent microsurgical clipping. Two patients with ICA stenosis up to 90% died in the early postoperative period. One patient (0.4%) had occlusion of one of the ICA in combination with IA, he underwent aneurysm clipping. The early postoperative period was complicated by vasospasm and ischemia, but the patient was discharged in a stable condition.

In the 2 group with vertebral artery stenosis (from 70 to 90%), according to CTA, 3 patients (1%) were identified. The implementation of the CAG to clarify the CTA data was needed in one case. All of these patients had clipped IA. One patient with 90% vertebral artery stenosis died in the early postoperative period on the background of vasospasm and ischemia.

In Group 3, pathological tortuosity of BCA was found in 74 patients (26.9% of the total number of patients with IA) (Figure 27). CAG after the ACT was required in 17 patients. Endovascular treatment of IA was performed in 6 patients, microsurgical clipping was performed in 68 patients. All patients from this group following endovascular treatment were discharged in stable condition with improvement.

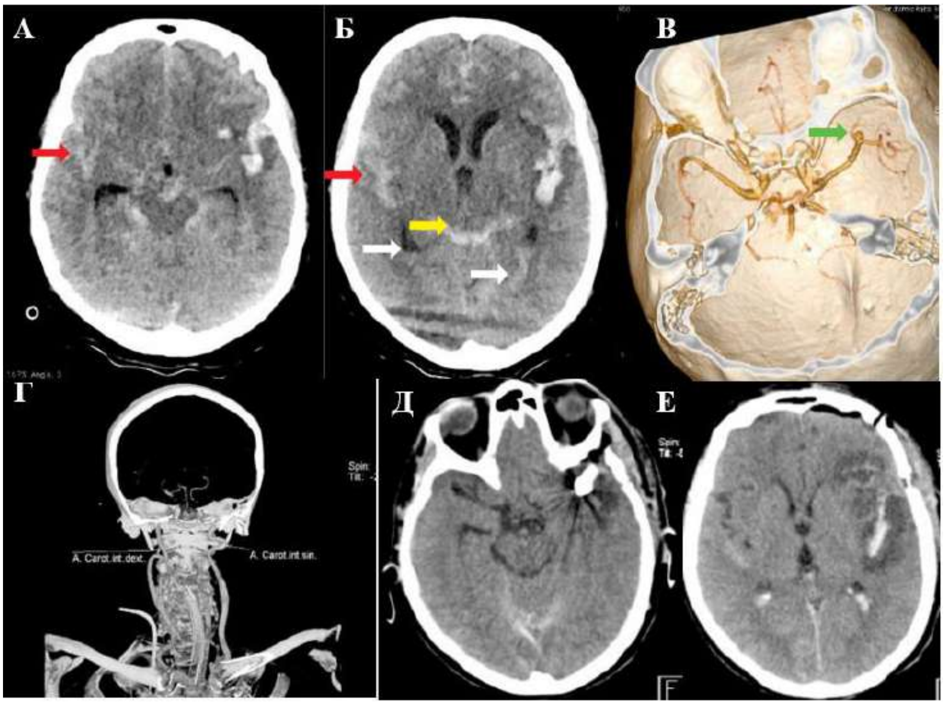


Figure 27 – Patient with nTSH, 59 years old. A, B: native CT, blood is detected in the lateral ventricles of the brain (white arrows), in cisterns (yellow arrow), in the fissures of both hemispheres (red arrows). C, D: CTA of BCA, aneurysm of the left medial cerebral artery (green arrow), ALL vascular loops (white arrows). D, E: native CT, condition after clipping of an aneurysm of the left middle cerebral artery

In Group 4, pathological tortuosity of the vertebral arteries was observed in 38 (13.8%) patients (Figure 28). In addition to CTA, CAG was performed in 12 patients. Endovascular IA treatment was performed in one patient, clipping was performed in 37 cases. 3 patients from this group died in the early postoperative period. The death of the deceased occurred against the background of vasospasm and secondary ischemia.

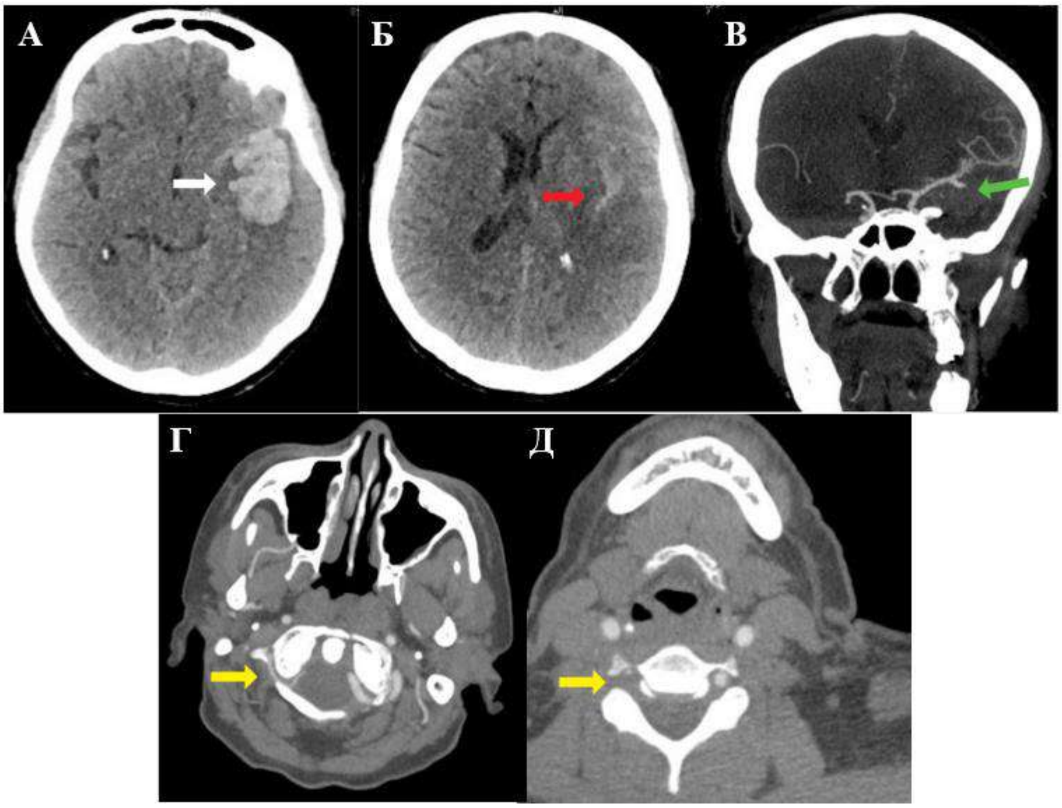


Figure 28 – A patient with nTSH, 63 years old. A-B: native CT, blood inside the parenchyma of the left temporal lobe (white arrow), in the furrows of the left hemisphere (red arrow). V-D: CTA of BCA, aneurysm of the left medial cerebral artery (green arrow), expressed hypoplasia of the right vertebral artery (yellow arrows)

In group 5, hypoplasia of the vertebral arteries was detected in 59 patients (21.5%). CAG was performed in 12 patients. Endovascular treatment of IA was performed in 2 patients, clipping was performed in 57 patients. In the early postoperative period, 6 patients died. In all the deceased patients, death occurred against the background of vasospasm, ischemia and cerebral edema.

Clinical case

A 49–year-old woman admitted to the reception department of the Research Institute - RCH No. 1, anamnesis collection was impossible due to the severity of the condition. According to the emergency medical service, she lost consciousness in a public place. The EMS team took this patient to the intensive care unit of the emergency department with the diagnosis: condition after syncope. Brain injury? Coma 1.

The state of admission (04/26/2020): the situation is forced. The skin is clean, pale. Correct physique, normosthenic. Breathing – ventilator, through ETT, no wheezing. BDD – 16/min. Hemodynamics is stable. Blood pressure 124/72 mm Hg. Heart rate 75/1 min. Pulse 75 / 1 min. Neurological status: level of consciousness – medical sedation, outside med. sedation – sopor. Corneal and brow reflexes are reduced on both sides, symmetrical. The eyeballs are set along the midline. Muscle strength, sensitivity, coordination sphere cannot be reliably assessed by the severity of the condition. Outside of sedation, increased convulsive activity in the form of generalized tonic-clonic seizures.

A CT of the brain and a CTA of BCA were performed on an emergency basis in the emergency room (Figure 29 A, B, C). According to CT (04/26/20): rupture of ACA aneurysm, massive basal subarachnoid-ventricular hemorrhage Fischer IV, Graeb 5. Stenosis/hypoplasia/spasm of vertebral arteries.

According to clinical and radiological data, the diagnosis was: a saccular aneurysm of the anterior connective artery (rupt). Massive basal subarachnoid-ventricular hemorrhage, Hunt-Hess V (IV+), Fischer IV. Graeb 5.

Surgical treatment (04/26/2020): pterionic craniotomy on the right, ventriculocysternostomy, clipping of a ruptured ACA aneurysm.

The course of the postoperative period: initially relatively stable. She was extubated, hemodynamically stable, neurologically – without paresis. On the 6th day after the hemorrhage – a sharp deterioration, coma, transferred to the ICU, intubated. According to the instrumental examination (05/02/2020): decompensated cerebral vasospasm with secondary ischemia of the brain stem. In the future, the condition remained extremely severe, with negative dynamics. Cerebral and cardiovascular insufficiency increased (Figure 29 B, D).

In the postoperative period, control CT of the brain was performed: CT control g/m 04/28/2020: condition after pterionic craniotomy on the right, ventriculocysternostomy, clipping of an aneurysm of the anterior connective artery. Pneumocephalus. Subarachnoid-ventricular hemorrhage. CT-picture of Varoliev bridge ischemia, midbrain.

CT control g/m 03.05.20: condition after pterionic craniotomy on the right, ventriculocysternostomy, clipping of an aneurysm of the anterior connective artery. Subarachnoid-ventricular haemorrhage – without significant dynamics. Stable CT picture of Varoliev bridge ischemia, midbrain (ischemia). Cerebral edema.

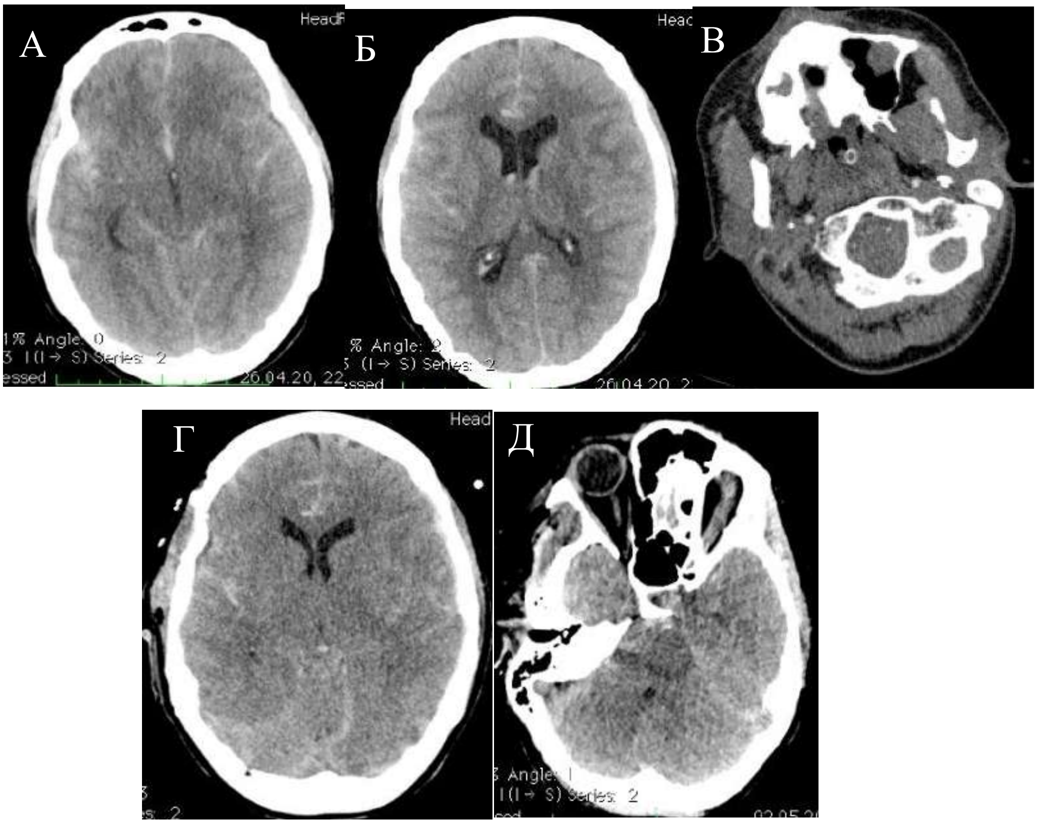


Figure 29 – Patient, 49 years old, acute nTSH. A, B, C – examination in the emergency department (A, B – native CT, B – CTA of BCA). D, D – native CT 6 days after admission. On native CT at admission (A, B), acute diffuse nTSH is determined. A weak point contrast of both vertebral arteries is noted on the CTA of ICA (B). On native CT (G, D), signs of cerebral edema, trunk secondary ischemia (against the background of vasospasm confirmed by ultrasound TG) are seen

Despite the ongoing therapeutic measures, the patient condition worsened, 05/06/2020: the patient passed away.

Cause of death: cerebral insufficiency, progressive severe widespread expressed cerebral vasospasm with extensive secondary ischemic brain damage (Figure 29G, D).

6.3 Patients with nSAH and concomitant intracranial vascular pathology

In clinical practice, there are cases with combination of different types of intracranial vascular pathology, and this comorbidity plays an important role in patient management tactics and risk assessment. In this study, two patients with nTSH and concomitant intracranial pathology were studied, and they were demonstrated in the form of clinical cases.

6.3.1 Clinical case 1

A woman, 51 years old, with suspected acute cerebrovascular accident. From the anamnesis: found unconscious on the street, taken by an ambulance team to the Research Institute – RCH No. 1.

The patient had no complains because of the severity of the condition. Objective examination in the emergency room: the general condition of the patient is severe, placed on a gurney. The patient has normosthenic build, average height. Skin and visible mucous membranes of physiological coloration. Support of external respiration was carried out. Blood pressure 140/80 mmHg, heart rate 85 beats per minute.

Neurological status: drug sedation. The productive contact is not available. Eye slits D = S, pupils D = S, narrow, photoreactions preserved. The sight is fixed straight. The face is externally symmetrical. Deep limb reflexes with no convincing difference, diffuse muscle hypotension (drug-induced myoplegia). Pathological foot reflexes and meningeal signs were not detected.

When the patient was taken to the emergency room, a native CT scan of the brain was performed, where blood was determined in the subarachnoid space of both hemispheres, parenchymal hemorrhage in the right frontal-temporal-subcortical region with a volume about 80 ml. Blood was also detected in the lateral, third and fourth ventricles (Figure 30).

Figure 30 – Brain CT without contrast, axial plane. Subarachnoid-parenchymal-ventricular hemorrhage. A – hemorrhage in the right frontal-temporal-subcortical region (long arrow), displacement of median structures by 10 mm from right to left (short arrow). B – blood in the interhemispheric sulcus (long arrow) and left ventricle (short arrow). B – blood in the subarachnoid space (short arrow)

Further, in the conditions of emergency rest, CTA of BCA was performed on a two-tube 256-slice Siemens Definition Flash tomograph. The thickness of the slice was 0.75 mm, the pitch was 0.2 mm. Images were obtained using high and low energy. The contrast agent was injected with an Ulrich Medical bolus syringe at a rate of 4 ml/s. A nonionic contrast agent with an iodine concentration of 350 mg/ml with a volume of 50 ml was used in this study. The area of study extended from the level of the aortic arch to the soft tissues of the cranial vault. Post-processing of the received images was performed on the VIA Multimodality workstation.

According to CTA data, the patient had two IA: anterior connective artery (12×19 mm), ophthalmic segment of the left internal carotid artery (4×4 mm) (Figure 31).

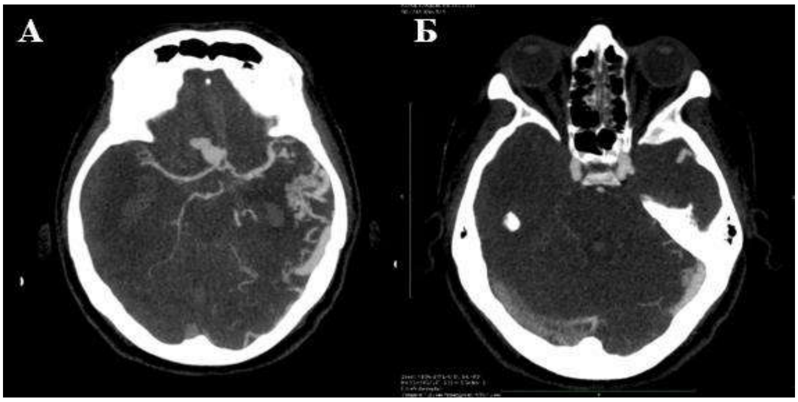


Figure 31 – CTA of BCA, axial plane. Multiple arterial aneurysms of the arteries of the Willis circle. A – anterior connective artery, B – ophthalmic segment of the left internal carotid artery

An aneurysm of the anterior connective artery closely adhered to parenchymal hemorrhage, had uneven contours – with protrusion in the bottom aspect. In the left temporal lobe, a conglomerate of pathological vessels (arteriovenous malformation) measuring 41×33 mm was observed with afferents from the left middle cerebral artery and efferents into the transverse sinus on the left (Figure 32). In addition, atherosclerotic changes of the carotid arteries were determined without hemodynamically significant stenoses.

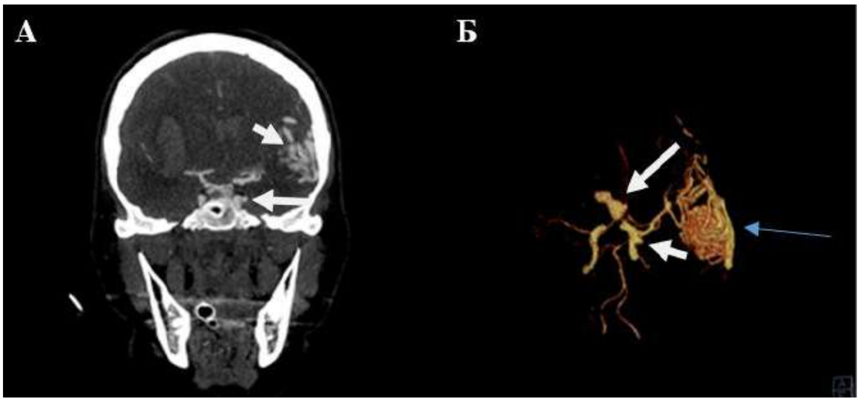


Figure 32 – CTA BCA, coronary plane (A), three–dimensional reconstruction of cerebral arteries (B). A - aneurysm of the ophthalmic segment of the left internal carotid artery (long arrow), arteriovenous malformation of the left temporal lobe (short arrow). B – the anterior connective artery aneurysm (long arrow), aneurysm of the ophthalmic segment of the left internal carotid artery (short arrow), arteriovenous malformation of the left temporal lobe (blue arrow)

The data obtained by CT and CTA allowed to establish the diagnosis: multiple cerebral aneurysms. Aneurysmal rupture, the anterior connective artery. Subarachnoid-parenchymal-ventricular hemorrhage with the formation of an acute intracerebral hematoma with a volume of about 80 ml. Fisher IV. Claassen IV. Graeb 10. Intact aneurysm of the ophthalmic segment of the left internal carotid artery. Arteriovenous malformation of the left temporal lobe.

The patient underwent emergency surgery. During the open operation, the fact of rupture of an anterior connective artery aneurysm was confirmed. The postoperative view is shown in Figure 33.

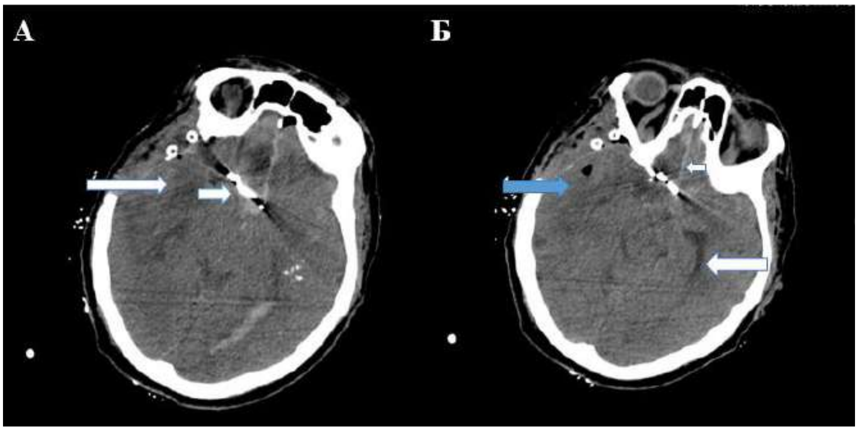


Figure 33 – CT of the brain without contrast, axial plane; the first postoperative day. A – clipped aneurysm of the anterior connective artery (short arrow), postoperative changes at the site of a removed intracerebral hematoma (long arrow). B – blood in the interhemispheric sulcus (short arrow) and lateral ventricle (long arrow), postoperative changes at the site of a removed intracerebral hematoma (blue arrow)

In 30% patients admitted to the emergency department with acute nTSH, multiple IA could be diagnosed. In the case of a combination of AVM and aneurysms, malformation is the source of bleeding in 93% cases, and an aneurysm is seen only in the remaining 7% [19].

Finding the source of bleeding is of paramount importance for providing timely assistance and determining treatment methods. In order to avoid unnecessary trepanations and repeated SAH, it is necessary to use modern and most informative neuroimaging techniques. Native CT is the initial method of research due to its simplicity and accessibility. The distribution of blood enables to suggest the aneurysm localization, however, attempts to determine the exact anatomical location of the suspected aneurysm, based only on the prevalence of intracranial hemorrhage by native CT, have a certain degree of error.

The presence of an intracerebral hematoma in one of the frontal lobes indicates a rupture of an anterior connective artery aneurysm, an anterior cerebral artery aneurysm, less often an aneurysm of the ophthalmic segment of the internal carotid artery with the upper direction of the dome. The presence of an intracerebral hematoma in the corpus callosum indicates a rupture of the aneurysm of the anterior connective or pericallous arteries, in the temporal lobe – a rupture of the aneurysm of the internal carotid or middle cerebral arteries. The presence of blood in the anterior horns of the lateral ventricles indicates a possible rupture of the aneurysm of the anterior connective artery, in the inferior horn of the lateral ventricle – a rupture of the aneurysm of the internal carotid or middle cerebral arteries; blood in the third ventricle indicates a possible rupture of the aneurysm of the internal carotid artery or the parting of the main artery (in the first case, the blood breakthrough occurs through the terminal plate, in the second second – through the bottom of the third ventricle).

To find the source of bleeding, it is necessary to perform an angiographic examination. More recently, in the examination of patients with nTSH, the main diagnostic approach was to perform native CT, and in case of a positive result, an aneurysm was searched using CAG. This algorithm of actions has gradually changed: CTA is used to detect or exclude IA, and CAG is used in extremely complicated cases [18, 93].

For patients with a diagnosed aneurysm, including those with concomitant vascular pathology, CT has a number of advantages over CAG. Its ability to identify the neck of an aneurysm can be useful when choosing treatment (surgical or endovascular). With the aid of 3D CT angiography, the aneurysm can be viewed in any projection, while the rotational CAG is limited to two planes. In addition, CT shows the thrombosed part of the aneurysm, calcifications on the wall and an adjacent clot that may make it difficult to install the clamp. Finally, establishing the relationship between the bone structures and the aneurysm enables to determine whether the aneurysm is intra- or extradural at the level of the cavernous sinus. This process requires consistence of the scanning with a dense contrast of the arterial bed, with the absence of venous blood in the cavernous sinus. If the scanning start time is chosen correctly, paraophthalmic and cavernous sinus aneurysms can also be visualized using CT angiography.

No clinical method can indicate with 100% accuracy in which of the aneurysms the bleeding occurred. The most probable risk of aneurysm rupture is noted when the following morphological parameters are detected: large size, irregular shape and/or the presence of diverticula, narrow aneurysmal neck, the ratio of the maximum size of the aneurysm to the diameter of the supporting artery is more than 2.05; the ratio of the height of the aneurysm to the diameter of the neck is more than 1.6 [148]. With CT, it is possible to determine the extravasation of the contrast agent, which indicates rupture of the detected aneurysms. Clinical signs are usually useless, although paralysis of the third nerve or unilateral retroorbital pain, for example, may indicate a rupture of the aneurysm of the orifice of the posterior connective artery. Delimited accumulations of subarachnoid blood may indicate an affected region [30].

The algorithm for detecting a ruptured IA should have been as follows: determine the site of hemorrhagic impregnation on CT scans, find masses or vasospasm on an angiogram, estimate the size and shape (larger aneurysms are more likely to bleed; if they are the same size, you need to look for violations of the contour of the sac or daughter loculus). CT should be compared with the native CT of the brain, compared with the blood accumulation in the subarachnoid space. If the native CT gives a positive result for the presence of nTSH, and the CT results correspond to the localization of the hemorrhage, there is enough evidence to consider the possibility of direct surgical intervention without obtaining preoperative CAG. In difficult cases, it is possible to use CAG, which is used to search for changes in aneurysms and, finally, an aneurysm with the highest probability of rupture is selected [30].

In the presented clinical case, the cause of hemorrhage was the largest of the two Willis circle aneurysms. To determine the localization of a ruptured aneurysm of the anterior connective artery using native CT, the maximum accumulation of blood during a contrast-free study (massive parenchymal hemorrhage in the right frontal-temporal-subcortical region) assisted. During the CTA, the features of the aneurysm shape of the anterior connective artery were revealed. Due to the severity of the condition and sufficient data for intervention, preoperative CAG was not performed. The diagnosis was confirmed intraoperatively. The first stage was clipping of the ruptured aneurysm.

6.3.2 Clinical case 2

Patient, 57 years old, had MRI of the brain due to a prolonged headache. According to the results, a large aneurysm of the left middle cerebral artery was revealed (Figure 34). After performing the study, the patient had a headache with a subsequent loss of consciousness. An ambulance team took her to one of the city hospitals in Krasnodar, where a massive subarachnoid hemorrhage with the formation of a peripheral-type hematoma of the left temporal lobe was verified by CT of the brain (Figure 35). For vital indications, she was transferred to the Research Institute – RCH No. 1 for surgical treatment.

Figure 34 – MRI of the brain without contrast, T2-weighted image mode, axial plane. An aneurysm (arrow) with an inhomogeneous MR signal is visualized in the projection of the left Sylvian fissure. There are no signs of hemorrhage

Figure 35 – CT scan of the brain without contrast, axial plane. Blood is visualized in the subarachnoid spaces, as well as a hematoma of the left Sylvian fissure, against which a large aneurysm of the left middle cerebral artery is noted (arrow)

Objective examination in the conditions of the admission department: the patient does not complain due to the presence of speech disorders. The general condition is severe, arterial hypertension (BP 160/90 mm Hg) is determined in the somatic status, otherwise without serious deviations from the norm. Neurological status: moderately somnolent, awake with open eyes, speech contact is difficult. Performs simple instructions "every other time". Gross meningeal syndrome. No focal symptoms were detected.

The study performed in the hospital of primary hospitalization was supplemented by CTA of BCA from the level of the aortic arch to the soft tissues of the cranial vault, according to which a large IA was found in the area of the parting of the left middle cerebral artery (14×9×13 mm in size), oriented laterally. Anomalies of the Willis circle structure were also revealed in the form of early infraoptic divergence of the A1 segment of the left anterior cerebral artery from the internal carotid and hypoplasia of the A1 segment of the anterior cerebral artery from the contralateral side (Figure 36).

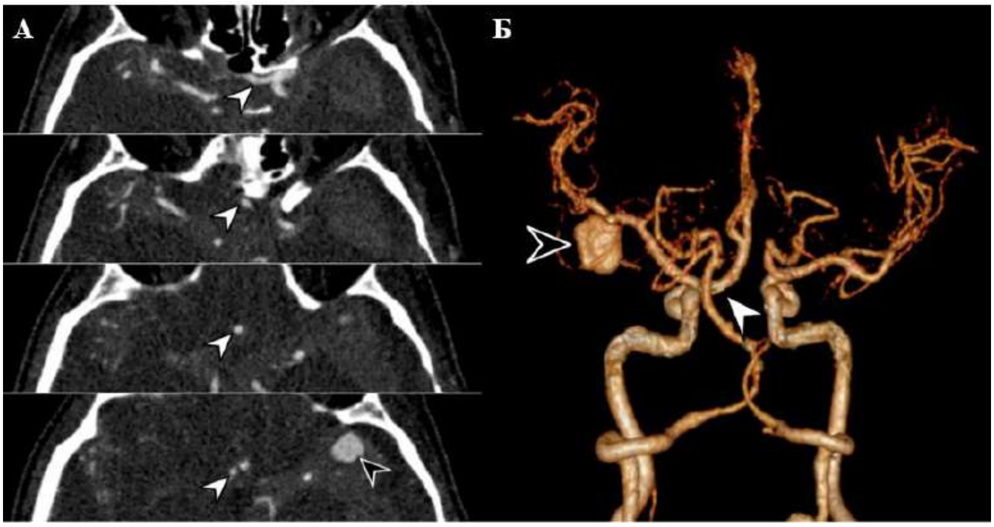


Figure 36 – CTA of the brachiocephalic artery: A – axial plane, B – three-dimensional reconstruction of the cerebral arteries. An abnormal infraoptic departure of the A1 segment of the left anterior cerebral artery (white arrow) is visualized. In the projection of the left Sylvian fissure, the IA of the left medial cerebral artery is determined (black arrow)

Considering the hemorrhagic type of the disease and the clinical and anatomical form of hemorrhage, the patient urgently underwent surgical intervention in the volume of preventive decompressive left-sided hemicranioectomy, ventriculocysternostomy, clipping of a large ruptured aneurysm of the left middle cerebral artery, dilating plasty of the dura mater with auto-tissues.

CT and MRI performed before the operation enabled surgeons to prepare an adequate amount of surgery and unexpectedly not encounter a rare variant of the structure of the arteries. Dissection of the basal cisterns, isolation and step-by-step cross-clipping of a large ruptured aneurysm of the branch of the left middle cerebral artery was performed using an operating microscope (Figure 37).

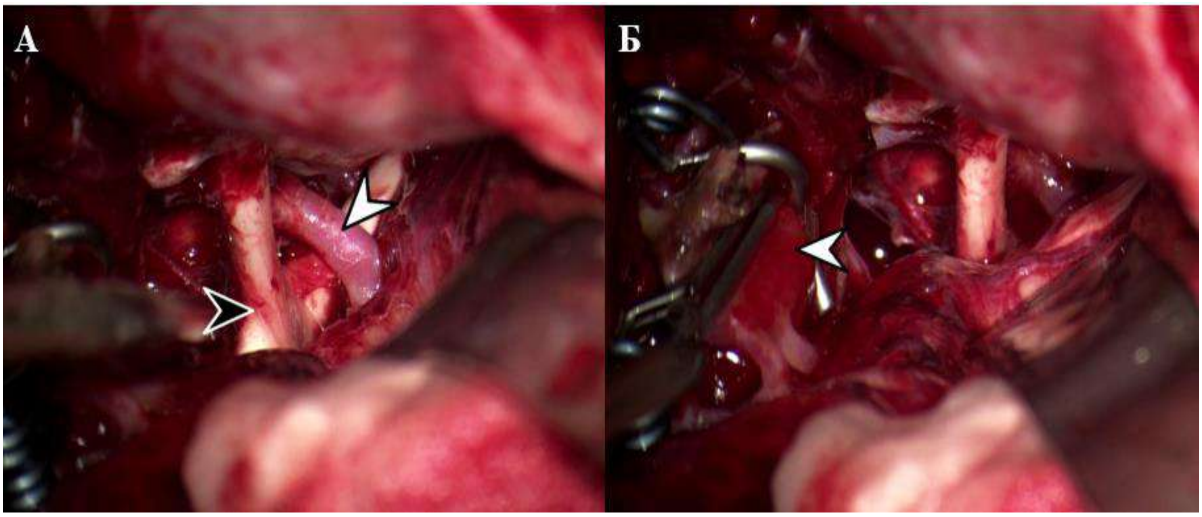


Figure 37 – Intraoperative views. A – abnormal departure of the left anterior cerebral artery (white arrow) anteriorly from the visual intersection (black arrow) in the interoptic interval. B – clipped aneurysm of the left middle cerebral artery (arrow)

The postoperative period was retarded. The patient fully regained consciousness, but speech contact was limited, the development of moderate right-sided hemiparesis, aggravation of sensorimotor aphasia was noted. Extubated on the 3 postoperative day. A partial regression of focal symptoms with preservation of sensorimotor dysphasia was noted. The postoperative wound was healed by primary tension, the cerebrospinal fluid was sanitized.

During the verticalization and expansion of the spectrum of rehabilitation treatment, the patient developed a clinic of "trepanned syndrome", which manifested itself in the form of diffuse headaches and a decrease in mental activity, as well as a visible retraction of the skin flap at the site of intervention. The patient became less active, adynamic. The control CT revealed an X-ray picture confirming the presence of the "drowned flap" syndrome ("sinking skin flap" syndrome) in the form of a pronounced sinking of the flap to the right (Figure 38A). In order to normalize spatial intracranial relationships and treat the "trepanned syndrome", which hinders further rehabilitation, it was decided to conduct early cranioplasty. As planned, the patient underwent cranioplasty of a large defect in the cranial vault with a mesh titanium biocompatible implant "Conmet". The postoperative course is uneventful, the clinical manifestations of the "trepanned syndrome" have regressed. The postoperative wound was healed by primary tension. In a control CT scan of the brain with CT, a clipped aneurysm of the left middle cerebral artery is determined without reliable signs of residual blood flow (Figure 38B).

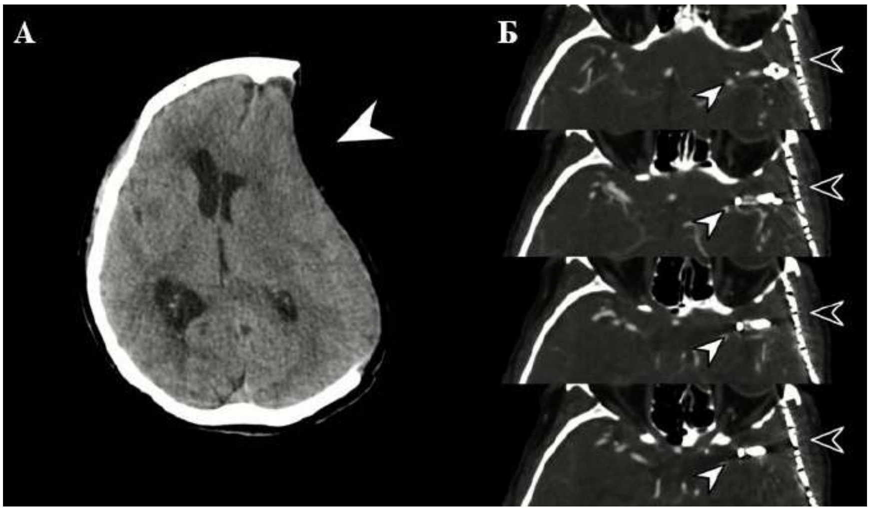


Figure 38 – CT and CTA of the brain after surgical treatment. A – postoperative CT of the brain without contrast, axial plane. On tomograms, a visual depression of the skin flap (arrow) is seen with a shift of the median structures to the right by 15.5 mm. B – CT angiography of cerebral vessels following surgery, axial plane. A clipped aneurysm of the left middle cerebral artery (white arrow) is visualized without signs of residual blood flow. A titanium mesh implant (black arrow) is also determined, which does not interfere with adequate visualization of blood vessels

For further rehabilitation treatment, the patient in a satisfactory condition was transferred to a rehabilitation hospital at the place of residence. This clinical case demonstrates an algorithm for diagnosing a rare combination of an abnormal course of the anterior cerebral artery with hypoplasia of the contralateral anterior cerebral artery and a ruptured aneurysm of the branch of the middle cerebral artery.

With the normal structure of the Willis circle, the anterior cerebral artery arises from the anterior semicircle of the internal carotid artery at right angles, goes in the anteromedial direction above the optic nerve and penetrates into the longitudinal cerebral sulcus where it communicates with the anterior cerebral artery of the opposite side through the anterior connective artery. As part of the anterior cerebral artery, there are proximal (A1) and distal parts (A2-A5), called the pericallous artery. The precommunicant segment (A1) extends from the bifurcation of the internal carotid artery, goes horizontally over the visual intersection up to the junction with the anterior connective artery. The subcalous segment (A2) passes around the rostrum of the corpus callosum within the cistern of the terminal plate to its genu (the place of a branch of the callosomarginal artery). The precalous segment (A3) wraps around the genu of the corpus callosum and at the level of its trunk passes into the supracalous segment (A4) and the postcalous segment (A5). A4 and A5 segments follow the upper edge of the corpus callosum and are conditionally divided by the plane of the coronal suture [102].

With the infraoptic departure of the A1 segment, the anterior cerebral artery originates from the ophthalmic (paraclinoid) segment of the internal carotid artery at the level of the branch of the ocular artery, passes under the ipsilateral optic nerve anteriorly from the optic intersection, and then turns upward between the optic nerves and flows into the anterior connective artery [155]. This type of structure of the A1 segment of the anterior cerebral artery is extremely rare, but it is almost always combined with cerebral aneurysms and other intracranial vascular anomalies [170].

At the moment, there is a single classification of the configurations of the infraoptic course of the anterior cerebral artery, based on a study by S. T. Wong et al. (2008) [170]. This classification systematizes the configurations of this anomaly based on the presence of the ipsilateral supraoptic segment A1 and the structure of the contralateral segment A1 (Figure 39). In our case, the patient is an example of the configuration of the infraoptic course of the anterior cerebral artery of type III.

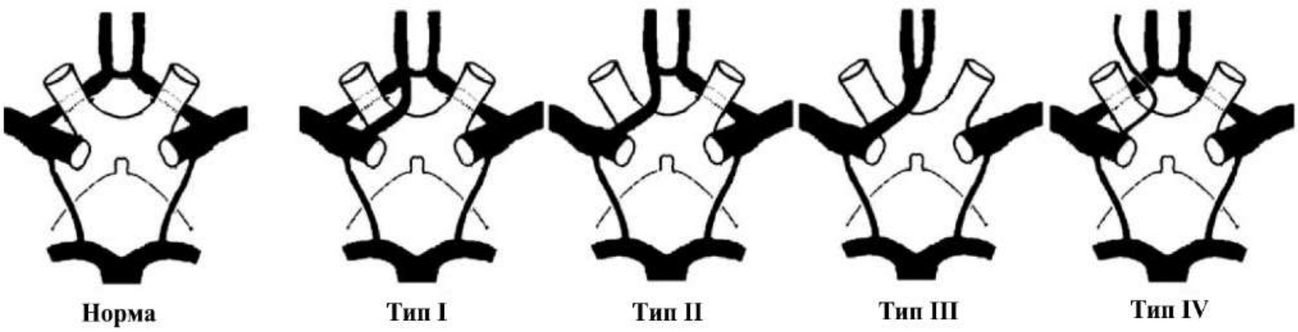


Figure 39 – Classification of configurations of the infraoptic course of the anterior cerebral artery. Type I - preservation of the normal anatomy of the internal carotid artery bifurcation with the presence of an additional infraoptic branch between the

internal carotid and anterior cerebral arteries. Type II - division of the internal carotid artery at the level of the ocular artery, there is no normal supraoptic segment A1. Type III is a combination of type II with hypoplasia or aplasia of the contralateral A1 segment. Type IV - the presence of an additional anterior cerebral artery with an infraoptic course of the A1 segment

The literature sources suggest that the abnormal infraoptic course of the A1 segment of the anterior cerebral artery is a consequence of the persistence of one of the two primitive ocular arteries forming an anastomotic loop around the optic nerve [31, 108]. However, now there is no objective data proving this theory or allowing us to put forward other reliable hypotheses to explain the occurrence of the anomaly.

As a rule, the infraoptic course of the anterior cerebral artery is combined with the intracranial aneurysm presence and other vascular anomalies. The most common associated anomaly is aplasia or hypoplasia of the contralateral anterior cerebral artery (35%) [123] that was observed in the case described above. It is also known that this vascular anomaly is prone to lateralization. Thus, according to previous clinical observations, in 75% of cases the infraoptic course of the anterior cerebral artery occurs on the right, in 15% on the left and in 10% demonstrates bilateral localization [38]. In most patients, the infraoptic course of the A1 segment of the anterior cerebral artery is detected accidentally during neurosurgical intervention for IA ruptures.

Domestic and foreign researchers of aneurysmal disease identify factors of the vascular wall that determine its resistive properties and factors of hemodynamic stress that cause local hemodynamic overload of limited areas of the cerebral artery vascular wall, leading, along with indicators of central hemodynamics, to the formation and rupture of IA. The analysis of the sectional material indicates that none of the factors of the vascular wall, which include: media defects, Rotter branching pads, "sutures" in the places of arterial branching, atherosclerosis and others, is leading to the occurrence of IA [24]. According to some modern studies, the formation of IA is caused by an unfavorable combination of biological and geometric features of blood vessels, mechanical and barometric stimuli, as well as factors of biochemical regulation of local hemodynamics, and the geometric features of the arteries of the Willis polygon play an important role in this process [77]. The results of hydrodynamic studies, which have now become very popular, indicate that any changes in the diameters of the adducting and diverting vessels, the angles of bifurcation, as well as the places and angles of departure of the lateral branches lead to very significant variations in the nature of cerebral blood flow, as well as changes in the configuration and size of hemodynamic load zones. Thus, the presence of specific anatomical variations of the Willis circle can equally modify the hemodynamics of cerebral blood flow. So, patients with extreme structural variants and rare anomalies of the Willis polygon are candidates for long-term follow-up due to the risk of developing de novo aneurysms. Currently, thanks to the use of the latest generation scanners and the introduction of modern postprocessing techniques, CTA is becoming a routine method of noninvasive assessment of the cerebral vascular network in the postoperative period [13]. It should be mentioned that in the described case, the presence of a mesh titanium implant in the immediate vicinity of the clipping zone caused no difficulties in visualization.

Conclusion

The present study showed that approximately one third of patients (30.4%) with nTSH had BCA atherosclerosis as a result of CT, 10.6% of those with hemodynamically significant stenoses and occlusion. Variants of BCA development were found in 21.5% patients. Hemodynamically significant BCA stenoses in most cases have become a contraindication to IA endovascular treatment. For this reason, when performing CT in patients with nTSH, the scanning area should be extended to the neck (up to the level of the aortic arch).

The demonstrated clinical cases showed that CT and CTA performed in the emergency unit made it possible in a short time to establish not only the presence of an aneurysm and intracerebral hemorrhage, but also to determine the level of aneurysm rupture. These data made it possible to carry out an immediate successful surgical intervention. The first observation shows that even if a large hematoma is detected with native CT, it is necessary to perform CTA to find the source of the hemorrhage.

The second clinical observation demonstrates the importance of the complex application of noninvasive radiation diagnostics methods to assess the structural features of the Willis circle. CTA of the BCA performed in the conditions of the admission department made it possible to prepare an adequate volume of surgical intervention, which, in turn, increases the safety of basal cistern dissection, releasing and clipping of IA in conditions of subarachnoid hemorrhage.

CHAPTER VII. POSTOPERATIVE CONTROL OF INTRACRANIAL ANEURYSMS

7.1 Postoperative Control of Clipped Intracranial Aneurysms

7.1.1 General Description of Patients

All patients were recommended dynamic observation by a neurosurgeon with CA at the end of hospitalization in the medical discharge report to monitor IA recovery. The follow-up period for the patients studied coincided with the pandemic of a new coronavirus infection. Thirty-seven patients came for postoperative follow-up.

The breakdown of patients by gender was as follows: 26 women (aged 32 to 77 years) and 11 men (aged 32 to 59 years). In total, these patients had 66 aneurysms, of which 45 were treated: clipping – 45, clipping + embolization – 1, resection – 2, stenting – 1, embolization – 5. Seven aneurysms were not treated, five aneurysms were discovered for the first time.

7.1.2 Postoperative Control with MRI and Dynamic MR Angiography

In total, MRI, MRA and dynamic MRA were performed in 34 patients, three patients refused the examination for various reasons. The patients included 23 women (aged 37 to 77 years) and 11 men (aged 44 to 58 years). In 34 patients, 57 aneurysms were subjected to a control examination: 51 aneurysms and 6 untreated aneurysms. Of the aneurysms treated, 43 were clipped, 5 embolized, 2 resected and 1 stented.

Of the 43 clipped aneurysms, 26 were treated in the acute phase of rupture, the remaining 17 – in the pre–hemorrhagic phase. Of the five embolized aneurysms, three aneurysms were treated in the acute phase of rupture, the remaining two – in the pre–hemorrhagic phase. Of the two resected aneurysms, one aneurysm was treated in the acute phase of rupture, the other was treated as planned.

Stenting of the aneurysm was performed in the acute phase of the rupture.

The time of the control examinations ranged from 8 to 49 months. All clips were made of titanium alloy manufactured by BBRAUN Aesculap.

After analysis, it was not possible to assess the extent of aneurysm clipping with 3D-TOF on MRI in 100% of cases, as the clips caused artifacts. In two cases (6 %) it was not possible to assess the vessels with TRICS, but this was mostly due to contrast agent defects; in most cases (94 %) the image quality was good (Table 20).

Table 20 – Comparison of images in 3D-TOF and TRICS

Image Quality	3D-TOF	TRICS
1 – assessment of vessels at the sites of clips, emboli and stents is not possible	34	2
2 – small artifacts do not interfere with the evaluation of vessels	–	1
3 – no artifacts	–	31

In the evaluation of dynamic MR angiography, the best contrast phases of the Willis circle were 5, 6 and 7. They were used for 3D processing and for the creation of multiplanar reconstructions.

Of the untreated aneurysms, three were located in the cavernous segments of the internal carotid artery, one in the posterior communicating artery, one in the superior cerebellar artery and one in the middle cerebral artery, all of which were intact and miliary. A detailed distribution of the localization of treated and untreated aneurysms is shown in Tables 20 and 21.

Table 20 – Localization of treated aneurysms

Aneurysm Localization	Qty of Clipped Aneurysms, %	Qty of Embolized Aneurysms, %	Qty of Resected Aneurysms, %	Qty of Stented Aneurysms, %
AComm	9	–	–	–
STA	4	–	–	–
PComm	8	–	–	–
PICA	1	1	–	–

Aneurysm Localization	Qty of Clipped Aneurysms, %	Qty of Embolized Aneurysms, %	Qty of Resected Aneurysms, %	Qty of Stented Aneurysms, %
PrcA	2	–	–	–
ICA	9	3	2	1
MCA	8	–	–	–
ACA	2	–	–	–
BA	0	1	–	–

Table 21 – Localization of untreated aneurysms

Localization	Untreated Aneurysms, %	New-Onset Aneurysms, %	Further Treatment, %
ICA	3	2	1
PComm	1	–	–
SCA	1	–	–
BA	–	1	–
ACA	–	1	–
AComm	–	1	–
MCA	1	–	–

After performing MRI and MRA a cerebral angiography a cerebral angiography was planned in all 34 patients, but during hospitalization, one patient refused the manipulation, the second patient contracted coronavirus and was transferred to a specialized hospital, the third patient had to postpone CA for the next hospitalization by one year.

As a result of MRI, MRA and TRICKS, near-neck parts were found in four clipped aneurysms and in two embolized aneurysms, which was confirmed by CA. The near-neck parts of the clipped aneurysms were located in AComm (n = 2), ICA (n = 1), STA (n =

1). Among the embolized aneurysms, the near-neck parts were found in BA and ICA (one in each artery). In addition, another five aneurysms were found: two in ICA, one in BA, ACA and AComm, also confirmed by CA.

The TRICKS data were compared with the CA data. In all cases the data matched completely, no discrepancies were found between them.

In one case, the TRICKS data showed a miliary aneurysm in the cavernous sinus of the ICA that was not noted in the CA protocol, so a second joint review of the images by a radiologist, a X-ray surgeon, and a neurosurgeon was required. The second review revealed a miliary aneurysm of in ICA with CA.

To determine the diagnostic value of TRICKS, its data were compared with the CA data with respect to two indicators: the presence or absence of an aneurysm neck and the presence or absence of a new aneurysm. The calculation results are listed in Table 22.

Table 22 – Determination of the diagnostic value of TRICS (MRI) based on the presence or absence of an aneurysm neck and the presence or absence of a new aneurysm

Indicators	Sensitivity, %	Specificity, %	Overall Accuracy, %	Positive Predictive Value, %	Negative Predictive Value, %
Aneurysm Neck	100.0 CI 74–100	100.0 CI 91–100	100.0 CI 93–100	100.0	100.0
New Aneurysm	100.0 CI 57–100	100.0 CI 87–100	100.0 CI 89–100	100.0	100.0

Thus, the TRICKS sensitivity reaches 100%, the specificity is 100%, the positive predictive value is up to 100% and the negative predictive value is 100%.

Two patients required further surgical treatment of IA after diagnosis: one patient underwent microsurgical clipping, the other embolization. In the case of an already embolized aneurysm, microsurgical clipping was performed. Embolization was performed for newly identified IA. In one of the patients, a local dissection of the vertebral artery was detected by MRI, which was not detected by CA and did not require treatment. A clinical case of postoperative follow-up in one of these patients is shown in Figure 40.

Clinical Case

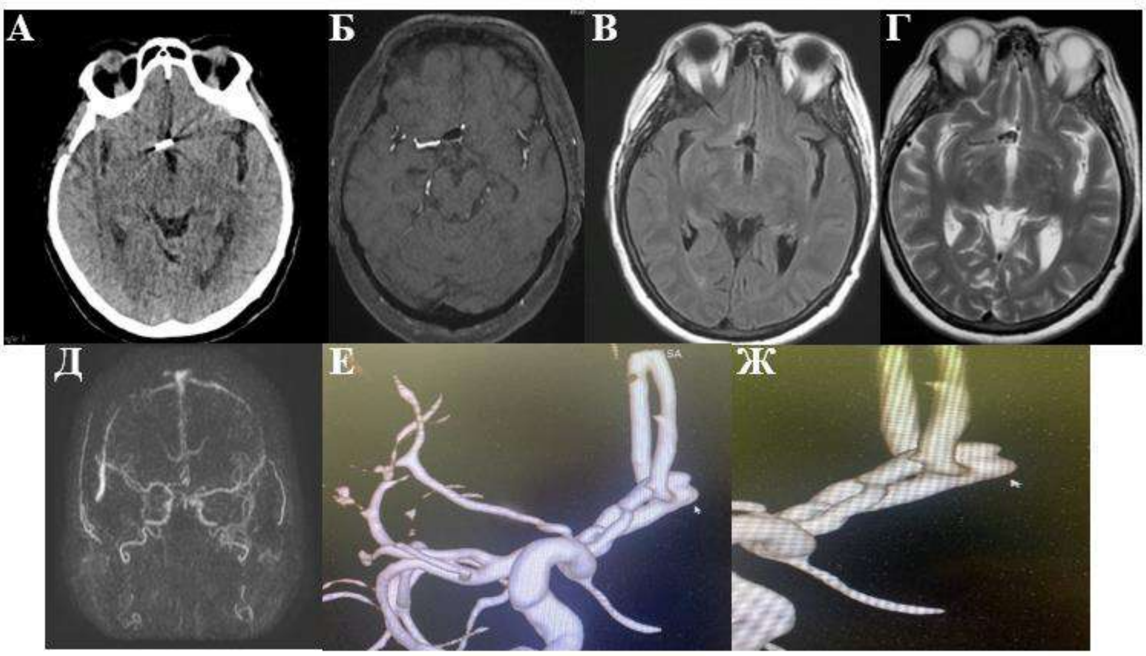


Figure 40 – Patient, 60 years, after microsurgical clipping of AComm aneurysm. The follow-up examinations were carried out 23 months after treatment: А – native CT, Б-Д – MRI (Б – 3D-TOF, В – FLAIR, Г – T2-ВИ, Д – TRICS), Е-Ж – CA. The native CT scan shows that the clip generates artifacts. On MRI (Б, В, Г), artifacts are visible at the location where the clip was placed. On MRA-TRICS (Д) there are no artifacts, the near-neck part of the aneurysm is visible, indicated by a white arrow, confirmed by the CA data (Е, Ж). In addition, an aneurysm of the wedge-shaped part of the left ICA (Д, yellow arrow) was confirmed

7.1.3 Postoperative Follow-Up with CT Angiography of the Brachiocephalic Artery

A postoperative follow-up examination with CTA BCA was performed in 35 patients, the remaining two patients refused the examination. The patients examined included 26 women (aged 32 to 77 years) and 9 men (aged 32 to 59 years). A total of 63 aneurysms were examined: clipping – 44, embolization – 4, resection – 2, clipping +

embolization – 1; 7 aneurysms were untreated, 5 aneurysms were discovered for the first time. Thirty-two aneurysms were treated in the acute phase of rupture, 29 aneurysms – in the pre-hemorrhagic phase. The quality of the CT images was assessed based on the contrast of the vessels and the presence of artifacts due to clips and emboli. Contrast was good in all patients and there were no errors in the administration. One patient had an allergic reaction after administration of the contrast agent, which prevented further CA; two patients refused to undergo CA and one patient developed a coronavirus infection. The control CA was therefore performed in 31 patients. In patients in whom the aneurysm was microsurgically clipped and resected, there were no artifacts during CT that impaired visualization. After embolization of the aneurysms, considerable artifacts occurred that prevented postoperative follow-up of aneurysm healing. The localization of the aneurysms and the methods of their treatment are listed in Table 23.

Table 23 – Localization of aneurysms and treatment methods

Localization	Qty of Clipped Aneurysms, %	Qty of Embolized Aneurysms, %	Qty of Resected Aneurysms, %	Qty of Aneurysms after Clipping + Embolization, %
AComm	9	–	–	1
STA	4	–	–	–
PComm	8	–	–	–
PICA	1	1	–	–
PrcA	2	–	–	–
ICA	9	2	2	–
MCA	8	–	–	–
ACA	2	–	–	–
BA	–	1	–	–

When comparing CTA BCA and the CA data, all intact, untreated aneurysms, including the miliary aneurysms, were found. The exception was only one miliary aneurysm in the cavernous sinus of ICA, which, however, had no clinical significance at the time of the examination and did not require any subsequent interventions. The localization of untreated and newly discovered aneurysms is shown in Table 24.

Table 24 – Localization of untreated and newly discovered aneurysms

Localization	Untreated IA, as per CT	Untreated IA, as per CA	Untreated IA, as per CTA	Untreated IA, as per CA	Further Surgical Treatment
AComm	–	–	–	1	–
PComm	1	1	–	–	–
ICA	2	3	1	2	1(embolization)
MCA	2	2	–	–	–
ACA	–	–	1	1	–
SCA	–	1	–	–	–
BA	1	–	1	1	–

The resected aneurysm was clearly visible, and a vascular anastomosis formed. The CTA method made it possible to assess the patency of the vessel and rule out parietal and occlusive thrombosis. The CT data in patients with aneurysm resection were confirmed during CA.

Due to artifacts caused by emboli in the aneurysm, we were unable to assess the degree of healing of the aneurysm, which is a limitation for the use of CTA BCA in patients with embolized aneurysms (four aneurysms in total).

The radiation exposure from CTA BCA was compared with the radiation exposure from the CA (Table 25).

Table 25 – Comparison of radiation exposure with CTA and CA of the brachiocephalic artery

Visualization	Min. Radiation Exposure (mSv)	Max. Radiation Exposure (mSv)	Average Value (mSv)
CT Angiography of Brachiocephalic Artery	2	8	4.09
CA of Brachiocephalic Artery	4	18	9.9

The minimum radiation exposure when performing CTA BCA was 2 mSv, which is two times less than when performing CA. The maximum radiation exposure during CTA of the brachiocephalic artery was 8 mSv, which is significantly lower than the radiation dose during CA (18 mSv). On average, the patient's radiation exposure is 2.5 times lower with CTA BCA than with CA.

To determine the diagnostic value of CTA BCA, its data were compared with the CA data with respect to two indicators: the presence or absence of an aneurysm neck and the presence or absence of a new aneurysm. The calculation results are listed in Table 26.

Table 26 –Determination of the diagnostic value of CTA BCA based on the presence or absence of an aneurysm neck and the presence or absence of a new aneurysm

Indicators	Sensitivity, %	Specificity, %	Overall Accuracy %	Positive Predictive Value, %	Negative Predictive Value, %
Aneurysm Neck	83.3 CI 55–95	97.6 CI 88–100	94.0 CI 55–98	90.9	95.3
New Aneurysm	60.0 CI 23–88	100.0 CI 89–100	94 CI 82–98	100.0	93.3

The comparison of the CTA BCA data with the CA data yielded values for sensitivity and specificity in the assessment of healing of clipped and resected IA: 83.3%

(sensitivity), 97.6% (specificity). The diagnostic value of a positive result was 90.9%, the diagnostic accuracy of a negative result was 95.3%.

Due to the pronounced artifacts caused by emboli, it is not possible to follow-up the healing of the embolized IA.

Conclusions

As a result of the examination, the high diagnostic value of non-invasive diagnostic methods (CT and dynamic MRA) in the postoperative follow-up of treated IA was demonstrated. The CTA method, with its high sensitivity and specificity, enables an average 2.5-fold reduction in radiation exposure compared to CA with similar accuracy. Embolized aneurysms represent a limitation for the use of CT angiography of the brachiocephalic artery. With dynamic MRA, both embolized and clipped aneurysms can be assessed with high diagnostic accuracy and without radiation exposure.

CHAPTER VIII. PROTOTYPE CONVOLUTIONAL NEURAL NETWORK IN DIAGNOSIS OF INTRACRANIAL ANEURYSMS AFTER CT ANGIOGRAPHY OF BRACHIOCEPHALIC ARTERY

8.1 Results of Prototype Convolutional Neural Network in Diagnosis of Intracranial Aneurysms

As a result of the research, a prototype of a neural network with CTA BCA of 456 patients was created, of which 45.2% (206 patients) with IA, 54.8% (250 patients) – without IA. Among them, 142 patients had a single IA and 64 patients had multiple IA (from 2 to 8 IA). Of the patients with multiple IA, 55 had 2 IA, 5 had 3 IA, 4 had 4 IA and 1 had 8 IA (Figure 41).

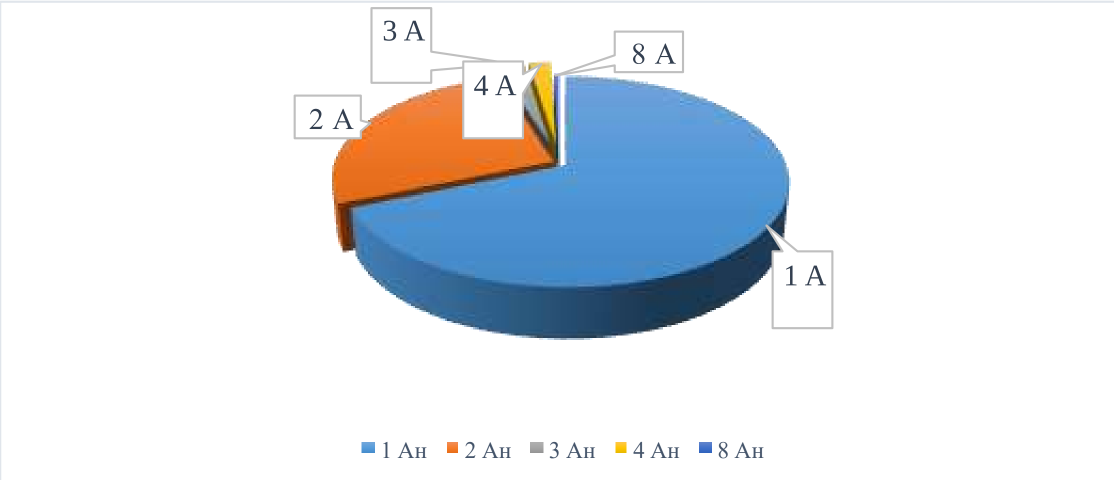


Figure 41 – Distribution of Patients Examined by IA Number

Twenty-six patients had an intact IA without signs of hemorrhage (13%), the remaining 180 patients (87%) had signs of acute non-traumatic SAH as a result of IA rupture.

The aneurysms were divided into three groups according to their size: miliary IA with a diameter of up to 3 mm (32 IA, 10.9%); IA with a diameter of 3 mm to 5 mm (126 IA, 43.3%); IA with a diameter of more than 5 mm (133 IA, 45.8%).

Depending on the localization of the IA, they were categorized as follows: Most IA were detected in the MCA (n = 118), the AComm (n = 81) and the ICA (n = 52), in 13 cases IA were detected in the PComm, in 11 cases – in the BA. The total number of IA cases in the PrcA, PICA, PCA, ACA, SCA and VA ranged from three to six cases for each of the listed arteries. The distribution of the identified IA by arteries is shown in Table 27.

Table 27 – Distribution of IA in arteries

Artery	IA Quantity	IA incidence, %
MCA	118	39.3
AComm	81	27.0
ICA	52	17.3
PComm	13	4.3
BA	11	3.7
PrcA	5	1.7
PICA	2	0.7
PCA	4	1.3
ACA	6	2.0
SCA	5	1.7
VA	3	1.0

The following values were determined as a result of the experiment:

$$TP = 183; FP = 18; FN = 25$$

$$Pression = \frac{183}{183+18} = \frac{183}{201} \approx 0{,}91 \quad (2)$$

$$Recall = \frac{183}{183+25} = \frac{183}{208} \approx 0{,}879$$

The experiment yielded values for the completeness and accuracy of the classification of 91% and 88% respectively.

In the group of patients with multiple IA, the artificial intelligence data indicated the presence of at least one IA with a probability of 51 to 100% in all cases: in four cases the probability was between 51 and 70%, in the remaining 60 cases – between 71 and 100%. In the group of patients with a single IA, the AI data showed a high probability of IA in 120 cases, a medium probability in 10 cases and a low probability in 11 cases.

The comparison of radiologist and AI data revealed five patients in whom the radiologists had missed miliary IA, while AI indicated a high probability of IA in four out of five patients.

In eight patients with single IA described by CT and confirmed intraoperatively, the probability of their presence according to AI was low. The missing IA were localized as follows: four aneurysms in AComm, two aneurysms in MCA, one aneurysm in ACA, one aneurysm in VA. In three out of eight cases, the intracranial aneurysms did not rupture; in the remaining cases, massive intraventricular hemorrhages and parenchymal hemorrhages occurred.

In the group of patients without IA, AI led to false positive results in 12 cases.

The analysis showed that the sensitivity of the developed neural network prototype was 85.1% (CI 78-90%), specificity – 95.1% (CI 88-94%), overall accuracy – 91%.

8.2 Effect of Prototype Convolutional Neural Network in the Detection of IA Using Brachiocephalic Artery CT Angiography Data in the Emergency Department

According to the data from the medical records (CA, intraoperative and autopsy data), there were a total of 13 patients without IA and 45 patients with aneurysms.

The results of the prototype test showed that the evaluation of CTA BCA by a resident in the first year identified 9 patients without IA and 49 patients with at least one aneurysm. With the prototype data, the number of patients without IA increased to 13 and the number of patients with IA decreased to 45. The diagnostic accuracy of the resident without the use of prototype data was as follows: sensitivity – 100% (CI 92-100%), specificity – 69.23% (CI: 42-87%), overall accuracy 93% (CI: 84-97%). The prognostic value of a positive result was 91.84%, the prognostic accuracy of a negative result was 100%. The diagnostic accuracy of the resident's conclusions increased when prototype data were used: Sensitivity and specificity up to 100% (CI 92-100% and 77-100%, respectively), overall accuracy up to 100% (CI 94-100%). The prognostic value of the positive and negative results was 100%.

Assessment of CT angiography of the brachiocephalic artery without prototype data by a neurosurgeon with more than 15 years of experience revealed 8 patients without aneurysm and 50 patients with IA. With the prototype data, the number of patients without IA increased to 12 and the number of patients without aneurysm decreased to 46. As a result of using the prototype data, the diagnostic accuracy of the neurosurgeon's reviews also changed. While the sensitivity, specificity and overall accuracy without using the prototype were 100, 61.54 and 91% respectively, the specificity increased to 92.31% and the overall accuracy to 98% when using the prototype, with a sensitivity of 100%. The evaluation of the assessments by radiologists also showed an improvement in diagnostic accuracy when prototype data was used. The diagnostic value of the reviews is shown in Tables 28 and 29.

Table 28 – Diagnostic value of reviews without prototype data

Specialists	Sensitivity (CI%)	Specificity (CI%)	Overall Accuracy (CI%)	Positive Predictive Value	Negative Predictive Value
Neurosurgeon	100 (92–100)	61.54 (36–82)	91 (81–96)	90	100
Medical Resident	100 (92–100)	69.23 (42–87)	93 (84–97)	91.84	100
Radiologist 1	100 (92–100)	76.92 (50–92)	95 (86–98)	93.75	100
Radiologist 2	100 (92–100)	100 (77–100)	100 (94–100)	100	100
Radiologist 3	100 (92–100)	76.92 (50–92)	95 (86–98)	93.75	100
Radiologist 4	100 (92–100)	84.62 (58–96)	97 (88–99)	95.74	100

Table 29 – Diagnostic value of reviews with prototype data

	Sensitivity (CI%)	Specificity (CI%)	Overall Accuracy (CI%)	Positive Predictive Value	Negative Predictive Value
Neurosurgeon	100 (92–100)	92.31 (67–99)	98 (91–100)	97.82	100
Medical Resident	100 (92–100)	100 (42–87)	100 (94–100)	100	100
Radiologist 1	100 (92–100)	84.62 (58–96)	97 (88–99)	95.74	100
Radiologist 2	100 (92–100)	100 (77–100)	100 (94–100)	100	100
Radiologist 3	100 (92–100)	100 (77–100)	100 (94–100)	100	100
Radiologist 4	100 (92–100)	100 (77–100)	100 (94–100)	100	100

The data obtained show that even experienced specialists working with neurosurgical emergency patients in multidisciplinary hospitals perceive discrepancies in CTA BCA. The use of an instrument in routine practice to determine the probability of aneurysms increases the diagnostic value of specialists' conclusions.

Conclusions

The results of the studies performed showed that the prototype has high sensitivity, specificity and overall accuracy (85.1, 95.1 and 91% respectively) in detecting IA from the CT angiography data. This model can be useful: as a first opinion to speed up the diagnostic process and support medical decision making and optimize workflow.

CHAPTER IX. RESULTS AND DISCUSSION

Due to the rapid development of diagnostic radiology, there is increasing evidence that invasive methods should also be replaced by non-invasive methods when examining patients with IA rupture in the acute phase.

The present study is based on the examination of patients with acute non-traumatic SAH by CTA BCA in the emergency department of the Krasnodar RVC and the subsequent analysis of the results obtained.

Until 2007, there was one center for head vessels in the Krasnodar Territory, where a native CT of the brain was performed around the clock to verify non-traumatic SAH, and to determine the source, CA was performed in all patients. Most patients at this time were transferred around the clock and underwent urgent microsurgical or intravascular procedures only in the main RVC (Research Institute / RCH No.1), regardless of age, severity of illness and time of diagnosis.

Over the past ten years, a “Package of measures to improve medical care for patients with acute cerebral circulatory disorders” has been implemented in various regions of the Russian Federation, and regional vascular centers and primary vascular departments have been established in the regions. As part of the implementation of the program, the vascular centers were equipped with high-tech devices for diagnosis and treatment [20, 27].

Thus, since 2011, thanks to the implementation of the Federal Vascular Program, 4 RVCs and 3 PVDs equipped with CT and C-Arcs have been opened in the Krasnodar Territory, where native CT and CA are performed.

Since 2017, in continuation of the vascular program, 6 RVCs and 12 PVDs have already been in operation in the Krasnodar Territory, where CTA BCA in non-traumatic SAH is performed according to native CT data.

Thanks to the re-equipping of the PVDs with CT scanners and the introduction of a telemedicine consultation system, the examination of non-traumatic SAH now takes place in the first admission department and no longer in the main RVC, as was the case in 2007 when the vascular program was just beginning. Thanks to the introduction of emergency CTA BCA in the emergency department, non-invasive verification of IA, which was the source of non-traumatic SAH, became possible. Figure 42 schematically shows the stages of implementation of the algorithm for the diagnosis and treatment of patients with non-traumatic SAH in the Krasnodar Territory over the years.

2007–2011	Suspected non-traumatic SAH Admission to the Central District Hospital Transfer to the Research Institute / RCH No.1 – all patients with IA (Native CT, CA for all patients, surgical treatment – 24/7)
2011–2017	Suspected non-traumatic SAH Admission to RVC (no neurosurgical care) – Native CT Transfer to the Research Institute / RCH No.1 – all patients with IA (Native CT, CA for all patients, surgical treatment – 24/7)
2017–2022	Suspected non-traumatic SAH Admission to RVC (neurosurgical care) – Native CT, CTA BCA for all patients, CA when necessary, surgical treatment – 24/7 Transfer to the Research Institute / RCH No.1 – only severe cases (2-3 per year)

Figure 42 – Stages of changes in the diagnostic algorithm, referral and triage of patients with non-traumatic SAH, in 2017–2022

The triage of patients with acute non-traumatic SAH is shown in Figure 43.

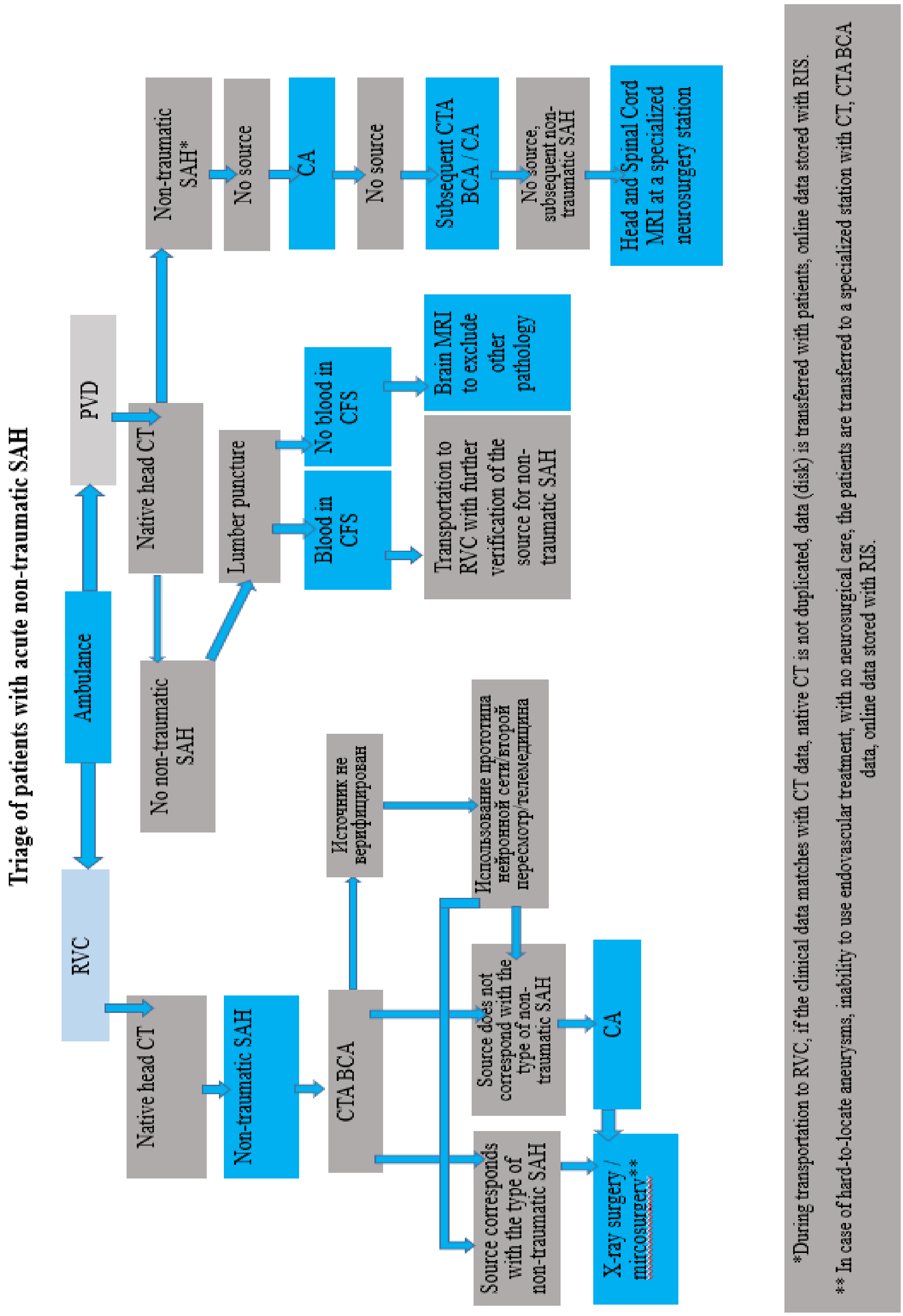


Figure 43 – Triage of patients with acute non-traumatic SAH, developed and implemented in the Krasnodar Territory since 2017

After the introduction of the new protocol, 650 case histories of patients with non-traumatic SAH who were diagnosed, medically treated and operated on at the Regional Neurosurgical Center of the Research Institute / RCH No.1 in the period from September 2017 to August 2020, were evaluated according to a uniform regional protocol. The causes of acute non-traumatic SAH in these patients were as follows: Rupture of intracranial arterial aneurysms, vascular malformations, vascular malformations in combination with IA, cavernomas; in some patients, the cause of non-traumatic SAH was not recognized. The study group included patients whose source of hemorrhage was a ruptured intracranial aneurysm. The algorithm for the study of patients with acute non-traumatic SAH is shown in Figure 44.

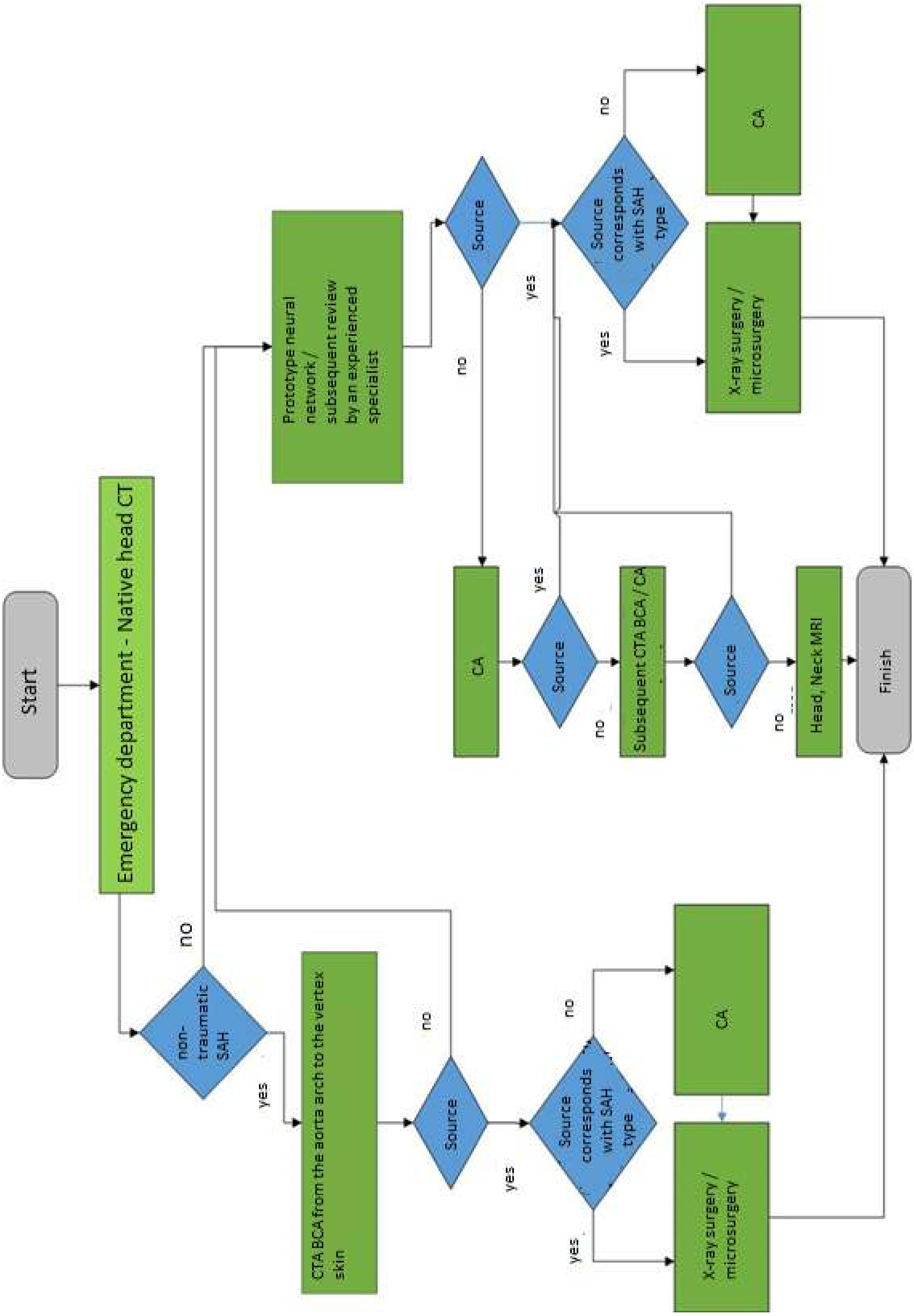


Figure 44 – Algorithm for the study of patients with acute non-traumatic SAH

Since the group of patients under study comes to the emergency department in a rather serious condition and needs immediate help, including surgical treatment, the main task at this phase is to find and eliminate the source of the SAH in order to stop the hemorrhage.

Non-contrast CT is used to detect non-traumatic SAH in the acute phase. This is a reliable method of diagnostic radiology that can confirm non-traumatic SAH with high sensitivity (approx. 93%) within the first 24 hours after the onset of clinical manifestations; the sensitivity of native CT reaches 100% in the first 12 hours [118]. Native CT can be used to assess the severity of SAH (Fisher scale) and IVH (Graeb scale), which is necessary for an objective assessment of the clinical picture with the possibility of preventing vasospasm [45, 75].

To identify the source of a non-traumatic SAH, it is recommended to perform CTA BCA. Its advantages include wide availability, speed of performance, convenience for the patient, diagnostic accuracy, non-invasiveness and relative safety. CTA enables the diagnosis of IA with high sensitivity (up to 94-98%) and specificity (95-100%) [111, 169, 174]. Native CT in combination with CTA of the heart makes it possible to determine with high accuracy which of the aneurysms is the source of the hemorrhage. According to literary sources, the largest aneurysm is the one that ruptures most frequently [94]. Other angiographic signs of rupture are vasospasm, irregular aneurysms or a blood clot inside the aneurysm.

Diagnostic difficulties in CTA BCA are most commonly associated with contrast agent errors, e.g. artifacts due to movement or incorrect timing of the delay in the administration of a bolus contrast agent. Problems can also occur with small aneurysms (usually due to those smaller than 3 mm) [111]. Difficulties in interpreting CT results explain the need for sufficient clinical experience of the specialist or double-checking of the data.

According to a study by G. Biddle et al. (2022), diagnostic errors occur in 2-8% of neuroradiology examinations, leading to significant potential morbidity and mortality. It was found that most errors in neuroradiology occur in the interpretation of MRI of the brain (30.3%), followed by CTA of the brachiocephalic vessels (27.9%) and native CT of the brain (26.1%). Errors in the interpretation of cerebral aneurysms were observed in 13.7% of cases. Most cerebrovascular diagnostic errors were perceptual and clinically significant, occurred in the emergency/inpatient setting, and were associated with a high workload of radiologists [44].

M.O. McCarron et al. (2014) investigated the extent of discrepancy between general radiologists and neuroradiologists in neuroimaging results. Discrepancies in diagnosis were found in 14.2% of patients [110].

In a study by J. Walls et al. (2009), the misinterpretation of CT scans of the brain by residents in the radiology departments of a level I trauma center was evaluated: the overall rate of misinterpretation was 41% [165].

Interestingly, the study by F. Caranci et al. (2015) showed that the highest percentage of errors occurred between 04:00 and 08:00 in the morning, i.e. in the last hours of the shift, which the authors attributed to fatigue. Numerous previous studies have shown a correlation between the incorrect interpretation of images and the level of training of residents: preliminary protocols written by first-year residents were most frequently incorrect [53].

According to M. Walton et al. (2022), it is impossible to extend the diagnostic accuracy of CTA BCA to medical institutions where there are no specialists in the field of neuroradiology. It is possible to improve outcomes in the treatment of patients with SAH through expanded neuroradiology training and the use of telemedicine involving other centers with relevant experience, as well as through the use of deep learning diagnostic algorithms (artificial intelligence), which in turn can potentially improve the coordination of activities between centers [166].

Unfortunately, there is no concept of "an experienced neuroradiologist or an expert-level neuroradiologist" in the national clinical recommendations. According to the RANZCR (Royal Australian and New Zealand College of Radiologists) and the Guidelines for Training in Neuroradiology, an experienced neuroradiologist is a radiologist who has completed five years of residency training in neuroradiology or one year of advanced training in neuroradiology (following completion of residency training in radiology) in medical institutions accredited by the RANZCR for neuroradiology. At the same time, the training must be fully supervised and carried out in an institution with at least two practicing neuroradiologists with more than 5 years of experience in neuroradiology. A radiologist trained in neuroradiology must work in a medical facility where there is a:

– Department of Neurosurgery/Vascular Surgery/Neurology, intensive care unit for neurological/neurosurgical/vascular surgery patients;

– CT, MRI and ultrasound equipment operating around the clock.

A neuroradiologist must participate in the analysis of fatal cases and complications as well as in consultations. Specialists trained in neuroradiology must attend at least one clinical conference per week in the relevant specialties (neurosurgery, neurology, vascular surgery, etc.). Preferably, a neuroradiologist should present a poster or verbal presentation at national conferences and participate in original research (series or participation in in vivo studies), however, it is not necessary [145].

The study showed that interpretation of the data by an experienced radiologist increased the sensitivity of CTA BCA compared to CA data from 78.36 to 84.95%, and the sensitivity compared to intraoperative data reached 95.56%.

When examining patients in the acute phase of a non-traumatic SAH, the question often arises as to the choice of the optimal imaging protocol. In particular, there is no consensus as to whether the scope of imaging should be limited to the brain or extended to the brachiocephalic artery and the aortic arch [10, 27, 79, 175, 176]. The latter makes it possible to diagnose concomitant vascular pathologies, which can be important for the choice of treatment.

There is evidence in the literature of a relatively high incidence of vascular pathology in patients with impaired cerebral perfusion [113, 136, 169]. Nevertheless, there are no specific data on the frequency of pathological changes in vascular structures in the acute phase of non-traumatic SAH. This paper investigated the role of CT angiography in the diagnosis of pathological changes in the brachiocephalic artery and vertebral arteries in patients in the acute phase of non-traumatic SAH and the clinical significance of these “incidental” findings.

Congenital or acquired pathological changes of the brachiocephalic artery are relatively common in patients with non-traumatic SAH: in about one third of patients there is evidence of an atherosclerotic lesion, including hemodynamically significant stenoses. Anomalies in the development of the brachiocephalic artery in the form of pathological curvatures or hypoplasia of the vertebral arteries were found in one fifth of the patients. The anomalies detected (atherosclerosis of the brachiocephalic artery, hypoplasia and pathological tortuosity of the vertebral arteries) were associated with unfavorable results of endovascular treatment of IA. The pathological tortuosity of the carotid arteries showed no such pattern.

One of the practical findings of the study is that brachiocephalic artery vascular pathology identified from CT angiography data in patients with non-traumatic SAH is generally not an obstacle to microsurgical clipping, even in emergency indications. Nevertheless, the presence and type of concomitant vascular pathology should be taken into account when planning the procedure.

In addition, the high efficiency of the CTA method in detecting pathologies of the brachiocephalic artery and vertebral arteries was demonstrated: only in a few cases was a CA required to clarify the changes [175].

The value of native MRI in the diagnosis of acute non-traumatic SAH is limited, but this method may be useful to detect concomitant changes in the brain parenchyma and to exclude other causes of acute symptoms. As for MRA, this method has high sensitivity (95%) and specificity (89%) in diagnosing IA. Diagnostic errors occurred mainly in aneurysms located at the base of the skull and in the middle cerebral artery, as well as in small aneurysms [140]. Factors that may affect visualization include vascular tortuosity, turbulent blood flow in the cavities of large aneurysms, and metal artifacts. Despite the advantages of the method, including the lack of radiation exposure to the patient due to the long examination time, possible artifacts due to movement and poorer accessibility, MRA does not apply to the methods for the diagnosis of non-traumatic SAH in the acute phase. In addition, the sensitivity and specificity of detecting IA by MRI is inferior to CTA and CA methods, especially for small IA [57].

CA is a proven method for the diagnosis of non-traumatic SAH and provides the optimal amount of information for planning further actions. Nevertheless, due to the invasiveness of the procedure, the radiation exposure and the probability of complications, which is not zero, the question of whether CA can be replaced by CT angiography is being asked more and more frequently. In the current study, this question was investigated using a large sample of patients with a clinical picture of SAH. The CTA method proved to be a reliable method for the detection of single and multiple aneurysms in the acute phase of non-traumatic SAH. The method has a high sensitivity and overall accuracy so that the data can be used for treatment planning.

In cases where the source of the non-traumatic SAH is not found on CTA, a second look at the images is required. If the result of the second look is negative, CA should be performed to detect aneurysms in hard-to-see locations or small aneurysms. Both methods – CTA and CA – have advantages and disadvantages, so it makes sense to combine them and, if possible, use them together depending on the specific clinical situation.

This research showed that the sensitivity of emergency CTA BCA is equally high for both single and multiple aneurysms: the accuracy of the method tends towards 100%. These data open up prospects for clinicians not only for a gradual empirical transition to non-invasive diagnostic methods, but also for the inclusion of these provisions in clinical recommendations.

A meta-analysis by W.J. Meurer et al. (2016), based on the results of various studies for the period 2008-2015, discusses the best possible combination of native CT and CTA as an algorithm for primary diagnosis and the prospects of replacing the previously accepted native CT and lumbar puncture in non-traumatic SAH with this combination [115]. This classic approach is known for its high sensitivity and high negative predictive value: A lumbar puncture after a native CT scan that has yielded a negative result can reveal the SAH missed on CT. Nevertheless, lumbar puncture is an invasive procedure that can lead to complications (mainly due to damage to various structures near the puncture site by the needle); in addition, this method often provides non-specific results. Considering the improvement of the CT procedure (especially in the first hours after the onset of the patient’s symptoms), lumbar puncture may not be effective enough to be included in the initial screening protocol for such patients in the near future.

An analysis conducted by H. Wu et al. (2016) showed that lumbar puncture is a more cost-effective method for the initial diagnosis of SAH. However, the difference between lumbar puncture and CT angiography was minimal, emphasizing the comparable clinical value of these methods [171]. The work of R.F. McCormack et al. (2010) showed the high sensitivity of CT angiography in detecting IA and concluded that this method is preferable to lumbar puncture. However, a potentially controversial point is that CT angiography is highly likely to detect IA, which is not a cause of SAH but an incidental finding, whereas lumbar puncture aims to directly detect blood in cerebral spinal fluid and thus confirm or refute the presence of SAH. The evidence showed that with a negative native CT, the probability of detecting an IA on CT angiography, which is the cause of the undetected SAH, is around 35% [111].

M.J. Ward et al. (2012) attempted to perform a comprehensive comparative analysis of the efficiency of different methods (native CT only, native CT followed by CTA, native CT followed by lumbar puncture, native CT followed by MRA) in the acute phase of SAH, but the mathematical model could not correctly estimate the occurrence of complications [167]. In particular, the complication rate of lumbar puncture was reported as 0 (whereas the actual occurrence of headache is about 4% [61]) and the occurrence of contrast-induced acute kidney injury after CTA was reported as 11% (in reality, it is much rarer with an incidence of about 0.02% [92]). The information on sensitivity also proved to be incorrect: this parameter for lumbar puncture proved to be 100% because it was taken as the standard, which is not a justified decision. Furthermore, there was no clear threshold between the detection of blood during lumbar puncture as a result of SAH and the complication of the procedure itself. Working to correct these inaccuracies in the model will make it possible to better answer the questions posed to researchers in the future.

Another important diagnostic dilemma concerns the comparative diagnostic value of CTA and CA, also in terms of economic feasibility. The American Heart and Stroke Association classifies CA as Class I evidence for the diagnosis of IA, CTA as Class IIb (because if the results of CTA are not sufficient to make a definitive diagnosis, CA must be performed) [57]. However, in the recommendations of the American College of Radiology, CA and CTA have the same evidence class, with CTA being ranked first (updated version of the 2020 recommendations [34]). So far, the general trend is that in older studies CA is recognized as the "first-line" method, but in more recent studies this place is taken by CTA, as its technique has been considerably improved in recent years [129, 139].

Despite the debate surrounding this issue, not enough analyzes have been performed on the cost-benefit ratio of CA and CTA in the primary diagnosis of IA, and their designs are heterogeneous. One of the most important studies was conducted by M. Salih et al. (2021). It concluded that if more than 47.2% of patients with IA are treated with the endovascular method, CA is a more economically reasonable strategy for the primary diagnosis; if endovascular treatment is chosen in less than 47.2% of patients, it is better to choose CTA. In the specific center where the study was conducted, 56.6% of patients underwent endovascular treatment, but this indicator depends on the experience of the institution and clinicians, as well as on the specifics of clinical recommendations of a particular country. The difference in patients' quality of life after CA or CTA (QALY scale) was insignificant [141]. Therefore, in most cases, the decision to carry out a particular procedure is currently made individually in each institution.

With regard to the economic aspects of CA in the case of negative CTA results, this question should also be clarified on a case-by-case basis, as the sensitivity of CTA is currently recognized as quite high, and CA is often an economically unjustified option that does not lead to an improvement in diagnostic quality [87].

The long-term follow-up of patients after surgical treatment of non-traumatic SAH due to IA rupture is an important but still unresolved issue. Traditionally, CA has been favored as the method of dynamic follow-up of such patients (although there are no recommendations that allow a definite conclusion), but recently CA is increasingly being replaced by CTA, a non-invasive and safer method. The main application of CTA is currently the postoperative follow-up of clipped aneurysms, while aneurysms treated with endovascular embolization are better monitored dynamically with CA, as metal artifacts are a serious obstacle to CTA imaging [63, 101, 150].

There are currently no recommendations for the frequency of imaging examinations after clipping of IA, so an individual algorithm is chosen for each patient depending on their condition and the characteristics of the IA. Optimal regular follow-up care helps to prevent recurrent IA rupture, reduce patients' anxiety and minimize their disability.

The study has shown that non-invasive imaging using CT and MRI provides important information about the pathological process and is necessary in various phases of patient treatment. Because visualization can be expensive, its use is justified when the goal is to provide unique data that contributes to a change in the course of treatment or provides specific information that is helpful in patient counseling.

The data obtained suggest that the niche for the use of CTA BCA in postoperative follow-up is quite large: the limitations of this method include a lower sensitivity of CTA for small necks and near-neck parts of the treated IA (less than 3 mm in size), but these changes are not a reason for subsequent surgery. In addition, CTA does not always detect small IA in the cavernous sinus of the internal carotid artery (these IA are also not treated surgically).

In the case of embolized aneurysms, there is currently the prospect of replacing the invasive method with a non–invasive method, in this case with MRA. This work demonstrates the application of TRICS – the TRICS data is perfectly reproducible compared to CA, making it a promising method for non-invasive monitoring of treated IA.

Experience with dynamic MRA shows that we can obtain valuable information about the intracranial vessels with this method, both after clipping of IA and after embolization.

The result, based on a small series of dynamic MRA examinations, has great potential to provide important new information about the intracranial arteries. Despite the small number of patients examined with the TRICKS method, data were obtained in two cases that contributed to the detection of pathological changes in the intracranial arteries:

in one case an aneurysm neck confirmed by CA data, in the other case a dissection of the vertebral artery. Conventional MRA did not allow us to obtain information about the rest of the aneurysm neck, which proved to be so important for a correct diagnosis.

Dynamic MRA therefore has a number of advantages: high resolution of the images of the intracranial arteries, non-invasiveness, no radiation exposure. In contrast to iodine-containing contrast media, gadolinium is generally better tolerated, although acute kidney failure can occur in rare cases. MRA with or without contrast medium is safer than CA.

Of course, the present research is limited to a small number of cases and the use of an MRI scanner from only one manufacturer. Other medical institutions may use other dynamic MRA programs, which may differ slightly from TRICS. There are plans to learn about other innovative visualization systems in the future.

However, the issue of postoperative follow-up of treated aneurysms has not yet been definitively clarified and there are no relevant clinical recommendations; research in this direction is actively underway.

An important aspect of the work of any medical institution is the economic component. Therefore, in this research, the cost of implementing the developed protocol was calculated and compared with the cost of implementing the current standard protocol, which includes CA. The new protocol has proven its cost-effectiveness: The use of CTA alone in 292 patients as the main method for the diagnosis of aneurysmal SAH resulted in significant cost savings, and this is without taking into account the savings resulting from not having to repeat the examinations at another institution. It is worth noting that the number of patients with non-traumatic SAH each year is much higher than the number of patients with aneurysmal SAH, namely around 350 patients. Therefore, the application of the method is fully justified from an economic point of view.

There is currently insufficient information in the literature on the cost-effectiveness of CTA compared to CA in the diagnosis of non-traumatic SAH. One of the largest studies in this field included 186 patients admitted to a medical facility with a clinical suspicion of non-traumatic SAH [85]. One group included 93 patients who underwent CTA on admission (74 of whom later required CA for diagnostic or treatment purposes), and the second group included 93 patients who underwent CA only at an earlier phase. The analysis showed that the costs for the diagnosis of non-traumatic SAH increased in the first group of patients. However, the cost-effectiveness analysis showed that the lower radiation exposure and the avoidance of the risks of invasive angiography (primarily radiation-induced cancers and neurological complications) fully justified the additional costs. The gradual expansion of the scope of application of CTA, including as a substitute for CA, therefore appears to be not only clinically but also cost-effective.

In modern reality, AI is increasingly being used in clinical practice by medical specialists. AI algorithms are able to shorten the time for image analysis and increase the efficiency of radiologists with high workloads [116]. The use of AI systems in the examination of patients with SAH will increase the likelihood of identifying the causal IA. The prototype three-dimensional convolutional neural network developed in this work, which determines the probability of the presence of IA based on CTA data, showed high sensitivity and specificity values that are comparable to the data available in the publications. In recently published papers, high sensitivity values of different AI methods have also been obtained in the detection of IA, but the common problem of such models so far is the presence of false positives. Further studies are needed to reduce this indicator, especially using CA as a reference technique. [39, 121, 147, 149, 173].

An overlooked IA can have catastrophic consequences, especially when you consider the likelihood of a rupture. Therefore, it is highly desirable for a specialist to have an automatic IA detection tool that improves work efficiency. The automatic IA detection tool presented in this research will not only significantly improve the accuracy of interpretation of CTA data but may also lead to a more favorable prognosis.

The results of the studies performed showed high values for sensitivity, specificity and overall accuracy (85.1, 95.1 and 91%, respectively) when using a neural network prototype to detect IA from CTA data. The resulting model makes it possible to expand the skills of radiologists and improve their diagnostic capabilities.

Of course, the research also has its limits. Firstly, the research focused only on IA in the preoperative phase. Therefore, the efficiency of the model in detecting IA in recurrences after coil or surgical clipping or IA associated with arteriovenous malformations has not been investigated. Secondly, no patients with surgical devices or appliances were examined in the research, so the effectiveness of the model for such patients is unknown. In clinical practice, CTA is generally used not only to detect IA, but also to assess many types of vascular disease. The high prevalence of IA in the test suite and the binary task of the radiologist could therefore cause an interpretation error. In addition, this research was conducted at a single center and with scanners from only two manufacturers and may not reflect effectiveness when extrapolated to data from other institutions with different scanners and imaging protocols. The research involved radiologists (including a resident) with extensive experience in scheduled and emergency CTA BCA. Nevertheless, the diagnostic value of their answers increased significantly when they used the prototype data. Given these data, the prototype can expand the possibilities and improve the diagnostic skills of specialists who rarely come into contact with this pathology, which is extremely important in the context of regional health care.

Undoubtedly, the prototype obtained must be improved by increasing the amount of data for training and classifying the IA into groups according to the fact of rupture (ruptured and unruptured), quantity (single and multiple IA) and localization. It is also necessary to continue the research and to test the hardware and software complex in the region's vascular centers on more patients and with devices from other manufacturers. This work continues as part of the implementation of the strategic academic leadership development program “Priority 2030” for the scientific project “Development of an artificial intelligence-based system for decision support in the assessment of vascular pathology using CTA”.

Modern AI algorithms aim not only to detect IA, but also to assess the risk of their rupture, with the most important criteria being the size and shape of the IA [158]. Automated algorithms are being developed to compensate for the subjective factor in the evaluation of these parameters [173]. An important parameter for the further management of the patient is also the determination of the IA neck area. The models are created on the basis of a topological analysis of the vascular structures [97]. It is already possible to calculate the size and shape of the IA with some modern models [131, 172].

A fundamentally new field of research in connection with AI is the prediction of the results of its treatment. For example, Paliwal et al. (2018) compared four AI algorithms for predicting outcomes for six months in patients after IA treatment by implanting a device to change the direction of flow; the maximum prediction accuracy was 90% [122]. However, there was no clear validation system for the results, so further research is needed to develop an accurate mechanism for selecting patients for IA treatment using this method. Although these systems are not yet widely used in practice, this area is developing rapidly and will be able to occupy its niche in the diagnosis of IA and non-traumatic SAH in the future.

CONCLUSIONS

1. The clinical and statistical analysis showed that the cause of the hemorrhage was the rupture of an intracranial aneurysm in 92% of cases. In 81% of cases, single aneurysms were found in the patients, in 19% – multiple aneurysms. Women are most frequently affected – 60%, while the share of working age individual is 95% for men and 84% for women. The RVC in the Krasnodar Territory operates on up to 200 patients in the acute phase of an IA rupture every year. A medical and social problem is the complication of the rupture – vasospasm – which occurs in 32% of cases; the consequences of vasospasm lead to disability. A fatal outcome is observed in 15.8% of patients.

2. Emergency CTA BCA has a high diagnostic accuracy in detecting IA in the acute period of rupture: its sensitivity in comparison with CA data was 78.36%, specificity – 60%, overall accuracy – 78%. Compared to intraoperative data, the sensitivity and overall accuracy of CTA BCA is 96-97%.

3. The reasons why the IA that caused the hemorrhage was overlooked are vasospasm, dynamic blurring due to the patient’s physical activity, small size of the aneurysm (less than 3 mm).

4. Atherosclerosis of the carotid and vertebral arteries is the most frequently detected pathology in patients in the acute phase of non-traumatic SAH (34.5%), including those with hemodynamically significant stenoses (10.6%). Anomalies in the development of the brachiocephalic artery were found in one fifth of patients (21.5%). Concomitant extracranial vascular pathology was associated with unfavorable outcomes of IA treatment. In CT angiography of the brachiocephalic artery, the scan area must include the extracranial segments of the artery (from the level of the aortic arch).

5. The experience of a radiologist has a significant impact on the results of the research analysis: when CTA BCA was reviewed by a radiologist with experience in describing such CTA, the values of sensitivity and overall accuracy increased compared to the intraoperative data. For single aneurysms, sensitivity and overall accuracy

increased by 1.8% and 2%, reaching 95.8% and 96%, respectively. In multiple aneurysms, the sensitivity and overall accuracy of CT angiography of the brachiocephalic artery improved by 5.5 and 5% and amounted to 100 and 98%, respectively.

6. It was found that the developed prototype of a three-dimensional, ultra-precise neural network made it possible to increase the detectability of IA with CTA BCA data (with sensitivity of 100%, specificity increased by 30.77% and overall accuracy – by 7%) leading to lower probability of rupture.

7. The diagnostic accuracy of CTA BCA in postoperative follow-up of IA was as follows: the sensitivity of the method is 83.3%, the specificity – 97.6%, the overall accuracy – 94%, the positive predictive value – 90.9%, the negative predictive value – 95.3%. The role of CTA BCA in detecting new intracranial aneurysms in treated patients is also shown: the sensitivity, specificity, overall accuracy, positive and negative predictive values reached 60, 100, 94, 100 and 93.9%, respectively.

8. The diagnostic value the dynamic MRA in postoperative follow-up of IA was as follows: the sensitivity of the method is 100%, the specificity – 100%, the overall accuracy – 100%, the positive predictive value – 100%, the negative predictive value – 100%.

9. The algorithm developed for diagnostic support has proven its effectiveness. Due to the high diagnostic accuracy, the use of CTA BCA made it possible to determine the course of the patient’s disease, avoid unnecessary invasive diagnostic procedures, reduce the time required to examine patients and apply management tactics. The economic effect of implementing the proposed algorithm for the diagnosis of non-traumatic SAH (the use of CTA BCA instead of CA) saved at least RUB 16,500 per patient and RUB 1,979,939 for 2 years of work in a multidisciplinary hospital.

PRACTICAL RECOMMENDATIONS

1. At the regional health facilities, all patients admitted to the emergency department of the RVC with an initial diagnosis of acute non-traumatic SAH must undergo an immediate native CT scan of the brain. If the diagnosis of acute non-traumatic SAH is confirmed by a native examination, it is necessary to perform a CT angiography of the brachiocephalic artery (CTA BCA). These diagnostic measures must be carried out in all patients with non-traumatic SAH, regardless of where the subsequent surgical treatment is to take place.
2. The protocol for CTA BCA must include the extracranial segments of the carotid and vertebral arteries, starting with the aortic arch.
3. If a non-traumatic SAH is present after a native CT of the head and the CTA results are consistent with the localization of the hemorrhage, then these data are sufficient to consider the possibility of direct surgical intervention without performing a preoperative CA, which is particularly important in severe patients.
4. If there is a lack of qualified professionals to assess CTA BCA, a second review with the help of a more experienced specialist is recommended; possibly using telemedicine resources, a radiologic electronic network and image analysis with AI based on a three-dimensional ultra-precise neural network.
5. The improvement of the studied prototype of a convolutional neural network for the search and analysis of IA by increasing the size of the database for training and setting more complex tasks will increase the diagnostic efficiency, namely: the localization of aneurysms, their number, the differentiation of ruptured and unruptured IA.
6. MRI and dynamic MRA (e.g. using TRICS or analogs) are recommended as a method for non-invasive postoperative follow-up of IA (embolized and clipped), especially in cases of intolerance to iodine preparations.
7. As a non-invasive postoperative follow-up for clipped IA, it is recommended to perform CTA BCA with a 64-row detector CT scanner or more.

LIST OF ABBREVIATIONS

ADPKD – autosomal dominant polycystic kidney disease

BCA – brachiocephalic arteries

SCA – superior cerebellar artery

SHA – superior hypophysial artery

IVH – intraventricular hemorrhage

WI – weighted images

HIV – human immunodeficiency virus

ICA – internal carotid artery

HCPT – heterogeneity of capillary passage time

CI – confidence interval

PCA – posterior cerebral artery

PICA – Posterior inferior cerebellar artery

PConA– posterior connective artery

IA – intracranial aneurysm

AI – artificial intelligence

MI – myocardial infarction

CMA – callosomarginal artery

CT – computed tomography

CTA – computed tomography angiography

MMP – matrix metalloproteinases

MRA – magnetic resonance angiography

MCAP – macrophage chemoadhesive protein

NSD – Neurosurgical Department

nTSH – non-traumatic subarachnoid hemorrhage

MA - main artery

AVCC – acute violation of cerebral circulation

VA – vertebral artery

STA – superficial temporal artery

PCA– pericallous artery

ACA – anterior cerebral artery

PVD – primary vascular department

ACA – Anterior Connective artery

RVC– Regional Vascular Center

SAH – subarachnoid hemorrhage

MCA – middle cerebral artery

SML – supraorbital-meatal line

CHF – chronic heart failure

COPD - chronic obstructive pulmonary disease

CAG – cerebral angiography

ECG – electrocardiography

EEG - electroencephalography

DWI – Diffusion-weighted imaging

FLAIR – Fluid attenuated inversion recovery

HH –Hunt-Hess scale

MIP – Maximum intensity projection

NASCET – North American Symptomatic Carotid Endarterectomy Trial

NF-kB – ядерный фактор каппа-B

SPGR – Spoiled gradient recalled

SSD – Single shot detector

SWAN – Susceptibility weighted imaging

TOF – Time-of-flight

QALY – Quality-adjusted life years

UTE – Ultrashort echo time

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