Research Article

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Surgical Treatment of Cerebral Aneurysms in the Acute Period of Subarachnoid Hemorrhage: Long-Term Result

I.M. Shetova[1], V.D. Shtadler[1] *, P.D. Matveev[2, 3], V.A. Lukyanchikov[1, 2], V.V. Krylov[1, 2]

Department of Neurosurgery and Neuroresuscitation
1 A.I. Evdokimov Moscow State University of Medicine and Dentistry
20 Delegatskaya St., Moscow 127473, Russian Federation
2 N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Health Department
3 B. Suharevskaya Sq., Moscow 129090, Russian Federation
3 Federal Center of Brain and Neurotechnology
1 Ostrovitjanova St., Moscow 117997, Russian Federation

***Contacts:** Vladislav D. Shtadler, Resident of the Department of Neurosurgery and Neuroresuscitation of the A.I. Evdokimov Moscow State University of Medicine and Dentistry. Email: vladislav.shtadler@gmail.com

ABSTRACT The influence of the consequences of aneurysmal subarachnoid hemorrhage on the human body in the long-term period has been insufficiently studied. Most studies indicate a high risk of developing cognitive impairment. Until now, there is no unified algorithm for the management of patients with aneurysmal subarachnoid hemorrhage, who need long-term comprehensive rehabilitation and supervision of specialists in various fields.

AIM OF STUDY To study the influence of the nature, severity, features of the clinical manifestation of aneurysmal subarachnoid hemorrhage, as well as the choice of the method of intervention in the acute period of the disease on the long-term results of treatment of aneurysms.

MATERIAL AND METHODS In the presented study, the observation group included 74 patients who were operated on in the emergency neurosurgery department of the N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Health Department from 2013 to 2019 in the acute period of subarachnoid hemorrhage (during the first 14 days after the rupture of the cerebral aneurysm). The average age of patients at the time of surgery was 47 [Me=46; min=27; max=76] years old. The ruptured aneurysm was turned off from the bloodstream by one of the following methods: microsurgical intervention with the application of a clip to the aneurysm neck (50 (67.6%) patients), the simultaneous open intervention of aneurysm clipping, and the formation of an extra-intracranial micro anastomosis from the side of the aneurysm access (8 (10.8%) patients), endovascular exclusion of the cerebral aneurysm from the bloodstream (16 (21.6%) patients). On average, after 2.4 [Me=2.5; min=1; max=6] years, patients were invited for a clinical and neurological examination, which included testing according to the Modified Rankin Scale (MRS), the Bartel Index, the Mini-mental State Examination (MMSE), and the Hospital Anxiety and Depression Scale (HADS). We analysed the changes in the professional activity and habitual lifestyle of patients, as well as the influence of the most common risk factors: arterial hypertension, diabetes mellitus, smoking, on long-term outcomes.

RESULTS In the long-term period of surgical treatment of cerebral aneurysms, on average after 2.4 [Me=2.5; min=1; max=6] years after subarachnoid hemorrhage, 30 (40.5%) patients scored 0 points on the Modified Rankin Scale, 27 (36.5%) patients – 1 point, 6 (8.1%) patients — 2 points, in 6 (8.1%) patients – 3 points, in 4 (5.4%) patients – 4 points and in 1 (1.4%) patient – 5 points. A statistically significant relationship of the disability degree assessed by mRs in the long-term period of SAH from the patient's condition severity assessed by the Glasgow outcome scale at discharge from the hospital ($p<0.001$) was revealed. The patient's age at the time of rupture of the aneurysm independently influenced cognitive functions and the ability to self-care in the long-term period. With an increase in age by 1 year, the score on the short scale of mental status and on the Bartel Index decreased by 0.08 ($p=0.03$) and by 0.3 ($p=0.04$), respectively. With the simultaneous presence of intracerebral hemorrhage and the severity of subarachnoid hemorrhage corresponding to grade III according to the Fisher classification, the likelihood of developing anxiety and depressive mental disorders according to the Hospital Anxiety and Depression Scale (HADS) increased significantly ($p<0.01$). The development of intracerebral hematoma with aneurysmal hemorrhage contributed to the appearance of hypertension ($p<0.05$).

CONCLUSION The revealed disorders that persist for several years after the intervention indicate the need for long-term follow-up of patients who underwent intervention for subarachnoid hemorrhage, the development of individual programs for physical and psychological rehabilitation, and clinical examination of persons at high risk.

Keywords: subarachnoid hemorrhage, aneurysm, follow-up, low-flow bypass, endovascular intervention

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Affiliations

Irma M. Shetova	Candidate of Medical Sciences, deputy director of the University Clinic of the A.I. Evdokimov Moscow State University of Medicine and Dentistry; https://orcid.org/0000-0001-8975-7875, shetova@gmail.com; 25%, participation in organizing the process, writing part of the article text
Vladislav D. Shtadler	Resident of the Department of Neurosurgery and Neuroresuscitation of the A.I. Evdokimov Moscow State University of Medicine and Dentistry; https://orcid.org/0000-0002-7584-3083, vladislav.shtadler@gmail.com; 25%, participation in organizing the process, writing part of the article text
Pavel D. Matveev	Head of the Department of X-ray Surgical Methods of Diagnostics and Treatment of the Federal Center of Brain and Neurotechnology; https://orcid.org/0000-0002-1114-6238, mpaveld@gmail.com; 20%, participation in organizing the process, writing part of the article text

Viktor A. Lukyanchikov	Doctor of Medical Sciences, Professor of the Department of Neurosurgery and Neuroresuscitation, Head Physician of the Clinical Center of the Maxillofacial and Plastic Surgery and Dentistry of the A.I. Evdokimov Moscow State University of Medicine and Dentistry; https://orcid.org/0000-0003-4518-9874, vik-luk@yandex.ru; 17%, participation in organizing the process, writing part of the article text
Vladimir V. Krylov	Academician of the Russian Academy of Sciences, Doctor of Medical Sciences, Professor, Honored Worker of Science of the Russian Federation, Head of the Department of Neurosurgery and Neuroresuscitation of the A.I. Evdokimov Moscow State University of Medicine and Dentistry, Chief Researcher of the Department of Emergency Neurosurgery of the N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Health Department, Chief Freelance Neurosurgeon of the Ministry of Health of Russia; https://orcid.org/0000-0001-5256-0905, manuscript@inbox.ru; 13%: organization of the process, correction and approval of the text of the article

DCT, decompressive cranial trepanation
CT, computed tomography
CVA, cerebrovascular accident
SAH, subarachnoid hemorrhage
MCA, middle cerebral artery
GOS, Glasgow Outcome Scale
EICMA, extra-intracranial microanastomosis
HADS, the Hospital Anxiety and Depression Scale
MMSE, Mini-mental State Examination
mRs, modified Rankin scale

INTRODUCTION

Subarachnoid hemorrhage (SAH) is one of the most severe types of acute cerebrovascular disease, most often affecting young and middle-aged people and leading to the loss of many years of productive life. The most common cause of SAH (up to 85% of cases) is a ruptured brain aneurysm [1]. Despite the fact that only 7% of acute cerebrovascular accidents (CVAs) are caused by a ruptured cerebral artery aneurysm with the SAH formation [2], SAH accounts for about a third of all stroke deaths in patients younger than 65 years of age [3]. The peak incidence of SAH is attributed to the age range of 40-60 years [4]. Over the recent decades, the survival rate after aneurysmal SAH has increased by an average of 17% due to improved measures for early diagnosis and specialized treatment for CVA [5, 6]. The mechanisms of SAH damaging effect and its complications (such as angiospasm and delayed ischemia) on the brain have been described in detail. Protocols of evaluation and treatment of patients in the acute phase of the disease have been developed and implemented [7].

However, the long-term effects of SAH on the human body have not been sufficiently studied. The results of most studies indicate a high risk of cognitive impairments after SAH in the long-term period after surgical treatment of brain aneurysms, even with good functional recovery and the absence of disability and dependence on others [8-10]. Mental disorders in the form of anxiety and depression, which aggravate cognitive deficits and hinder active socialization of patients, are frequent companions of cognitive impairment in patients who have had SAH [11-12]. Risk factors for an incomplete functional recovery of patients in the long-term period of aneurysm surgery may include severe conditions at admission to the hospital, massive SAH, the presence and extent of angiospasm, and the development of hydrocephalus [13-19].

To date, there is no uniform algorithm for managing patients with SAH consequences. Meanwhile, it is obvious that the very fact of hemorrhage and its complications do not pass without a trace for the brain substance, and a patient who has suffered aneurysmal SAH needs a long-term comprehensive rehabilitation and observation by specialists of various profiles (neurologist, neuropsychologist, speech therapist, occupational therapist).

The aim of this study was to investigate the impacts of the SAH nature and severity, the specific features of the hemorrhage clinical manifestations, and the choice of intervention technique in the acute stage of the disease on the long-term outcomes of aneurysm treatment.

MATERIAL AND METHODS

Since 2019, within the framework of the Russian Study on Aneurysm Surgery [20] a prospective follow-up of patients who suffered SAH resulted from ruptured brain aneurysms has been conducted.

In the presented study, the observation group included 74 patients who were operated on in the acute stage of SAH (during the first 14 days after a brain aneurysm rupture) in the Department of Urgent Neurosurgery of N. V. Sklifosovsky Research Institute for Emergency Medicine in the period from 2013 to 2019. The mean age of patients at the time of surgery was 47 [Me=46; min=27; max=76] years. The study included 30 men and 44 women. The mean follow-up period after surgery was 2.4 [Me=2.5; min=1; max=6] years.

Upon admission to the clinic for the surgical treatment of a ruptured brain aneurysm, all patients underwent a standard clinical and instrumental examination, which included:

1. Computed tomography (CT) of the brain with the reconstruction of 0.5 mm sections. In the presence of SAH, it was graded by Fisher Scale (C. M. Fisher, 1980); the localization and volume of intracerebral and intraventricular hemorrhages, and the severity of hydrocephalus were also evaluated.

According to the SAH intensity and extent, the patients were distributed as follows: the hemorrhage was assessed as Fisher Grade I in 5 patients (6.7%), Fisher Grade II in 11 patients (14.9%), Fisher Grade III in 19 patients (25.7%), and Fisher Grade IV in 39 patients (52.7%).

2. CT angiography of intracranial arteries with the reconstruction of 0.5 mm sections after intravenous administration of contrast agent, 60 mL. CT angiography was used to visualize the brain aneurysm, its localization, and anatomical features for planning surgical intervention.

In the study population, 20 patients (27%) had internal carotid artery aneurysms, 29 (39.2%) had middle cerebral artery (MCA) aneurysm, 14 (18.9%) had anterior cerebral artery aneurysm, 4 (5.4%) had vertebrobasilar aneurysm, and 7 (9.5%) had multiple aneurysms.

3. The Hunt and Hess Scale (W.E. Hunt, R.M. Hess, 1968) was used to assess the severity of patients in the acute period of SAH and the risk of postoperative mortality.

The condition severity before surgery corresponded to grade I–II in 36 patients (48.7%), grade III in 34 patients (45.9%), and grade IV in 4 patients (5.4%).

4. We analyzed the onset of the disease, taking into account the acute symptoms (intense "thunderous" headache, vomiting, loss of consciousness) to determine the impact of these factors on in-hospital and long-term outcomes.

5. The categorization of outcomes with an assessment of the patient's level of consciousness was made using the Glasgow Outcome Scale (GOS, B. Jennett, M. Bond, 1975).

The condition severity was scored 5 by GOS in 46 patients (62.1%); in 15 patients (20.3%), moderate disorders of brain function were detected and scored 4 by GOS, in 13 patients (17.6%), the condition severity at discharge corresponded to score 3 by GOS.

Based on the results of the examination, a decision was made on the choice of the intervention approach for cerebral aneurysm rupture.

Microsurgical intervention with the clip application on the neck of the aneurysm and the exclusion of the aneurysm from the bloodstream was performed in 50 patients (67.6%). Decompressive cranial trepanation (DCT) was performed in 18 patients (36%) operated on using microsurgical techniques.

A simultaneous open intervention for clipping the aneurysm and forming an extra-intracranial microanastomosis (EICMA) between the branches of tegmental or cortical MCA segments and the parietal branch of superficial temporal artery from the side of the access to the aneurysm were performed if the cerebral perfusion disorders had been detected in the aneurysm-carrying artery pool in the form of a decreased cerebral blood flow (CBF) by 20% or more compared to the contralateral side, as assessed by a single-photon emission CT or CT-perfusion [21]. The method of simultaneous intervention was used in 8 patients (10.8%), 4 (50%) of whom underwent DCT.

Endovascular exclusion of the cerebral aneurysm from the bloodstream was performed in cases of cerebral aneurysms that were difficult to access via open intervention, also taking into account the capabilities of the clinic. Endovascular intervention was performed in 16 patients (21.6%).

The intervention was performed at 1–3 days after the aneurysm rupture in 30 patients (40.5 %), at 4-7 days after the aneurysm rupture in 26 patients (35.2%), at 8-11 days in 10 patients (13.5 %), and at 12-14 days in 8 patients (10.8%).

After a mean of 2.4 [Me=2.5; min=1; max=6] years, the patients who underwent surgery for the rupture of cerebral aneurysm were invited to a clinical and neurological follow-up examination, which included evaluations by using neurological scales to assess the degree of disability, dependence on others, quality of life, ability of self-care, and the severity of cognitive impairments and mental disorders (anxiety and depression).

1. The Modified Rankin Scale (mRs, 1988) was used to assess the degree of disability, independence and outcomes of rehabilitation, as well as to analyze the patient's functioning in a real-world environment, and the patient's need for help from other people.

2. To analyze the daily life activities, the Barthel Activities of Daily Living Index (1955) was used as a tool for assessing independence in everyday life.

3. The Mini-mental State Examination (MMSE, 1975) was used to assess the patient's cognitive functions and identify possible cognitive impairments, in particular dementia.

4. The Hospital Anxiety and Depression Scale (HADS, 1988) was used to determine the anxiety and depression level, as well as to assess the patient's emotional state and well-being.

5. We conducted a survey of patients and analyzed medical records (outpatient records and discharge epicrises), which revealed the most common risk factors: arterial hypertension, diabetes mellitus, smoking, before surgery and after discharge from the hospital and before visiting the clinic in the long-term follow-up. We analyzed changes in professional activity after the intervention for cerebral aneurysm (inability to perform professional activities, changes in labor intensity), as well as changes in patient's usual way of life: hobbies, marital status; we took into account the assignment of a disability group after the intervention.

For statistical data processing, we used the licensed version of STATISTICA 12, Microsoft Office Excel 2007.

RESULTS

A multivariate regression analysis was performed, in which the impact of demographic parameters, the condition severity according to the Hunt and Hess Scale, the timing and method of surgery, the SAH severity according to Fisher Scale, the presence of intracerebral or intraventricular hemorrhage, and hospital outcomes by GOS on the degree of patient functional recovery were assessed in a long-term period, the ability to fulfill previous professional duties, change in the lifestyle (change in hobbies, marital status), allocation to a disability group, and the dynamics of the present main vascular risk factors after mean of 2.4 [Me = 2.5; min = 1; max = 6] years post-SAH.

The analysis of the condition severity at discharge according to GOS in patients whose aneurysm was excluded from the bloodstream by different methods revealed the predominance of favorable outcomes (GOS score 5) among patients who had the aneurysm excluded by using a simultaneous technique of aneurysm clipping with applying EICMA (75%) and using endovascular technique (68%) compared to the patients who underwent microsurgical aneurysm clipping only (58%). In the group of patients whose aneurysm was excluded from the bloodstream by using microsurgical techniques, a severe brain function disorder (corresponding to score 3 by GOS) was more often (in 20% of cases) detected at discharge compared to the patients who used simultaneous and endovascular techniques (score 3 by GOS was observed in 12.5% of cases when using both methods). However, due to the small sample size of patients who underwent EICMA, this correlation was not statistically significant (Figure 1).

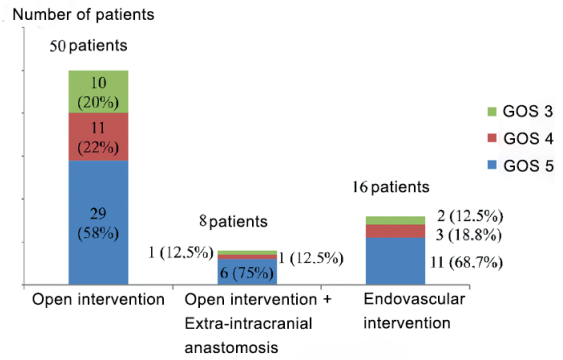

Fig. 1. Hospital outcomes at discharge according to the Glasgow Outcome Scale depending on the type of surgery (n=74)

In the long-term postoperative period after the surgical treatment of cerebral aneurysms, after a mean of 2.4 [Me=2,5; min=1; max=6] years after suffering SAH, 30 patients (40.5 %) had no difficulties in daily life activities or disability; these patients were completely independent from the others in everyday life (scored 0 by the modified Rankin Scale); 27 patients (36.5 %) had a minimum of difficulties in daily life activities, scored 1 by the mRs, which did not affect the performance of daily duties; 6 patients (8.1 per cent) had mild

degree of difficulties in daily life (score 2 by the mRs); moderate disability and the difficulties in daily life, assessed as score 3 by the mRs were also identified in 6 patients (8.1 %); 4 patients (5.4 %) had severe difficulties in daily life activities assessed by mRs score 4; and there was 1 patient (1.4 %) diagnosed with severely impaired human life and a complete dependence from others in everyday life (score 5 according to the mRs).

The relationship of the disability degree to the choice of the method of excluding the aneurysm from the bloodstream was found in the patients in the long-term period of surgical treatment: severe and gross disorders in daily life activities and complete dependence on others in everyday life were revealed only in patients whose aneurysm was excluded from the bloodstream by using a microsurgical technique (in 10% of cases, gross and pronounced disorders of daily life activities were observed assessed by mRs scores 4 and 5) (Fig. 2). Complete functional recovery (score 0 or 1 by Rankin scale) was recorded in 81% of cases after endovascular intervention, in 87.5% of cases after EICMA, and 74% after microsurgical treatment.

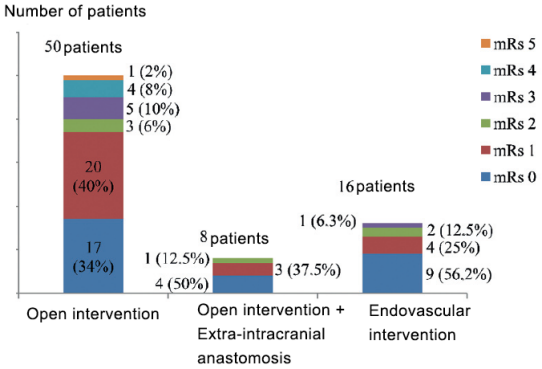

Fig. 2. Disability degree according to the modified Rankin scale in the long-term period of surgical treatment (n=74)

A statistically significant relationship of the disability degree according to the modified Rankin scale in the long-term period of SAH to the severity of the patient's condition at discharge from the hospital according to GOS was revealed ($p < 0.001$). In the patients with severe functional disorders of the central nervous system at discharge from the hospital, pronounced and gross impairments of daily life activities in the long-term period were statistically significantly more often detected (Fig. 3).

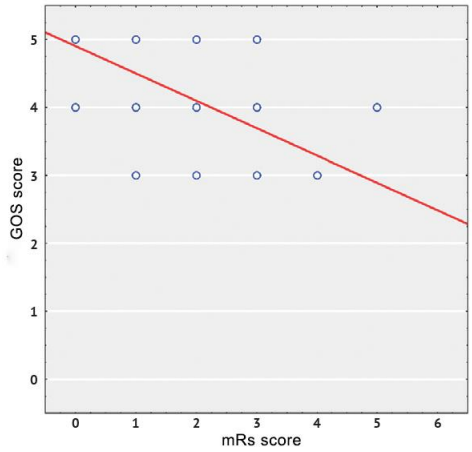

Fig. 3. Disability degree of patients according to the modified Rankin scale in the long-term period of surgical treatment of cerebral aneurysms (n=74)

According to the results of our study, the patient's age at the time of aneurysm rupture independently affected cognitive functions in the long-term period of the disease (p=0.03, statistically significant); with an increase in age by 1 year, the MMSE score decreased by 0.08 (Fig. 4).

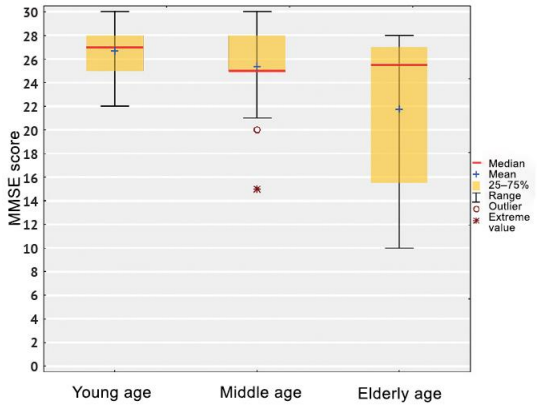

Fig. 4. Cognitive functions of patients of different ages in the long-term period of hemorrhage (n=74)

The age of patients at the time of aneurysm rupture also independently affected the ability to self-care in the long-term period, according to the evaluation results by using the Bartel Index (p=0.04, statistically significant). With an increase in age by 1 year, the Barthel Index decreased by 0.3 (Fig. 5).

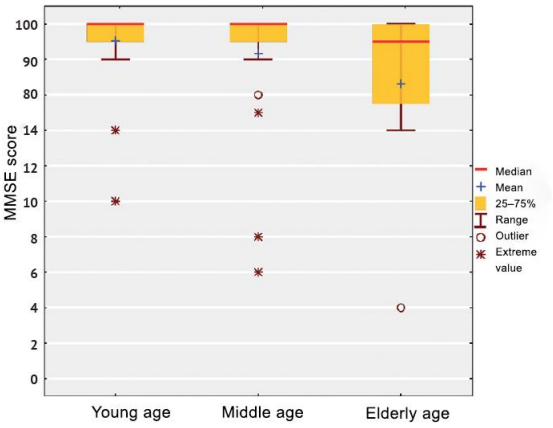

Fig. 5. The ability for self-care according to the Barthel Index in the long-term period of SAH in patients of different ages (n=74)

When analyzing the severity of the anxiety and depression manifestations in patients in the long-term period of the surgical treatment, we identified the simultaneous impact of intracerebral hemorrhage and the extent of basal SAH assessed by the Fisher scale on the occurrence of anxiety in the long-term period. With the simultaneous presence of intracerebral hemorrhage and the SAH severity assessed as Grade III by the Fisher classification, the probability of developing anxiety and depressive mental disorders statistically significantly increased ($p<0.01$).

The development of intracerebral hematoma in aneurysmal SAH contributed to the occurrence of hypertension at mean 2.4 years after hemorrhage ($p<0.05$; statistically significant).

We analyzed the impact of the SAH onset (dynamics of symptom development) on patients' recovery in the long-term period. We noted that adverse outcomes by GOS estimation were more likely to occur in patients whose disease onset was characterized by "thunderous" headache, vomiting, and loss of consciousness. All patients (100%) whose severity was assessed as Grade IV–V by Hunt and Hess Scale in the first hours of the disease had an acute onset of SAH accompanied by intense headache, vomiting, and subsequent loss of consciousness. These patients, even after successful surgery, developed severe disability in the long-term of the disease corresponding score 4-5 by the modified Rankin scale ($p<0.05$; statistically significant). Poor functional outcomes in this group of patients were due to vascular spasm and subsequent cerebral ischemia or the aresorptive hydrocephalus development.

According to the results of the presented study, the timing of surgical intervention for cerebral aneurysm rupture did not affect the long-term outcomes of the disease.

According to the results of this study, the probability of changing hobbies (the appearance of new hobbies and leisure options) in the long-term period of surgical treatment was higher in the patients with Grade I–II SAH severity by the Hunt and Hess Scale, whose surgical intervention was performed within 7-14 days from aneurysm rupture ($p<0.03$; statistically significant).

DISCUSSION

Improvements in the system of care for patients with acute CVA, including the increase in surgical activity in acute brain pathology, the development of emergency care, intensive care, and early rehabilitation have led to decreased mortality and disability in operated patients [14]. However, as for the patients who underwent surgery for a ruptured cerebral aneurysm, the issues of their management after the discharge from a neurosurgical hospital are still debated.

The results of present day studies indicate the development of cognitive and mental disorders, which, along with incomplete functional recovery, are most likely to cause low resocialization of patients after SAH [11-12, 22-24].

We found that the risk factors for cognitive impairments aggravated by mental disorders such as anxiety and depression, asthenia, mood disorders, and sleep disorders, are most often the severity of neurological symptoms during cerebral aneurysm rupture, preoperatively as well, and a massive SAH in combination with intracerebral and intraventricular hemorrhages. The obtained data are consistent with the results of other investigators [25-28].

According to the results of our study, the choice of intervention approach in the acute period of SAH was crucial for the patient recovery both at discharge and in the long-term period of surgical treatment: 68% of patients who had the aneurysm excluded from the bloodstream using endovascular techniques and 75% of patients who underwent aneurysm clipping and EICMA did not have a pronounced neurological deficit at discharge (score 5 by GOS). Patients who underwent microsurgical aneurysm clipping did not have a deficit in only 58% of cases. The same trend retained in the long-term period of surgical treatment (mean at 2.4 years after the discharge).

The lack of statistical significance in the advantage of one of the methods of surgical treatment for aneurysms over the other in our study is most likely caused by a small number of patients who underwent EICMA (8 patients), which indicates the need for further analysis in order to establish the effect of the method chosen for the cerebral aneurysm exclusion from the bloodstream on patient recovery in the long-term period. In our opinion, the EICMA applied in the acute period of surgical treatment for a brain aneurysm rupture can improve the brain tissue perfusion, which contributes to better functional recovery in the early and long-term periods after the discharge.

The literature describes the advantage of using the endovascular technique over microsurgical aneurysm exclusion for the long-term prognosis of patient recovery based on the results of a retrospective analysis of multiple studies that included data from 2458 patients [29]. After one year of follow-up, 24% of patients randomized for endovascular treatment and 32% of patients randomized to the microsurgical treatment group showed an incomplete functional recovery and disability corresponding to score 3-6 by the modified Rankin scale. Based on the results of the ISAT (International Subarachnoid Aneurysmal Trial) study in patients who underwent endovascular surgery, the survival and independence at home 10 years after the intervention was higher (83%) than in patients who underwent microsurgical intervention (79%). However, the patients after endovascular intervention were more likely to have recurrent bleeding within 1 year after treatment [30].

According to the results of the presented study, an unfavorable factor affecting the ability to self-care and cognitive functions in the long-term period of the disease was the patient's age at the time of aneurysm rupture: with increase in age, the prognosis for a functional outcome and recovery of cognitive functions worsened, which was also confirmed by the results of previous studies [26, 31].

The revealed association of the acute onset of SAH symptoms ("thunderous headache", loss of consciousness, and vomiting at the onset of the disease) with the severity of the patient's condition and the outcome by GOS most likely indicates the severity of general cerebral symptoms due to massive basal and parenchymal hemorrhage, brain edema, the dislocation of brain structures as prognostically unfavorable factors for patient recovery.

CONCLUSION

After the surgical treatment of brain aneurysms in the acute period of hemorrhage, 59.6% of patients have an incomplete functional recovery in the long-term. Such patients develop cognitive and mental disorders that reduce the quality of life, interfere with their full-fledged social adaptation and determine their dependence on others.

Risk factors of incomplete functional recovery in the long-term postoperative period are the patient's severe condition before surgery, widespread basal subarachnoid hemorrhage in combination with intracerebral hematoma, and advanced age.

The best functional recovery in the long-term period was observed after endovascular treatment of aneurysms.

The identified disorders that persist for several years after the intervention indicate the need for a long-term follow-up of patients undergoing surgery for subarachnoid hemorrhage, the development of individual programs for physical and psychological rehabilitation, and medical examinations of high-risk individuals.

FINDINGS

In the long-term period of surgical treatment for brain aneurysms, at mean 2.4 [Me=2.5; min=1; max=6] years after the subarachnoid hemorrhage:

1. A statistically significant relationship of the disability degree by mRs in the long-term period of subarachnoid hemorrhage to the patient's condition severity assessed by Glasgow Outcome Scale at hospital discharge was revealed ($p<0.001$).

2. Patient's age at the time of aneurysm rupture independently affected cognitive functions and the ability to self-care in the long-term period. With an increase in age by 1 year, the scores in the Mini-mental State Examination and the Bartel Index statistically significantly decreased by 0.08 ($p=0.03$) and 0.3 ($p=0.04$), respectively.

3. With the simultaneous presence of intracerebral hemorrhage and the grade III severity of SAH assessed by Fisher Scale, the probability of developing anxiety and depressive mental disorders statistically significantly increased ($p<0.01$) as assessed by the Hospital Anxiety and Depression Scale.

4. The development of intracerebral hematoma in aneurysmal hemorrhage contributed to the occurrence of hypertension ($p<0.05$).

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