факторов травматического остеомиелита нижней челюсти. Волгоградский научно-медицинский журнал. 2010;4:41-44. [Fomichev E.V., Kirpichnikov M.V., Podolsky V.V. Analysis of the etiological factors of traumatic osteomyelitis of the lower jaw. Volgograd Scientific Medical Journal. 2010; 4: 41-44. (In Russ.).] https://readera.ru/analiz-jetiologicheskih-faktorov-travmaticheskogo-osteomielita-nizhnej-cheljusti-142148866

8. Фомичёв Е.В., Островский О.В. Кирпичников М.В. Эффективность лечения больных травматическим остеомиелитом нижней челюсти с помощью эфферентных методов. Волгоградский научно-медицинский журнал. 2010;3:42-45. [Fomichev E.V., Ostrovsky O.V. Kirpichnikov M.V. Effectiveness of treatment of patients with traumatic osteomyelitis of the lower jaw by means of efferent methods. Volgograd Scientific Medical Journal. 2010. 3:42-45. (In Russ.).] https://cyberleninka.ru/article/n/effektivnost-lecheniya-bolnyh-travmaticheskim-osteomielitom-nizhney-chelyusti-s-pomoschyu-efferentnyh-metodov

9. Ярыгина Е.Н., Смотрова Е.В., Кирпичников М.В. Диагностика эндогенной интоксикации у больных атипично текущими флегмонами и челюстно-лицевой области и травматическим остеомиелитом нижней челюсти. Вестник Российского государственного медицинского университета. 2006;2: 202. [Yarygina E.N., Smotrova E.V., Kirpichnikov M.V. Diagnosis of endogenous intoxication in patients with atypically flowing phlegmon and maxillofacial area and traumatic osteomyelitis of the lower jaw. Bulletin of the Russian State Medical University. 2006; 2:202. (In Russ.).] https://cyberleninka.ru/article/n/sovremennye-osobennosti-klinicheskih-proyavleniy-odontogennogo-i-travmaticheskogo-osteomielita-nizhney-chelyusti

10. Mihara M, Uchiyama M, Fukuzawa K. Thiobarbituric acid value on fresh homogenate of rat as a parameter of lipid peroxidation in aging, CCl4 intoxication and vitamin E deficiency. *Biochem. Med.* 1980; 3 (23):302–311. https://www.ncbi.nlm.nih.gov/pubmed/7417237

11. Prieto P, Pineda M, Aguilar M. Spectrophotometric Quantitation of Antioxidant Capacity through the Formation of a Phosphomolybdenum Complex: Specific Application to the Determination of Vitamin E. *Anal Biochem.* 1999;269:337-41. https://www.ncbi.nlm.nih.gov/pubmed/10222007

Information about authors:

Fomichev Evgeniy Valentinovich - Doctor of Medical Sciences, Professor, Head of the Department of Surgical Dentistry and Maxillofacial Surgery FGBOU VO "Volgograd State Medical University", Volgograd, 400081, st. Angarskaya 7B - 44, f3vstom@yandex.ru. 89375541234 .

Weisheim Lyudmila Dmitrievna - doctor of medical sciences, professor, head of the chair of the FUV FGBOU VO "Volgograd State Medical University", Volgograd, 400117, st. Sheksninskaya 40-77, elyarygina@yandex.ru, 89272512731.

Kirpichnikov Mikhail Viktorovich - Candidate of Medical Sciences, Associate Professor of the Department of Oral and Maxillofacial Surgery FGBOU VO "Volgograd State Medical University", Volgograd, 400081, st. Tvardovsky 10-55, kirpichnikov-m@yandex.ru, 89026592098.

Yarygina Elena Nikolaevna - Candidate of Medical Sciences, Associate Professor of the Department of Oral and Maxillofacial Surgery FGBOU VO "Volgograd State Medical University", Volgograd, 400131, Lenin Avenue 15-73, elyarygina@yandex.ru, 89272512731.

Mikhalchenko Aleksey Valerevich - Candidate of Medical Sciences, Associate Professor of the Department of Therapeutic Stomatology FGBOU VO "Volgograd State Medical University", Volgograd, 400005, Lenin Avenue 68-33, alekseymiha@yandex.ru,89023625065.

Yurkevich Alexander Vladimirovich - doctor of medical sciences, associate professor, head of Department of orthopedic stomatology of the "Far East state medical university", Khabarovsk, 680000, st.Muravieva-Amurskogo 35-233, dokdent@mail.ru, 89655025888.

Ushnitsky Innokenty Dmitrievich - doctor of medical sciences, professor, head of the Department of therapeutic, surgical, orthopedic dentistry and pediatric dentistry of M. K. Ammosov NEFU Medical Institute., Yakutsk, 677000,st.Oyunsky 27-420, incadim@mail.ru, 89241708940.

N.A. Sokolova, A.F.Potapov, A.A. Ivanova, A.G. Zolotareva, T.S. Makarova

PATTERNS OF COMPLICATIONS IN THE PERIOPERATIVE PERIOD AND MORTALITY IN PATIENTS WITH ANEURYSMAL SUBARACHNOID HEMORRHAGE

ABSTRACT

The article presents the results of studying the patterns of complications and mortality from aneurysmal subarachnoid hemorrhage (aSAH) at the Anesthesiology, Reanimation and Intensive Care Unit (ARICU) of the Republic's Hospital No. 2 – Center for Emergency Medical Aid (ARICU RH No. 2 – CEMA) of the Sakha Republic (Yakutia) for the period of 2015-2017. During the study period, various complications were diagnosed in the preoperative period in 67.3% of the patients and in 64.7% of cases following surgery, and the mortality rate of this group of patients was 5.8% (9 patients).

The dominating pattern of the preoperative complications was cerebral vasospasm, with the specific gravity of 81.9%. Other complications of this period included ruptured aneurysms and cerebral edema with dislocation syndrome, 9.0% and 4.8% of the complications, respectively.

The complications during surgeries were of a technical nature and observed in 12.8% of the cases, leading to changes in surgical planning. These included ruptured aneurysm (85% of intraoperative complications), as well as pronounced cerebral edema and the impossibility of applying clips.

In the postoperative period, 64.7% of the patients had various intra- and extracerebral complications, which amounted to 61.38% and 38.6%, respectively, in the patterns of complications. Among the intracerebral complications, delayed cerebral ischemia (DCI) with 39.60% ranked first. This complication was more often observed in patients transported by air ambulance from district hospitals (32.1%) than among patients from the city of Yakutsk (19.2%). Among the extracranial complications, nosocomial pneumonia (NP) and severe cerebrocardiac syndrome (CCS) were more often diagnosed, making 20.79% and 12.87% in the patterns of postoperative complications.

Of the total number of treated patients, 62.2% of the patients were discharged with full recovery, 21.1% - with mild neurological deficit, 10.3% - with moderate neurological deficit, and 0.6% - in the vegetative state.

The data presented indicate the relevance of the issues related to treating patients with aSAH in the region, as well as the importance of measures for further improvement of the treatment, diagnostic and organizational-tactical approaches aimed at reducing complications and mortality in this group of patients.

Keywords: aneurysmal subarachnoid hemorrhage, intracerebral complications, extracerebral complications, cerebral vasospasm, nosocomial pneumonia.

Introduction. Currently, aSAH is diagnosed in over 75-85% of all hemorrhages in the subarachnoid space, posing a real threat to the lives of patients and remaining one of the topical issues in the neurological stage of reanimatology [13].

The recent studies show that the annual aSAH frequency in the world varies from 2-22.5 cases per 100,000 of population depending on a region, is more common in people over 50 years of age and develops mostly in women [9, 10, 13]. According to statistics from the Ministry of Health of the Russian Federation, the frequency of newly diagnosed subarachnoid hemorrhages (SAH) among adults in recent years has averaged 11.44 per 100,000 of population (in 2015 -13.69; in 2016 - 9.37; 2017 - 11.25 per 100,000 of population). In the Sakha Republic (Yakutia), the frequency of newly registered SAH among the adult population for the same period was 13.60, 11.31 and 12.86 per 100,000 of the population, respectively [3].

The median aSAH mortality rate in developed countries is as follows: the United States – 32%, England – 18%, European countries – 44%, Japan – 27% [13]. In Russia, the SAH mortality, given the latest management protocols, is at the level of 14.5% [6]. According to Chugunova S.A. and co-authors, in 2015, the Sakha Republic had the share of hemorrhagic strokes at 26.2% [8]. Our previous studies revealed that at the Center for Emergency Medical Aid of the Sakha Republic (Yakutia) in the period 2011-2015 ruptured aneurysms were observed in 50.75% of patients having been operated for non-traumatic SAH, and the mortality rate in this category of patients made 34.21% [1].

The modern approach to the treatment of aSAH involves active neurosurgical tactics and the use of various methods of intensive observation and therapy. Moreover, the right timing of surgery, objective neurological monitoring in the immediate postoperative period, monitoring the effectiveness of therapy, as well as prevention of complications are recognized as the main factors for the successful outcome of this severe pathology [7, 9]. It is proved that the main causes of disability and mortality of this group of patients are due not only to the direct effect of hemorrhage (55% of patients), or its recurrence (up to 17% of patients) [11], but also delayed cerebral ischemia, which is observed in 20-40% of patients [14, 15].

Cerebral vasospasm and ischemic cerebral damage should be attributed to the most common and severe complications during ruptured aneurysms. According to the Fisher grading scale, with grade 2 basal hemorrhage, cerebral vasospasm develops in 100% of cases, and cerebral ischemia occurs in over 50% of patients. Cerebral vasospasm, forming on days 3–4 from the onset of the disease and reaching the maximum by days 7–14, can lead to total obliteration of the vascular bed in 20% of cases. Cerebral infarction develops in more than 60% of patients with cerebral vasospasm [5, 7, 14, 15].

The next most frequent and severe complication is aSAH recurrence, developing in 17-26% of patients with aneurysm, in 5% of patients with arterio-venous malformation and very rarely with SAH of a different etiology. Most often, repeated hemorrhage occurs due to lysis of a blood clot at the ruptured aneurysm location, most often on day 1 (4%) and in the following 4 weeks (1–2% per day) [6, 9, 11].

Extracerebral complications such as pulmonary edema, myocardial ischemia, cardiac arrhythmias, hyperthermia of noninfectious genesis, venous thrombosis with complications, hyponatremia, which are observed in 10–20% of patients [6, 9, 11, 15], should be also taken into consideration.

Thus, the treatment of patients with SAH, and with aSAH in particular remains a topical issue in practical health care. From this point of view, a study of treatment results, an analysis of the frequency of development and patterns of complications, and mortality of aSAH patients in the specialized center of the Sakha Republic (Yakutia) is relevant.

The research objective is to study the patterns of intra- and extracerebral complications and mortality in aSAH patients having been operated at the specialized center of the Sakha Republic (Yakutia) in the period 2015-2017.

Materials and Methods. We conducted a retrospective analysis of the perioperative complications in 156 patients having been operated for aSAH and treated at the Anesthesiology, Reanimation and Intensive Care Unit (ARICU) of the Republic's Hospital No. 2 – Center for Emergency Medical Aid in the period 2015- 2017.

The age of the patients ranged from 19 to 79 years (mean age 51.4 ± 10.7 years); there were 52 men (33.3%) and 104 women (66.7%). All the patients were admitted for emergency reasons, with 78 (50.0%) patients having been transported by air ambulance from district hospitals of the republic.

The diagnosis of aSAH was confirmed in the preoperative period by instrumental studies with the X-ray computed tomography (CT); the diagnostic measures were carried out in accordance with the guidelines for the management of patients with SAH [7, 9, 12].

The neurological status of the patients was assessed at admission and in dynamics by the Glasgow Coma Scale (GCS) and the Hunt-Hess scale, before discharge – by the Glasgow Outcome Scale [7, 9, 12].

All the patients underwent surgical treatment: craniotomy for resection, hematoma removal, and arterial aneurysm clipping. The clinical guidelines for the management of patients with aSAH [9] were used for determining indications and scale of a surgery, anesthesia administration and postoperative intensive care.

Results and Discussion. The assessment of the patients' condition by the conscious state (GCS) and the severity (Hunt-Hess scale) at admission showed the following. The conscious state by GCS was 15 points (full consciousness) in 107 (68.6%) patients, 14-11 points (stupor) – in 38 (24.4%), 10-9 points (semicoma) – in 7 (4.5%), 8-6 points (moderate coma) – in 3 (1.9%), 4-5 points (deep coma) – in 1 (0.6%) patient. There were no patients in the terminal coma (Table 1).

Assessing the severity of a patient's condition at the beginning of treatment by the Hunt-Hess scale is of significant predictive value in terms of survival. In the study group, at admission, the severity of state of most patients was assessed at 1 (66 patients, or 42.3%) and 2 points (55, or 35.3%). These were the patients with full consciousness, minimal neurological deficit and prediction of survival at 60-70%. The number of patients with 3 points was 25 (16.0%) (prediction of survival at 50%); with 4 points - 7 (4.5%) patients (prediction of survival at 20%). The distribution of the patients by the studied years showed that while the share of the patients with 1 and 2 points did not change significantly, the share of the patients with 3 and 4 points increased in 2016-2017, and there were 3 (1.9%) patients with 5 points. These were the patients in a state of deep coma, with the prediction of survival at 10% (Fig. 1).

During the study period, an increase in the number of patients transported by the Republic's Center for Disaster Medicine (RCDM) was observed: in 2015 - 14 (29.2%), in 2016 - 30 (50.0%), in 2017 - 34 (70.8%). However, the transportation time of these patients to the specialized

Table 1

Assessment of the patients' conscious state by GCS at admission

ШКГ (баллы)	Год			Итого
	2015	2016	2017	
15	33 (68,7)	42 (70,0)	32 (66,7)	107 (68,6)
14-11	13 (27,1)	15 (25,0)	10 (20,8)	38 (24,4)
10-9	2 (4,2)	1 (1,7)	4 (8,3)	7 (4,5)
8-6	-	1 (1,7)	2 (4,2)	3 (1,9)
5-4	-	1 (1,7)	-	1 (0,6)
3	-	-	-	-
Всего	48	60	48	156

center from the onset of the ruptured aneurysm showed a decreasing trend: 5.4 ± 3.4 days in 2015, 5.5 ± 3.8 in 2016 and 3.0 ± 2.4 in 2017.

The great majority of the patients (108, or 69.2%) were operated within the first 5 days from the onset of hemorrhagic stroke, with 45 (28.8%) patients undergoing surgery in the acute period (in the first 2 days). The remaining patients underwent delayed surgeries: on days 6-10 - 25 (16.0%) patients, on days 11-15 - 8 (5.1%) patients, and in 16 days or more - 16 (10.3%) patients. The delayed surgery tactics was applied to the patients in critical condition with initial scores by the Hunt-Hess scale at 4 and 5 points (without intracerebral hematomas requiring emergency surgery), as well as in the cases of progressing concomitant pathologies.

The studies of the nature and localization of aneurysms indicated that single aneurysms (78.2% of the cases) and aneurysms of the middle cerebral artery (MCA) (47.4%) prevailed. Aneurysms of the anterior cerebral artery (ACA) and the internal carotid artery (ICA) made 34.6% and 18.0%, respectively (Table 2).

In 21 (13.5%) patients, hemorrhage was accompanied by the formation of intracerebral hematomas with a volume of over 50 cm^3, and 70 (44.9%) patients suffered blood breakthrough into ventricles of cerebrum.

A study of the patterns of complications during the management of patients with aSAH revealed the following results. In the preoperative period, complications were noted in 105 (67.3%) patients. Cerebral vasospasm (from functional to severe) was most frequent in the preoperative period and was diagnosed in 86 (55.1%) patients, being verified by instrumental studies (transcranial Doppler study with calculating the linear blood flow velocity, angiography or CT in the angio-mode). Accounting for 81.9%, the specific gravity of this complication among other preoperative complications was significantly higher. According to the recent studies, the pathogenesis of vascular spasm and ischemic changes associated with it during aSAH is complex and diverse. Its most important elements are intracranial hypertension, increased intracellular Ca^{2+} in smooth muscle cells and neurons, disruption of cell energy supply, dysfunction of ion channels, and inflammatory changes due to the blood-brain barrier breakthrough. The severity of vasospasm depends on the scale of a hemorrhage [5, 11].

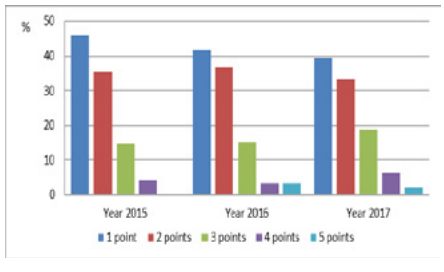

Fig. 1. Distribution of the patients by the Hunt-Hess scale at admission

In addition, in the preoperative period, the risk of repeated ruptured aneurysms remained due to the tactics of delayed surgeries. Within different periods (from 1 to 10 days), 14 (9.0%) patients experienced repeated ruptured aneurysms (13.3% of the preoperative complications).

Before the surgery, 5 (3.0%) patients had pronounced cerebral edema with dislocation syndrome (4.8% of the preoperative complications).

The complications during surgery were observed in 20 (12.8%) cases; they were of a technical nature and led to changes in the surgical planning. These were cases of ruptured aneurysm in 17 patients (85% of the reasons for the change in operational tactics); thus, the final clipping was performed on the second stage, after the application of temporary clips on the artery in order to stop the blood flow. Due to pronounced cerebral edema and the impossibility of applying clips in 3 patients (15% of the changes in operational tactics), the scope of the surgery was limited to decompression trepanning. In these cases, two patients underwent successful embolization later, and one patient died of a repeated hemorrhage.

In the postoperative period, 101 (64.7%) patients experienced various intra- and extracerebral complications, which accounted for 61.38% and 38.6% in the patterns of complications, respectively (Table 3).

The patterns of intracerebral com-

Table 2

Nature and localization of arterial aneurysms

Nature and localization of aneurysms	Years						Total	
	2015		2016		2017			
	number	SG (%)	number	SG (%)	number	SG (%)	number	SG (%)
Nature of aneurysm								
Single	37	77.1	47	78.3	38	79.2	122	78.2
Multiple	11	22.9	13	16.7	10	20.8	34	21.8
Total	48	100	60	100	48	100	156	100
Localization of aneurysm								
ACA	20	41.7	10	16.7	24	50.0	54	34.6
MCA	19	39.6	36	60.0	19	39.6	74	47.4
ICA	9	18.7	14	23.3	5	10.4	28	18.0
Total	48	100	60	100	48	100	156	100

Table 3

The patterns of complications in aSAH patients in the postoperative period

Complications	Years			Total number, (%)
	2015	2016	2017	
Intracerebral complications	17 (16.83)	18 (17.82)	27 (26.73)	62 (61.38)
Delayed cerebral ischemia	8 (7.92)	10 (9.90)	22 (21.78)	40 (39.60)
Postoperative epi- and subdural hematomas	1 (0.99)	2 (1.98)	1 (0.99)	4 (3.96)
Repeated hemorrhage due to clip disposition	2 (1.98)	-	1 (0.99)	3 (2.97)
Occlusive hydrocephaly	2 (1.98)	-	-	2 (1.98)
Meningitis	1 (0.99)	-	2 (1.98)	3 (2.97)
Central diabetes insipidus	3 (2.97)	6 (5.94)	1 (0.99)	10 (9.90)
Extracerebral complications	10 (9.90)	17 (16.83)	12 (11.88)	39 (38.61)
Infectious complications, including: - nosocomial pneumonia, - sepsis	6 (5.94) 6 (5.94) -	10 (9.90) 8 (7.92) 2 (1.98)	8 (7.92) 7 (6.93) 1 (0.99)	24 (23.76) 21 (20.79) 3 (2.97)
Pulmonary embolism	-	1 (0.99)	1 (0.99)	2 (1.98)
Severe cerebrocardial syndrome	4 (3.96)	6 (5.94)	3 (2.97)	13 (12.87)
TOTAL	27 (26.73)	35 (34.65)	39 (38.61)	101 (100)

plications of the postoperative period were dominated by DCI – 39.60% of all the complications (40 patients). Moreover, this complication increased by more than 1.5 times in 2017 compared to the years 2015-2016. This can be explained by the increase in the share of the patients with 3 and 4 points on the Hunt-Hess scale, which is demonstrated in the diagram above (Fig. 1). In addition, the analysis of each DCI case showed that this complication was more often observed in the patients transported by air ambulance from district hospitals than among patients from the city of Yakutsk — 32.1% and 19.2%, respectively. This fact indicates the importance of adequate prevention and treatment of cerebral ischemia during the management of patients in district hospitals, as well as their transportation, taking into account all aspects of its pathogenesis (vascular spasm, intracranial pressure, energy supply of neurons, etc.).

Another serious complication occurred in 10 (9.90%) cases of central diabetes insipidus (DI). Polyuria, characteristic of this syndrome, leads to pronounced water-electrolyte imbalance, requiring large-volume infusions, the introduction of potassium solutions, antidiuretic drugs, and lengthening the duration of ICU treatment of these patients. In our study, we observed a female patient with polyuria up to 34 liters a day. Previously, we published a clinical case of DI with severe polyuria (maximum daily diuresis of 22.7 liters) for 12 days in a female patient with aSAH [4].

Being diagnosed in 21 patients and making 20.79% in the patterns of postoperative complications, NP stands out in the extracranial complications. This pathology was confirmed by clinical, instrumental (plain radiography and CT of the chest) and microbiological studies. These data indicates that the problem of NP for ICU patients remains relevant. Thus, in a study conducted at the ARICU CEMA in 2015 on patients with acute impairment of cerebral circulation, it was found that NP complicated the course of the disease in 36% of cases, and ventilator-associated pneumonia was found in 27% of the patients [2]. Gram-negative microorganisms were the causative agents of the hospital pneumonia: *Pseudomonas aeruginosa (MBL)* – 56%, *Klebsiella pneumonia (BLRS)* – 82%, *Escherichia coli (BLRS)* – 51% of the cases, and gram-positive microorganisms: *Staphylococcus aureus (MRSA)* – 10. 5% of the cases.

Severe CCS complicated the course of disease in 13 patients and amounted to 12.87% in the patterns of complications. This group included the patients without concomitant coronary heart disease (CHD), and they had to undergo targeted pharmacological correction due to CCS. These cases were combined with an extensive hemorrhage, severe brain damage and occurred in all the patients with the unfavorable outcome.

The mortality of aSAH patients over the study period was 5.8% (9 patients died): in 2015 – 4.2% (2 patients), in 2016 – 6.7% (4 patients) and in 2017 – 6.3% (3 patients). The analysis of the mortality confirmed the adequacy of the Hunt-Hess scale, used for assessing the severity of patients in the acute period of SAH (Fig. 2).

As can be seen in the diagram, the highest mortality was observed in the patients with 4 and 5 points by the Hunt-Hess scale: 2 patients died in each group, making 28.6% and 66.7%, respectively.

The analysis of mortality showed that intracranial complications were the direct cause of death in 6 (3.9%) patients: large-scale hemorrhage with cerebral edema and dislocation syndrome (3 patients) and repeated hemorrhage (3 patients). Severe extracranial complications caused the deaths of 3 (2.9%) patients: NP complicated by sepsis (1 patient), PE (1 patient), and pseudomembranous colitis complicated by peritonitis and abdominal sepsis (1 patient). Comorbidity contributed a lot to the outcome of treatment. First, these were diseases of the cardiovascular system, which in fact caused hemorrhages (CHD, hypertension, etc.) and were present in majority (98.7%) of the patients. Among other concomitant pathologies in the patients, there were diseases of the digestive (12.8%), endocrine (7.1%), and respiratory (5.8%) systems.

The patients stayed in the ARICU for 6.3 ± 6.0 bed-days, and as in-patients in hospital – for 28.5 ± 11.1 bed-days.

Of the total number of the patients who received treatment, 62.2% of the patients

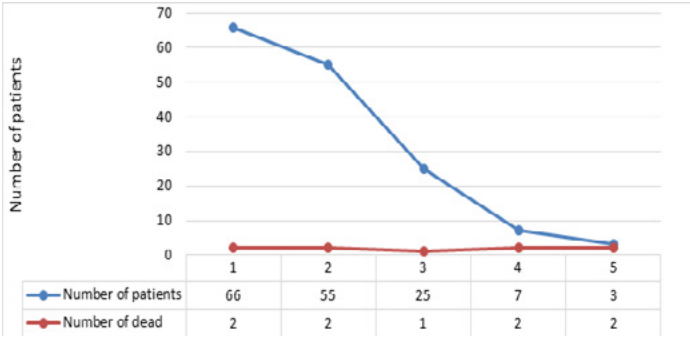

Fig. 2. ASAH mortality depending on the initial severity by the Hunt-Hess scale

were discharged with full recovery. 21.1% and 10.3% of the patients were discharged with mild and moderate neurological disability, respectively. One (0.6%) patient was discharged in the vegetative state (Table 4).

Conclusion

Thus, the study of the patterns of complications and mortality of aSAH at the ARICU, RH No. 2-CEMA of the Sakha Republic (Yakutia) in the period 2015-2017 showed that complications of a different nature were diagnosed in the preoperative period in 67.3% of the patients and in 64.7% of the cases following surgeries, and the mortality rate for this group of patients was 5.8% (9 patients).

In the patterns of the complications of the preoperative period, the dominant one was cerebral vasospasm, with the specific gravity of 81.9%. Other complications of this period included ruptured aneurysms and large-scale cerebral edema with dislocation syndrome, 9.0% and 4.8% of the complications, respectively.

During surgical treatment of the patients, in 12.8% of the cases there were changes in the surgical planning due to a ruptured aneurysm (85% of the reasons for changing the operational tactics), as well as pronounced cerebral edema and the impossibility of applying clips.

In the postoperative period, 101 (64.7%) patients had various intra- and extra-cerebral complications, which accounted for 61.38% and 38.6% in the patterns of complications, respectively. Among the intracerebral complications, DCI with 39.60% ranked first. Moreover, this complication was more often observed in the patients transported by air ambulance from district hospitals (32.1%) than among patients from the city of Yakutsk (19.2%). Of extracranial complications, NP and severe CCS were most common, comprising 20.79% and 12.87% in the patterns of the postoperative complications.

Of the total number of the treated patients, 62.2% of the patients were discharged with full recovery, 21.1% with a mild neurological disability, 10.3% with a moderate neurological disability, and 0.6% in the persistent vegetative state.

The data presented indicate the relevance of the issues related to treating patients with aSAH in the region, as well as the importance of measures for improved treatment, diagnostic and organizational-tactical approaches aimed at reducing complications and mortality in this group of patients.

References

1. Макарова Т.С., Соколова Н.А., Потапов А.Ф., Иванова А.А. Анализ результатов лечения больных с нетравматическими внутримозговыми кровоизлияниями. *Успехи современной науки*. 2016;8(1):196-201. [Makarova TS., Sokolova NA., Potapov AF., Ivanova AA. The analysis of treatment outcomes of patients with non-traumatic cerebral hemorrhages. *Uspekhi sovremennoj nauki*. 2016; 8(1):196-201 (In Russ.)].

2. Слепцова Н.Ф., Портнягина У.С., Шамаева С.Х., Матвеев А.С., Татаринова О.В. Госпитальные пневмонии у пациентов с острыми нарушениями мозгового кровообращения. *Материалы III Республиканской научно-практической конференции «Совершенствование оказания медицинской помощи пациентам с сосудистыми заболеваниями в Республике Саха (Якутия)», посвященной 5-летию открытия Регионального сосудистого центра*. 2016:37-38. [Sleptsova NF., Portniagina US., Shamaeva SKh., Matveev AS., Tatarinova OV. Hospital-acquired pneumonia in patients with acute cerebrovascular disorders. *Materialy III Respublikanskoj nauchno-prakticheskoj konferencii «Sovershenstvovanie okazaniya medicinskoj pomoshchi pacientam s sosudistymi zabolevaniyami v Respublike Saha (YAkutiya)», posvyashchennoj 5-letiyu otkrytiya Regional'nogo sosudistogo centra. Yakutsk*. 2016; 37-38 (In Russ).]

3. Заболеваемость взрослого населения России в 2016 г.: Статистические материалы, 2015, 2016, 2017. [Morbidity in the adult population in Russia: statistical materials, 2015, 2016, 2017 (In Russ.).] DOI: https://www.rosminzdrav.ru

4. Золотарева А.Г., Соколова Н.А., Потапов А.Ф., Иванова А.А. Интенсивная терапия центрального несахарного диабета. *Вестник Северо-Восточного университета имени М.К. Аммосова. Серия «Медицинские науки»*. 2016; 3(04):39-42. [Zolotareva AG., Sokolova NA., Potapov AF., Ivanova AA. Intensive therapy of central diabetes insipidus. *Vestnik Severo-Vostochnogo universiteta imeni M.K. Ammosova. Seriya «Medicinskie nauki»*. 2016; 3(04):39-42. (In Russ).]

5. Крылов В.В. Калинкин А.А., Петриков С.С. Патогенез сосудистого спазма и ишемии головного мозга при нетравматическом субарахноидальном кровоизлиянии вследствие разрыва церебральных аневризм. *Неврологический журнал*. 2016;5:4-12. [Krylov VV., Kalinkin AA., Petrikov SS Pathogenesis of vasospasm and cerebral ischemia following non-traumatic aneurysmal subarachnoid hemorrhage. *Nevrologicheskij zhurnal*. 2016; 5:4-12. (In Russ).]

6. Рудник Е.Н., Белкин А.А., Громов В.С. Анализ летальности пациентов с нетравматическим субарахноидальным кровоизлиянием, предрасполагающие факторы, причины, осложнения. *Научно-практический журнал: «Анестезиология и реаниматология»*. 2018;63(1):68-72. [Rudnik EN., Belkin AA., Gromov VS. The analysis of mortality of patients with non-traumatic subarachnoid hemorrhage, underlying factors, causes, and complications. *Nauchno-prakticheskij zhurnal: «Anesteziologiya i reanimatologiya»*. 2018;63(1):68-72. (In Russ).]

Table 4

The conscious state of the in-patients at discharge by the Glasgow Outcome Scale)

Glasgow Outcome Scale (points)	Years			Total number, (%)
	2015	2016	2017	
5 points Full recovery	29 (60.4)	40 (66.7)	28 (58.3)	97 (62.2)
4 points Light neurological disability	14 (29.2)	7 (11.7)	12 (25.0)	33 (21.1)
3 points Moderate neurological disability	3 (6.2)	8 (13.3)	5 (10.4)	16 (10.3)
2 points Persistent vegetative state	0	1 (1.7)	0	1 (0.6)
1 point Death	2 (4.2)	4 (6.6)	3 (6.3)	9 (5.8)
Total	48	60	48	156

7. Савин И.А., Фокин М.С., Лубнин А.Ю. Рекомендации по интенсивной терапии у пациентов с нейрохирургической патологией. *Пособие. Издание четвертое. – М: НИИ нейрохирургии им. акад. Н.Н. Бурденко*. 2016;200. [Savin IA., Fokin MS., Lubnin Alu. Guidelines for intensive therapy of patients with neurosurgical pathologies. *Posobie. Izdanie chetvertoe. – M: NII nejrohirurgii im. akad. N.N. Burdenko*. 2016; 200. (In Russ).]

8. Чугунова С.А., Николаева Т.Я., Кузьмина З.М., Егорова Т.С., Клочихина О.А., Стаховская Л.В. Эпидемиология инсульта в Якутске по данным территориально-популяционного регистра за 2015 год. *Дальневосточный медицинский журнал*. 2017;3:80-85. [Chugunova SA., Nikolaeva TIa., Kuz'mina ZM., Egorova TS., Klochikhina OA., Stakhovskaia LV. Epidemiology of stroke in Yakutsk according to the data from the Regional Registry of Population for the year 2015. *Dal'nevostochnyj medicinskij zhurnal*. 2017;3:80-85. (In Russ).]

9. AHA/ASA Guideline. Executive Summary: Guidelines for the Management of Aneurysmal Subarachnoid Hemorrhage. E. Sander Connelly Jr, Alejandro A. Rabinstein, J. Ricardo Carhuapoma, Colin P. Derdeyn. Stroke. 2012; 43:1711–1737 DOI: 10.1161/STR.0b013e3182587839

10. Aneurysmal subarachnoid hemorrhage—diagnosis and treatment. Petridis AK. Kamp MA, Cornelius JF, Beez T, Beseoglu K, Turowski B, Steiger HJ. Dtsch Arztebl Int. 2017; 114:226–236. DOI:10.3238/arztebl.2017.0226

11. Complications and follow up of subarachnoid hemorrhages. Danière F. Gascou G., Menjot de Champfleur N., Machi P., Leboucq N., Riquelme C., Ruiz C. Diagnostic and Interventional Imaging. 2015; 96:677—686. DOI:10.1016/j.diii.2015.05.006

12. Matthew Cordingly, John Hell. Wessex Neuro ICU guidelines. 2016; 103-110. http://www.neuroicu.org.uk

13. Stanlies D'Souza. Aneurysmal Subarachnoid Hemorrhage. Journal of Neurosurgical Anesthesiology. 2015; 3(27):222–240. DOI: 10.1097/ANA.0000000000000130.

14. Subarachnoid blood acutely induces spreading depolarizations and early cortical infarction. Hartings JA. York J, Carroll CP, Hinzman JM, Mahoney E, Krueger B, Winkler MKL, Major S, Horst V, Jahnke P, Woitzik J, Kola V, Du Y, Hagen M, Jiang J and Dreier JP. A Journal of Neurology "Brain" – Oxford. 2017;140:2673-2690. DOI:10.1093/brain/awx214.

15. Tomoya Okazaki, Yasuhiro Kuroda. Aneurysmal subarachnoid hemorrhage: intensive care for improving neurological outcome. Journal of Intensive Care. 2018;6:2-8. DOI:10.1186/s40560-018-0297-5.

The authors:

M. K. Ammosov North-Eastern Federal University, Sakha Republic's Hospital No. 2 – Center for Emergency Medical Aid:

SOKOLOVA Nadezhda Aleksandrovna – post-graduate student, Department of Anesthesiology, Reanimation and Intensive Care, Institute for Post-graduate Medical Training, Institute of Medicine, M. K. Ammosov North-Eastern Federal University, e-mail: nadyusha.sokolova2606@list.ru, phone: +79644190795;

POTAPOV Aleksandr Filippovich, Doctor of Medical Sciences, Head, Department of Anesthesiology, Reanimation and Intensive Care, Institute of Medicine, Ammosov North-Eastern Federal University, e-mail: potapov-paf@mail.ru, phone: +79248625525;

IVANOVA Albina Ammosovna, Doctor of Medical Sciences, Associate Professor, Department of Anesthesiology, Reanimation and Intensive Care, Institute of Medicine, Ammosov North-Eastern Federal University, e-mail: iaa_60@mail.ru, phone: +79247622916;

ZOLOTAREVA Aleksandra Grigorievna – Associate Professor, Department of Anesthesiology, Reanimation and Intensive Care, Institute for Post-graduate Medical Training, Institute of Medicine, M. K. Ammosov North-Eastern Federal University; Head, Anesthesiology, Reanimaton and Intensive Care Unit, Sakha Republic's Hospital No. 2 – Center for Emergency Medical Aid, e-mail: zlata15.8@mail.ru, phone: +79142354581.

MAKAROVA Tatiana Semenovna – Candidate of Medical Sciences, Associate Professor, Department of Anesthesiology, Reanimation and Intensive Care, Institute for Post-graduate Medical Training, Institute of Medicine, M. K. Ammosov North-Eastern Federal University; Head, Anesthesiology and Reanimation Unit, Research Center of Phthisiology, e-mail: mtc712@mail.ru, phone: +79246617750.

O.V. Dolgikh, K.G. Starkova, A.V. Krivtsov, O.A. Kazakova, A.A. Mazunina

IMMUNOGENETIC MARKERS OF THE SIBERIA SOUTHERN REGIONS POPULATION UNDER THE EXPOSURE OF TECHNOGENOUS FACTORS

ABSTRACT

Peculiarities of the population health, characteristic for the newly emerging endemic provinces in Russia, are formed by the anthropogenic pollution conditions of the environment and determine the need to identify the indicator of immunological and genetic indicators that reflect the population health of industrial regions.

The aim of the work is to analyze the population immune and genetic indicators in the conditions of the anthropogenic impact of the urban environment on the example of the Southern Siberia region.

Materials and methods. Laboratory immunological and genetic examination of the adult population living in a combined influence of a chemical factors number of habitat zone is carried out. The content of specific antibodies to benzo(a)pyrene, aluminium, formaldehyde was detected by allergosorbent testing with an enzyme label. Cell populations were determined by CD markers on a flow cytometer. Biochemical markers were studied by enzyme immunoassay. Genetic features were detected by real-time polymerase chain reaction and allele discrimination, based on the diagnosis of single-nucleotide polymorphisms.

Results. There was a significant decrease in the number of $CD3^+CD25^+$- lymphocytes relative to the reference interval, and there were lower concentrations of $CD16^+CD56^+$ -, $CD3^+$- and $CD4^+$-cells relative to the comparison group. The decrease in serum IgG and IgM levels was combined with an increase in the level of IgG to aluminium and benzo(a)pyrene, IgE to formaldehyde relative to the values in the comparison group. There was a significant (p=0.02) increase in the frequency of occurrence of the minor allele of the enzyme eNOS rs1799983 gene associated with a decrease in serum levels of nitric oxide, which indicates the formation of additional risk factors under technogenic exposure.

Findings. The established changes in immune reactivity and genetic polymorphism indicate their population peculiarities of the technogenic chemical province of the Southern Siberia region, which can be used as formation of pathological health disorders markers associated with oxygen-associated processes in the vascular endothelium, the implementation of which can contribute to the identified imbalance of cellular and humoral immunity ($CD3^+CD25^+$- lymphocyte deficiency and IgG hyperproduction to aluminum and benzo(a)pyrene, IgE to formaldehyde).

Keywords: immune regulation, genetic polymorphism, *eNOS* gene rs1799983, technogenous factors.