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In accordance with the resolution of the Higher Attestation Commission of the Ministry of Education and Science of the Russian Federation, the Problems of Neurosurgery named after N.N. Burdenko was included in the List of Leading Peer-Reviewed Journals and Periodicals issued in the Russian Federation where the main results of Candidate and Doctor Theses are recommended to be published.

**Topics to be covered in our next issue**

- Quality of life of patients with pituitary adenomas
- Management of neurogenic tumors of the sacrum and sacral area
- Additive technologies in neurosurgery
Intraoperative Mapping of Long Association Fibers in Surgery of Gliomas of the Speech-Dominant Frontal Lobe

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Surgery of intracerebral tumors involving long association fibers is a challenge. In this study, we analyze the results of intraoperative mapping of the superior longitudinal, arcuate, and frontal aslant tracts in surgery of brain gliomas.

Material and methods. Twelve patients with left frontal lobe gliomas were operated on: 11 patients were right-handed, and one patient was a left-hander retrained at an early age. Histological types of tumors were represented by Grade II diffuse astrocytomas (6 patients), Grade III anaplastic astrocytomas (1 patient), Grade IV glioblastoma (1 patient), Grade II oligodendroglioma (1 patient), and Grade III anaplastic oligodendrogliomas (3 patients). The mean age of patients was 45 (29―67) years; there were 6 males and 6 females. All patients underwent preoperative and postoperative MRI with reconstruction of the long association fibers and determination of the topographic anatomical relationships between the fibers and the tumor.

Surgery was performed using the asleep-awake-asleep protocol with intraoperative awakening of patients. All patients underwent cortical and subcortical electrophysiological stimulation to control the localization of eloquent structures and to clarify the safe limits of resection. For intraoperative speech monitoring, a computerized naming test was used with naming of nouns or verbs, and automatic speech was evaluated (counting from 1 to 10, enumeration of months and days of the week), which was complemented by a talk with the patient. Speech disorders before, during, and after surgery were evaluated by a neuropsychologist.

Results. The association fibers were intraoperatively identified in all patients (SLF/AF in 11 patients; FAT in one patient). In 4 patients, the cortical motor speech area was intraoperatively mapped; in three cases, tumor resection was accompanied by speech disturbances outside the stimulation. During direct electrical stimulation, speech disturbances developed in 7 of 12 cases. All patients underwent control MRI within the first 48―72 h; total resection (more than 90% of the tumor) was performed in 7 cases; subtotal resection was achieved in two patients; partial resection was performed in two cases. According to postoperative MR tractography, the resected tumor bed was adjacent to the SLF/AF complex in 7 cases, located near the SLF/AF complex in three cases, and adjacent to the FAT in two cases.

Postoperatively, 11 out of 12 patients had worsening of neurological symptoms in the form of various speech disturbances. In one patient, speech disturbances developed 2 days after surgery, which was associated with an increase in edema. On examination 3 months after surgery, severe speech disturbances remained in 1 patient.

Conclusion. Resection of frontal lobe tumors in the speech-dominant hemisphere using early postoperative awakening is associated with a high rate of complex speech disorders due to injury to the SLF/AF complex and FAT. In these cases, intraoperative speech mapping with allowance for the course of long association fibers is an essential procedure. Preoperative tractography in combination with intraoperative speech mapping enables identification of association fibers of the SLF/AF complex and FAT, which may help to avoid severe conduction aphasia with poor speech recovery after tumor resection.

Keywords: glioma, long association fibers, awake surgery.

Abbreviations:
SLF — superior longitudinal fasciculus
AF — arcuate fasciculus
FAT — frontal aslant tract

The first awake surgeries of the brain were performed in the first half of the XX century by an outstanding Canadian neurosurgeon W. Penfield on patients with epilepsy. During the surgery, he stimulated the surface of the cerebral cortex with electrical discharges and recorded his observations. After gaining experience and performing more than 750 awake surgeries, W. Penfield formulated the modern description of the topography of cortical representations of motor and sensory functions. Later G. Ojemann used awake surgeries to map the white matter pathways associated with the cortical speech zones. In particular, he described nominative (amnesic) aphasia after subcortical stimulation of the parietal lobe and development of sudden neurological deficit when performing memory tasks during the stimulation of thalamic structures [1].

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Direct stimulation of the cortical zones and pathways is currently the standard in resection of intracerebral tumors. According to the European recommendations [1], an expansion of tumor resection significantly prolongs the overall survival of patients with gliomas of both low and high malignancy. On the other hand, brain functions must be mapped to preserve patient’s quality of life. Therefore, in case of diffuse tumors, such as gliomas, the main task is to remove the part of the brain affected by tumor cells, based on individual functional boundaries rather than "oncological" boundaries, which are essentially absent in gliomas, which always have invasive growth [1].

In other words, it is extremely important to map the cortex and the white matter pathways responsible for sensorimotor, visual-spatial and linguistic functions. To confirm this new concept, a recent meta-analysis, which presented the results of surgical treatment of 8091 patients with brain gliomas, demonstrated that the use of intraoperative mapping made it possible to achieve statistically significant reduction in permanent neurological deficit, despite the increase in the frequency of resections in functionally important areas; in addition, the degree of resection has been increased [1].

Gliomas are common tumors of the CNS and most often (in 40% of cases) they are localized in the frontal lobes [2], where various functionally important zones are located as well, including those responsible for motor functions and speech.

Surgical treatment of gliomas in functionally significant areas of the brain is a very challenging task. In addition to detailed knowledge of the functional anatomy of the cerebral cortex by a neurosurgeon, he or she also need to take into account the anatomy of the pathways during the surgery. Historically, the neurosurgeons and neurophysiologists focused on the functional anatomy of the cerebral cortex and only to a lesser extent on the pathways, of which the pyramidal tract is the most often mapped during surgeries [3]. The long association fibers involved in ensuring speech function have been less studied in the surgery of intracerebral tumors.

Despite significant progress in understanding the structure of the long association pathways of the brain, which has been achieved over the past 30 years due to the invention of diffusion-tensor imagine (DTI) and the improvement of mathematical models for receiving and processing the signal, such as HARDI, HARDI Q-ball, HARDI-CSD, their accuracy remains insufficient to definitely resolve the issue of anatomical structure of the associative fibers [4, 5]. Nevertheless, modern capabilities of the HARDI-tractography make it possible to identify the terminals of the tracts, the intersection of various bundles, and the course of fibers in the zone of tumor infiltration and edema [6]. Based on these data, it is possible to develop a preoperative representation of the topographic-anatomical relationship between the tract and the tumor (variants of displacement, infiltration, destruction, intact bundle).

Studied of the tract fibers course using Klingler dissection on autopsied brain specimen is important for understanding the microsurgical anatomy of the tracts [7].

Currently, awake craniotomy is the standard for intraoperative mapping of functional speech zones [8, 9].

The literature describes numerous cases of transient postoperative Aphasia during surgical resection of gliomas with awakening, if gliomas are located in the dominant speech hemisphere. According to H. Duffau et al. [8], nearly 80% of patients experience speech disorders immediately after awake surgeries on the dominant hemisphere. After 3 months, up to 95% of patients no longer have neurological deficits. According to the results of other authors [10], permanent speech disorders can persist in almost 10% of patients. Intraoperative mapping is used to reduce the likelihood of postoperative speech disorders not only for cortical speech zones, but also for long association fibers.

The study purpose was to compare the results of intraoperative mapping and the postoperative speech function in patients with gliomas of the premotor area of the speech-dominant frontal lobe, which involved the superior longitudinal, arcuate, and frontal aslant tracts, who were operated on using awake craniotomy.

1. The SLF/AF and FAT topography

The topography and segmentation of long association fibers (SLF, AF, FAT) and their functional significance [11–13] are presented in Table 1 (they were described in more detail in our previous papers [6, 14]).

The superior longitudinal fasciculus (SLF) is a complex tract consisting of three segments: SLF I, SLF II, SLF III. The data on the structure, functions and symptoms detected in case of damage to these tracts are presented in Table 1. This segmentation may seem convention-based, especially for SLF I, which is anatomically separated from the rest of the segments. This approach is explained by the data of autoradiography on primates and the common function of all segments: establishing the connection between the frontal, parietal lobes and temporal lobes.

Currently the arcuate fasciculus (AF) is divided into two segments: dorsal and ventral. The dorsal segment connects the middle and inferior temporal gyri with the inferior frontal one; damage to it leads to disruption of the lexical and semantic aspects of speech and transcortical motor aphasia. The ventral segment connects the superior and middle temporal gyri with the lower frontal one (pars triangularis). The damage to this segment causes phonemic (literal) paraphasias, as described by Karl Wernicke in the XIX century. Some authors [11] describe the AF as part of the SLF.

The SLF and AF fibers run in parallel, however the AF, unlike the SLF, does not switch in the parietal lobe.
The anatomy, segmentation and symptoms of damage to the main long association fibers have been described in more detail earlier in both Russian and foreign studies [11—13, 15, 16].

The frontal aslant tract (FAT) has been discovered later than all other pathways, using MRI tractography. It runs aslant from the inferior frontal gyrus (pars opercularis) to the medial surface of the additional motor cortex. Normally, excessive motor speech activity is suppressed through the frontal aslant tract and articulation is initiated. Partial damage or intraoperative stimulation of this tract causes stuttering or speech arrest, and full damage leads to the development of the specific Foix-Chavany-Marie syndrome (paresis of the face, larynx and jaw). It is assumed that FAT plays an important role in the initiation of spontaneous speech, linking Broca’s area and the SFG [17].

The exact structure of the bundles described above remains unclear, their segmentation is not fully understood and mainly based on the difference in neurological deficits observed during intraoperative mapping of these fibers, which in itself is a rather controversial decision, since association pathways exhibit the greatest variability. Their structure and segmentation are described in detail in our previous work [16].

Topographically, the SLF II, SLF III and both AF segments run in parallel in the frontal lobe, closely adjoining each other, and the FAT intersects them at a right angle, as a result of which most clinical cases involve all the above-described bundles, and the intraoperative differential diagnosis of the pathway lesion is difficult. It is made even more challenging in the presence of preoperative or intraoperative aphasia, which blur the pattern of speech monitoring and makes it difficult to monitor the patient’s neurological status. The layout of the main association tracts is shown in Fig. 1.

### 2. Materials and Methods

#### 2.1. Patients’ series

The inclusion criteria for this study were over 18 years of age, supratentorial glioma in the dominant hemisphere (speech), awake surgery, and the mandatory identification of the functionally significant pathways during the surgery (SLF, AF, FAT). In this article, we described a series of 12 clinical observations (6 men and 6 women, mean age of 45 years (29—67)) of patients with gliomas located in the left frontal lobe near the speech zones, of whom 6 patients had diffuse astrocytomas (Grade II), 1, anaplastic astrocytoma (Grade III), 1, glioblastoma (Grade IV), 1, oligodendroglioma (Grade II) and 3 had anaplastic oligodendroglioma (Grade III). In 6 patients clinical presentation included structural epilepsy with focal seizures, in 2 it was represented by speech disorders before the surgery, and in 4 by general cerebral symptoms (headache).

#### 2.2. Pre- and postoperative contrast-enhanced MRI and MR-tractography

All 12 patients underwent MRI with contrast enhancement and re-construction of long association fibers according to the HARDI (High Angular Resolution Diffusion Weighted Imaging) method with establishing the topographic-anatomical relationship between the fibers and the tumor before the surgery and within the first 72 hours after its completion.

#### 2.3. Neurophysiological control and awake craniotomy technique

All patients underwent surgical interventions with awakening according to the asleep-awake-asleep protocol using cortical and subcortical stimulation in order to localize functionally significant structures and clarify the possible amount of resection. The average current for direct electrical stimulation of the cortex and association

---

**Table 1. Basic information about the superior longitudinal and arcuate tracts**

<table>
<thead>
<tr>
<th>Tract</th>
<th>S</th>
<th>Terminals</th>
<th>Terminals</th>
<th>Involvement in ensuring a function and symptoms of injury</th>
<th>Lateralization</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLF I</td>
<td>PreCu</td>
<td>Cing</td>
<td></td>
<td>Involvement in the coordination of movements, the initiation of movements</td>
<td>None</td>
</tr>
<tr>
<td>SLF II</td>
<td>AG</td>
<td>MFG</td>
<td></td>
<td>Unknown / concentration of attention</td>
<td>Left (in case of dyslexia in children) / Normally right, provides audio-visual lateralization of the right hemisphere</td>
</tr>
<tr>
<td>SLF III</td>
<td>SMG (pars opercularis)</td>
<td>IFG</td>
<td></td>
<td>Speech (articulation component). In case of injury: spatial neglect syndrome</td>
<td>None</td>
</tr>
<tr>
<td>AF</td>
<td>MTG 100%, ITG 40%</td>
<td>PCG 80%, IFG 60%, MFG 20%</td>
<td></td>
<td>Phonemic, lexico-semantic, proseptic</td>
<td>Strong left for right-handers and left-handers</td>
</tr>
<tr>
<td>FAT</td>
<td>SMA, pre-SMA (pars opercularis)</td>
<td></td>
<td></td>
<td>Not studied. Destruction leads to the development of Foix-Chavany-Marie syndrome</td>
<td>Towards the dominant hemisphere</td>
</tr>
</tbody>
</table>

**Footnote.** S — tract segments, PreCu - precuneus, Cing — cingulate gyrus, AG — angular gyrus, MFG — middle frontal gyrus, SMG — supramarginal gyrus, IFG — lower frontal gyrus, MTG — middle temporal gyrus, ITG — inferior temporal gyrus, PCG — precentral gyrus, SMA — additional motor area.
tracts was 3 mA (1.9–6.5 mA). Direct electrostimulation was performed using a bipolar electrode. In all cases, electrocorticography was used during the surgery to control the epileptic activity of the cerebral cortex. Intraoperative ultrasound and fluorescent navigation with 5-aminolevulinic acid (5-ALA, Alasens) were used for the intraoperative identification of tumor boundaries in 6 cases.

2.4. Pre-, intra- and postoperative speech assessment

The state of speech functions was assessed before, during and after surgery by a neuropsychologist.

A comprehensive neuropsychological study was carried out according to the method of A.R. Luria before the surgery and before the discharge [18]. This method allows for a detailed qualitative analysis of the detected disorders, and it also allows to establish the topological affiliation of the identified symptoms. Different types of praxis, qualitative features of speech functions (including writing and counting), spatial functions, auditory and visual gnosis, as well as cognition were examined. The particular emphasis was placed on the study of speech function. Spontaneous speech, naming, understanding, repetition, and dictation were evaluated. Vocabulary and inertia of speech functions were assessed using a fluency of speech test with naming of words of a given character for 1 minute (“red” or “green” objects, “nouns starting with letter C or S”). In addition, a computerized naming test, which was used for intraoperative testing, was used for all patients before and after the surgery.

The leading hand was determined by the questionnaire of M. Annett [19], according to which 11 patients were right-handed, and 1 was re-trained at an early age left-hander, who completely switched to the right hand. The dominance of the hemisphere in terms of speech was determined using dichotic listening with the determination of the corresponding coefficient.

A computerized naming test [20] was used for intraoperative speech monitoring with naming of nouns or verbs using presentation of simple black-and-white pictures (a total of 30 pictures representing actions or objects); automated series were also evaluated (counting from 1 to 10, listing of months, days of the week). During the entire awake period, the patient was engaged in free dialogue in the absence of electrostimulation during the resection of the tumor.

3. Results

3.1. Preoperative neuropsychological study of patients

Prior to the surgery, 10 out of 12 patients had normal speech. One patient (No 3) had mild efferent motor aphasia (according to A.R. Luria) or Broca’s aphasia, which manifested as individual perseverations in spontaneous speech and writing. Another patient (No 11) had normal speech, but had isolated perseverations of letters and syllables when writing. All patients had varying degrees of impairment of aural-speech memory and dynamic praxis.

3.2. Intraoperative mapping of functional speech zones of the cortex

The cortical area of motor speech was identified intraoperatively in 4 out of 12 patients. Its detection during the electrical stimulation was accompanied by speech arrest or perseverations of previous words, which was characteristic of efferent motor aphasia according to A.R. Luria (Broca’s aphasia). In 2 cases, the cortical motor speech zone was located in the posterior regions of the inferior frontal gyrus, which coincided with the generally accepted anatomical borders of the Broca’s area; in 2 other cases, it was localized in the middle and posterior parts of the middle frontal gyrus, respectively. In the remaining 8 observations, no cortical speech zones were detected during the surgery.

3.3. Intraoperative fluorescence diagnostics

Visible fluorescence was observed in 3 cases out of 6 patients operated on with the use of 5-ALA: One observation had a bright character (a patient with glioblastoma) and in 2 cases it was moderate (patients with Grade III gliomas). In 1 case, the fluorescence of the tumor was observed on the cerebral cortex. The fluorescence was absent in 3 patients with diffuse astrocytomas. Fluorescence was not used in 6 remaining cases.

3.4. Intraoperative mapping of the long association fibers

During the intraoperative mapping of the speech zones, the detected speech disorders were similar to those in efferent motor aphasia (Broca’s), e.g., perseveration, speech arrest, as well as acoustic-mnemonic aphasia (nomi- native, forgetting words). Less commonly, speech disorders occurred within the framework of the subcortical injury, e.g. dysarthria, slowdown. Speech disorders occurred for the first time outside of stimulation during free dialogue in 6 of 12 observations, as the tumor was being removed (paraphasia of a different nature, perseveration, pronouncing of words by syllables, dysarthria and slowdown, forgetting words). Of these 6 observations, direct electrostimulation was performed only in 2 cases, in which the speech disorders occurred again. In the remaining 6 observations, speech disorders occurred for the first time directly during the direct electrical stimulation. Therefore, speech disorders during the direct electrical stimulation were observed only in 8 out of the 12 observations: speech arrest, verbal and literal paraphasias when naming pictures, perseveration of previous words, forgetting words, slowing down and impaired speech articulation (Table 2). In 11 cases, the complex of the superior longitudinal and arcuate fascicula (SLF/AF)
was localized in the bed of the tumor being removed; in one patient the frontal aslant tract (FAT) was located in the area. In our study we considered the complex of the SLF and the AF as a whole, without distinguishing these tracts from one another and segmentation of the SLF into individual fascicles. The detailed data on speech disorders before the surgery, during the surgery and after it at different time points are presented in Table 2. Without presenting pictures, we didn’t catch the naming disorders (temporal component); after the surgery it was the one that could have become predominant.

As can be seen from the Table 2, after the surgery certain speech disorders were identified in 11 of 12 patients. In one of them, speech disorders appeared 1 day after the surgery, which can be associated with an increase in postoperative cerebral edema. One patient developed moderate right-sided hemiparesis, mainly in the arm, after the surgery.

Table 2 also demonstrates that aphasia, detected after the resection of the frontal lobe tumor of the left hemisphere, had a complex character in 10 patients in the studied series. Only two patients did not have aphasia after the surgery. One of them (No 1) had subcortical speech disorders (slowing down, non-gross dysarthria) and writing (“disrupted” writing, non-flowing, micrography). His tumor was small, located mainly in the dorsomedial prefrontal area, during testing there were speech disorders similar to postoperative ones. In another patient (No 7), speech remained normal during the observation period. Her tumor was small, located near the Broca’s area (according to functional MRI). During the intraoperative testing, perseveration and paraphasia were detected when naming actions, which made it possible to identify the Broca’s area.

The analysis of complex speech syndrome in 10 patients is of particular interest. Eight of them had disorders typical for injuries to the temporal lobe, in addition to the perseverating syndrome of varying severity (efferent motor aphasia according to Luria, Broca’s aphasia) typical for injuries to the left frontal lobe. These were primarily naming disorders, very similar to those in acoustic-mnestic aphasia (according to Luria). They were pronounced, accompanied by a description of the functional purpose of the presented object, in nearly all 8 patients. Verbal paraphasia, which the patients used instead of the real names of the objects, were also very characteristic; the paraphasias were often very far in meaning from the real name. In one case, such paraphasias were noted already during the intraoperative mapping (presentation of pictures with actions). An alienation of the meaning of words was observed In 4 out of these 7 patients, sometimes even in pronounced form (when asked to show parts of the face, objects in the room, pictures in an album, etc.). Such features of speech disorders made one think about the onset of conductive aphasia due to the severance of connections between the speech zones of...
the temporal and frontal lobes of the left hemisphere caused by damage to the long association fibers (SLF/AF complex).

After the surgery, patient No 2 had clear transcortical motor aphasia (dynamic). During the testing of the SLF/AF tracts, speech arrest and perseveration were noted. However, the postoperative picture better corresponded to the FAT involvement, which can be attributed to close spatial arrangement of the SLF/AF and FAT tracts in the area of the medial frontal gyrus. Another patient (No 5) had complicated motor aphasia (efferent motor - Broca’s aphasia) and afferent motor aphasia after the surgery, accompanied by impaired oral praxis and blurred speech. This component is characteristic of a parietal injury. The patient had a tumor predominantly of the median frontal gyrus, to a lesser extent of the lower frontal gyrus. Perseverations and speech blurring were also detected during the intraoperative testing. We could associate the onset of the parietal component in aphasia with the involvement of the parietal component of the superior longitudinal fasciculus.

The average Karnofsky index before surgery was 90 points, by the time of discharge, 70 points.

3.5. Magnetic Resonance Imaging

MRI conducted in all patients within the first 48—72 hours after the surgery showed that total resection was performed in 7 (more than 90% of the tumor) cases, subtotal, in 2, partial, in 2, and open biopsy was performed in 1 case. According to the postoperative MR tractography, the bed of the removed tumor was immediate adjacent to the SLF/AF complex in 7 cases, was located near the SLF/AF complex in 3 cases, and was immediately adjacent to FAT in 2 cases.

3.6. Clinical examples

Clinical example 1

Patient A, female, 29-year-old (observation No 7) The disease manifested in the form of attacks of speech disorders with subsequent short-term loss of consciousness. MRI of the brain revealed a tumor in the left frontal lobe (posterior parts of the inferior frontal gyrus - near Broca’s area) (see Fig. 2). Examination by a neuropsychologist before the surgery: speech functions normal; auditory and visual memory at the lower limit of the norm. The removal of the left frontal lobe tumor was performed with electrophysiological monitoring and awakening. The brain cortex was mapped intraoperatively: the Broca’s area was detected upward from the tumor (speech arrest was detected). Immediately towards the end of the tumor resection, during the electrical stimulation, in the region of the lower lateral surface of the surgical bed at a depth of about 3.5 cm from the cortex, speech disorders appeared in the form of incorrect naming of actions, and isolated perseverations; there were no visible tumor residues in this area. Topographically, this zone in the bed of the removed tumor corresponded to the course of the SLF/AF complex (which also corresponded to the data of both pre- and postoperative MR tractography). After the surgery, MRI with contrast enhancement showed total resection of the tumor; speech disorders were not detected during the examination by a neuropsychologist. Histological diagnosis: anaplastic oligodendroglioma.

Clinical example 2

Patient M, female, 60-year-old (observation No 4). Was admitted to the hospital with general cerebral symptoms. MRI before the surgery revealed glioma of the posterior portions of the inferior frontal gyrus on the left. In a preoperative neuropsychological study speech and writing were normal; the only disorders were clear defects of aural-speech memory with impaired selectivity of traces and disorders of dynamic praxis. The syndrome corresponded to the lesions of the posterior parts of the left frontal lobe.

The cortical motor zone of the arm was identified during the surgery (Fig. 3). During subcortical electrostimulation at a depth of about 4 cm from the cortex, specific errors were identified in the naming of the actions shown in the pictures. Specificity consisted in the fact that the patient used verbs that are very far in semantics from the correct ones to refer to the actions shown in the pictures. For example, when a patient was shown a picture where a girl strokes a cat, she said: “Scratching the ground”, when she was shown a picture where the girl was brushing her teeth, she said: “Strokes the sand.”

On Day 2 after the surgery, the efferent motor aphasia with verbal perseverations, naming disorders which were SLF/AF complex-specific and verbal paraphasias of similar nature were observed. Speech disorders had clear signs of damage to both the frontal and temporal lobes, which could be associated with the damage to the SLF/AF complex. Control MRI with contrast enhancement after the surgery, showed subtotal removal of the tumor.

Final histological diagnosis: diffuse astrocytoma Grade II.

Clinical example 3

Patient K, female, 48-year-old (observation No 9) The diagnosis of a tumor of the left frontal lobe was established 9 years ago after a single convulsive attack, which did not reoccur. All this time the patient abstained from the surgery and was under dynamic observation. At the next brain MRI, a significant increase in the size of the tumor was identified. The tumor had the following localization: the prefrontal regions and the poles of the left frontal lobe, the middle and anterior sections of the middle frontal and partially superior frontal gyri. Examination by a neuropsychologist before the surgery: speech is normal, other cognitive functions are preserved. The removal of the left frontal lobe tumor was performed with electrophysiological monitoring and awakening. During
### Table 2. Localization of the tumor and the dynamics of speech disorders in the examined patients

<table>
<thead>
<tr>
<th>No</th>
<th>Gender</th>
<th>Age</th>
<th>Gyri and areas of the frontal lobe (according to preoperative MRI)</th>
<th>Speech disorders prior to the surgery</th>
<th>Speech disorders during free dialogue without electrical stimulation during the tumor resection</th>
<th>Speech disorders during the electrical stimulation</th>
<th>Increase in aphasia after the surgery</th>
<th>Relationships to association tracts (according to postoperative MR tractography)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>39</td>
<td>Posterior sections of the MFG and partly the SFG (premotor region)</td>
<td>None</td>
<td>Dysarthria, slowing of the speech</td>
<td>Not stimulated</td>
<td>Mild dysarthria, slowdown and impaired smoothness of speech, low voice</td>
<td>The SLF/AF complex is immediately adjacent to the postoperative cavity</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>66</td>
<td>Posterior sections of the MFG (premotor region)</td>
<td>None</td>
<td>None</td>
<td>Disruptions in rendering of automated series (stops, perseveration)</td>
<td>Impaired active speech (transcortical motor or dynamic aphasia)</td>
<td>The SLF/AF complex is immediately adjacent to the postoperative cavity</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>61</td>
<td>Posterior sections of the IFG (Broca’s area)</td>
<td>Yes (light motor Broca’s aphasia)</td>
<td>Paraphasia and perseveration during the surgery in deep segments</td>
<td>Paraphasias and perseverations</td>
<td>Efferent motor aphasia (Broca’s) + clear inability to comprehend the meaning of words and naming disorders of the temporal type (conductive aphasia)</td>
<td>The SLF/AF complex is immediately adjacent to the postoperative cavity</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>60</td>
<td>Posterior sections of the IFG (Broca’s area)</td>
<td>None</td>
<td>None</td>
<td>Specific errors in naming the actions shown in the pictures</td>
<td>On Day 2: efferent motor aphasia (Broca’s) with verbal perseverations, naming disorders with specific verbal paraphasias</td>
<td>The SLF/AF complex is immediately adjacent to the postoperative cavity</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>33</td>
<td>Posterior sections of the MFG and partly the SFG (premotor + Broca’s)</td>
<td>None</td>
<td>None</td>
<td>Perseveration, blurred speech</td>
<td>Disruption of oral praxis + efferent motor aphasia (Broca’s) with perseverations and paraphasias</td>
<td>The SLF/AF complex is immediately adjacent to the postoperative cavity</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>37</td>
<td>The middle and posterior sections of the IFG (Broca’s area + partially prefrontal cortex)</td>
<td>None</td>
<td>None</td>
<td>Literal paraphasia and speech arrest when listing months</td>
<td>Gross efferent motor aphasia (Broca’s) + naming disorders, inability to comprehend the meaning of words and writing disorders of the temporal type (fluent writing, verbal and literal paragraphias)</td>
<td>The SLF/AF complex is near the postoperative cavity</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>29</td>
<td>Posterior sections of the IFG (Broca’s field)</td>
<td>None</td>
<td>None</td>
<td>Action’s naming disorders, isolated perseverations, when counting transition from Russian to Chuvash (bilingual)</td>
<td>Normal speech</td>
<td>The SLF/AF complex is immediately adjacent to the postoperative cavity</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>49</td>
<td>Posterior sections of the SFG (dorsomedial area)</td>
<td>None</td>
<td>None</td>
<td>Irregular and unclear speech slowdown</td>
<td>No aphasia, writing disorders of the subcortical type (micrographies)</td>
<td>The SLF/AF complex is immediately adjacent to the postoperative cavity</td>
</tr>
</tbody>
</table>

*The Table is continued on the next page*
Characteistically, during the perseverations, either objects or actions properly and she constantly persevered. During the test, she used the same verbs as during stimulation during the surgery. The temporal component of aphasia during the surgery in the region of the middle and superior frontal gyri of the cortical-subcortical level of the left frontal lobe indicates dissociation of the frontal and temporal lobes due to damage to the SLF/AF complex. This may be attributed to the large size of the tumor and the development of postoperative edema in the area of the not only the FAT, but also the SLF/AF. The results of the examination and identified disorders are presented in Fig. 4.

In this clinical example, the FAT mapping is interesting. Intraoperatively, the patient developed perseverations and paraphasias, these speech disorders could have been caused by electrical stimulation of the FAT, which links the extra motor cortex and Broca’s area. The path of the fibers of the tract identified during the surgery corresponded anatomically to the FAT’s course along the posterior contour of the tumor, obtained by MR tractography. However, in the postoperative period, due to the

Table 2. Localization of the tumor and the dynamics of speech disorders in the examined patients (continued)

<table>
<thead>
<tr>
<th>No</th>
<th>Gender</th>
<th>Age</th>
<th>Gyri and areas of the frontal lobe (according to preoperative MRI)</th>
<th>Speech disorders prior to the surgery</th>
<th>Speech disorders during free dialogue without electrical stimulation during the tumor resection</th>
<th>Speech disorders during the electrical stimulation</th>
<th>Increase in aphasia after the surgery</th>
<th>Relationships to association tracts (according to postoperative MR tractography)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>F</td>
<td>48</td>
<td>Middle and anterior sections of the MFG and partially SFG (prefrontal cortex + frontal lobe area)</td>
<td>None</td>
<td>Isolated literal paraphasias</td>
<td>During electrical stimulation of the white matter of the superior and middle frontal gyri - verbal paraphasias when naming verbs</td>
<td>Aphasia of complex genesis: non-gross efferent motor aphasia (Broca’s) with naming disorders, inability to comprehend the meaning of words (as in temporal aphasia) and verbal naming paraphasias with different meanings (conductive aphasia)</td>
<td>The FAT is immediately adjacent to the postoperative cavity</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>35</td>
<td>Posterior sections of the MFG and partly IFG (prefrontal cortex + Broca’s area)</td>
<td>None</td>
<td>Perseveration and verb naming disorders</td>
<td>No electrical stimulation was performed.</td>
<td>Some deterioration of naming (nomination) of the temporal type (conductive aphasia)</td>
<td>The SLF/AF complex and FAT are immediately adjacent to the postoperative cavity</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>28</td>
<td>Middle sections of the IFG (prefrontal cortex + Broca’s area)</td>
<td>Isolated perseverations when writing</td>
<td>No impairment of speech were detected on the surface of the cortex.</td>
<td>Naming disorders, gross writing defects with word sound analysis disorders of the temporal type. The motor side of speech is normal</td>
<td>The SLF/AF complex near the postoperative cavity</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>56</td>
<td>Posterior sections of the MFG and partly IFG (premotor cortex + Broca’s area)</td>
<td>None</td>
<td>In the depth of the wound, stopping and perseveration when listing months.</td>
<td>No impairment of speech were detected on the surface of the cortex.</td>
<td>Naming disorders, gross writing defects with word sound analysis disorders of the temporal type. The motor side of speech is normal</td>
<td>The SLF/AF complex near the postoperative cavity</td>
</tr>
</tbody>
</table>
The large size of the tumor and the development of perifocal edema, the onset of clinic presentation associated with injury to the SLF/AF complex was observed, which was dominated by temporal aphasia.

**Discussion**

The modern understanding of the neuroanatomical basis of linguistic functions has been established through models involving many areas of the cerebral cortex, functioning as part of a large network, including those consisting of the superior frontal gyrus, inferior parietal lobe, middle temporal gyrus, inferior temporal lobe region and other white matter tracts such as the SLFs, IFOFs, and fibers in the deep parts of the frontal lobe [21].

It should be noted that in general the function of the white matter pathways is not as well studied as that of the cortical structures of the brain. One of the reasons is the limitations of such research since it is usually difficult to find a patient with selective lesions of a particular tract. In addition, although the cortex can be mapped using surface electrodes, for example, as a method of preoperative study in patients with epilepsy or brain tumors, subcortical fibers are not as easy to evaluate this way [22].

The stimulation zone is considered functionally significant when speech disorders are noted three times in a row after subsequent stimuli, and speech function is re-
covered after the end of the stimulation. The type of speech disorders is verified by a neuropsychologist, and the nature and severity of speech disorders are assessed based on the tests used. The next stage is the resection of the tumor, taking into account the mapping data; periodic subcortical stimulation is performed to search for functionally significant white matter pathways.

Therefore, the use of intraoperative mapping and electrophysiological monitoring allows surgeons to remove the maximum possible volume of the pathological focus while maintaining neurological functions and minimizing the rate of postoperative complications [23—25].

The frontal lobe is the largest lobe of the human brain, its volume is up to 40% of the whole brain, and in terms of gliomas, it ranks first ahead of other brain lobes [10]. The main association fibers of the frontal lobe include the superior longitudinal fasciculus (SLF), which is divided into three segments (SLF I, II, III), the frontal aslant tract (FAT) and the lower frontal-occipital fasciculus (IFOF), which we did not review in our work. The variable anatomy of these tracts has been shown in the earlier works [14, 16].

In our series of 12 patients, all tumors were located in the left frontal lobe. The group included 7 patients with low-grade gliomas (Grade II) and 5 with high-grade gliomas (Grade III — IV). In 6 cases, speech disorders were observed without direct electrical stimulation during the resection of the tumor in the subcortical parts. In 8 patients, speech disorders developed during the electrical stimulation. The nature of speech disorders was diverse. In one patient, speech disorder was delayed (on Day 2) and reversible. In our opinion, this may be attributed to transient perifocal edema caused by the proximity of the SLF/AF fibers. The symptoms fully regressed after anti-edema therapy.

In this study, we observed reproducible speech symptoms in 8 patients during the electrical stimulation of the white matter of the frontal lobe. Our results showed that 11 patients had speech disorders without motor disorders of the extremities or tongue (except for 1 observation with the development of right-sided hemiparesis in the postoperative period). It means that aphasic disorders were not associated with damage to the motor component (the cortex and pyramidal tract).

After the surgery, an increase in speech disorders was noted in all patients (except 1 patient, observation No 7). It is noteworthy that in most cases aphasia was complex and combined focal symptoms of injury to both the frontal and temporal lobes, and in one patient (observation No 5) to the frontal and parietal lobes. It indicates partial damage to the long association fibers, leading to symptoms of dissociation of these brain lobes. The speech disorders described by us are fully aligned with the descriptions of conductive aphasia presented in the literature [26—28].

As a rule, if an intraoperative damage is not gross and incomplete, speech disorders are transient in nature and regress in a period from several days to several weeks. In these situations, the work of a speech therapist in the postoperative period is of particular importance.

Thus, 11 out of 12 patients had various variants of speech disorders in the postoperative period, despite the fact that the studied tracts were identified during the awake surgery and this information served as the basis for stopping the resection of the tumor. Our results correspond to the data presented in international literature, according to which patients have speech disorders after awake surgery with an incidence of up to 95%. (Such surgeries are, in principle, are performed when the speech cortical zones or vocal tracts are close). When the resection is methodically performed with mapping of the tract, speech disorders regress within 3 months after the surgery and remain permanent in only 5% of patients.

In one of the observations, it was impossible to reconstruct a part of the SLF/AF fibers in the tumor itself with the help of MR-tractography. When measuring the distance from the surface of the cortex to the fibers of the tract in the pre-operative images, we see a discrepancy with the distance from the tract to the cortex measured during the surgery. The tract was detected at a closer distance to the cortex, which indicates the impossibility of reconstructing fibers of the long association tract in the tumor itself. Any preoperative tractography is provisional (it is a mathematical model), because it has significant limitations in the reconstruction of fibers passing inside the tumor.

A number of researchers use different current strengths (from 2 to 10 mA) and different pulse amplitudes during the intraoperative stimulation. K. Seidel et al. [29] suggest to stop tumor resection in case of response to stimulation with a current strength of 2 mA. H. Duffau et al. [30] also use a current of 2 mA and considers the method of direct electrostimulation safe, accurate and reliable mean to identify pathways. It is well known that the strength of a current is interdependent with the distance over which it spreads; with an approximate ratio of 1 mm to 1 mA (the “golden rule” of neurophysiology) [31]. The parameters and the strength of the current are of great importance when stimulating the association fibers. In our series of observations, the current strength was 2–5 mA, which is in agreement with the data of foreign authors.

In patients with malignant gliomas, focal neurological symptoms are significantly more frequent before the surgery. In case of localization of long association fibers or the functional cortical speech zone near the tumor, it usually manifests as aphasia. In case of gross aphasia before the surgery, the awake craniotomy is contraindicated. At the same time, in case of the infiltrative nature of tumor growth, long association fibers can be involved in its structure, and their function can be preserved, especially in benign gliomas [32]. In case of malignant gliomas there is a destruction zone with an already formed focal neurological deficit in the white matter. In low-
Fig. 3. Magnetic resonance imaging of the brain of the patient M.

a, b — MRI with contrast enhancement before the surgery in T1 and T2 modes, axial sections; c — positron emission tomography of the brain with methionine: accumulation index of RFP 1.3; d — functional MRI: orange color indicates Broca's area; e, f — preoperative MR-tractography: green color indicates the pyramidal tract, blue, arcuate fiber; g — intraoperative photo: 0 — right hand movement zone; h — intraoperative photo: visible fluorescence of the tumor; i — intraoperative photo: the arcuate fasciculus identified during the electrical stimulation in the depth of the tumor bed; j — MRI with contrast enhancement in the first 72 hours after surgery, axial section; k, l — postoperative MR-tractography: green color indicates the pyramidal tract, blue, arcuate fiber.
grade gliomas, the main symptoms before the surgery are focal epileptic seizures, aphasic disorders are extremely rare, which increases the complexity of the surgery and requires mandatory mapping of not only cortical zones, but also long association fibers.

In our series, the SLF/AF complex was found in 9 out of 12 patients during the surgery. We consider it unreasonable to differentiate these tracts during the surgery due to their close topographic-anatomical location and parallel course of the fibers. The difference between these tracts is that the SLF fibers switch in the parietal zone of Geschwind’s zone, while the AF fibers go directly from the frontal lobe to the temporal lobe. In addition, during the surgery, it is difficult to identify the SLF segments due to their close proximity to each other and the similarity of the neurological symptoms of a lesion. However, anatomical separation of the SLF and AF fibers and the possibility of distinguishing between individual SLF segments have been shown in a number of papers [33]. In our opinion, studying the course of the fibers on anatomical preparations is necessary for a neurosurgeon-neurooncologist, however, distinguishing individual closely

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**Fig. 4. Magnetic resonance imaging of the brain of the patient K.**

a, b — MRI before the operation in T1 and T2 modes, axial sections; c — fMRI - Broca's area is marked in orange; d — preoperative MR-tractography: AF is denoted with yellow, FAT with violet, a postoperative cavity is highlighted with green. The FAT is located at the posterior border of the tumor and closely adjacent to it; e — intraoperative photo: 0, 2, 3, 41 — zones of speech disorders in the wound bed, obtained by direct electrical stimulation; the topography of the identified zones, corresponding to the course of the FAT fibers, attracts particular attention; f — MRI after the surgery within the first 72 hours The arrow indicates the hemostatic mark (a fragment of hemostatic gauze left in the cavity of the bed along the posterior contour of the tumor in the zone of speech disorders identified during the electrical stimulation), g — postoperative MR-tractography: AF is denoted with yellow, FAT with violet, remnants of the tumor are highlighted with green.
located tracts, and especially their segments, from each other is hardly possible during a real surgery. Therefore, we can agree with the opinion of a number of colleagues that intraoperatively it is reasonable to identify the SLF and AF fibers as a single complex. This is due not only to the proximity and contours of their course, but also to the similar symptoms in case of damage [32].

Therefore, clinical significance of such detailed intraoperative differential diagnosis of lesions to specific segments of association tracts remains controversial, since damage to any of the above described fibers is an indication for stopping tumor resection regardless of the specifically affected segment. However, understanding of the topography of the above fibers and their functions can provide valuable intraoperative information about the degree of involvement of each particular segment and influence the decision to continue with the tumor resection.

Conclusions

1. In case of intracerebral tumors of the frontal lobe of the dominant speech hemisphere, it is advisable to perform MR tractography with the reconstruction of long association fibers (SLF/AF complex and FAT) to assess their relationship with the tumor and their electrophysiological identification in conditions of awake craniotomy.

2. In surgery of tumors of the frontal lobe of the dominant hemisphere in awake conditions, after identifying functionally significant cortical structures at all stages of tumor resection, it is advisable to maintain continuous speech contact with the patient, complementing it with electrical stimulation, since the likelihood of speech disorders is high. The segmentation of the SLF fibers and distinguishing the SLF from the AF is difficult in real operating conditions.

3. In the majority of observations, patients experience an increase in speech disorders in the early postoperative period (11 out of 12 patients). These speech disorders eventually regress in the vast majority of patients.

4. In case of damage to the long association fibers of the dominant hemisphere during the surgery, a syndrome of separation of the frontal, temporal, and less often the parietal lobes may develop followed by development of complex types of aphasias, which may increase in the early postoperative period.

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Limitations:

The follow-up interval was insufficient in patients operated on in 2017 (less than 12 months). The study did not include any left-handed persons. We did not consider patients with bilateral speech representation in tumors of the subdominant hemisphere and cross aphasia.

Authors declare no conflict of interest.

REFERENCES


ORIgINAL ARTICLES


Commentary

One of the important problems in neurooncology is surgical tactics in the treatment of gliomas of functionally significant areas of the brain. Neurosurgery focuses on the mapping of the cerebral cortex. Methods for mapping pathways, especially the long association fibers of the brain, have been studied to a lesser extent and are not implemented into practice to the same degree. These conductors support the most important functions of the human brain, which was confirmed by a number of studies (H. Duffau et al., M. Berger et al., S. Sarubbo et al., 2015).

The article summarizes the experience of mapping the complex of the superior longitudinal and arcuate tracts in 12 patients with gliomas of the left frontal lobe. The authors continue to summarize the clinical observations after 2 previous publications on the anatomy of the long association fibers (S.A. Goryainov, V.Yu. Zhukov, A.A. Potapov, 2014 and 2017).
A review of the literature and clinical examples are provided, with particular attention on the details of mapping of long association fibers, features of neuropsychological tests and postoperative speech disorders. The work is illustrated with clinical examples of patients with gliomas of the left frontal lobe with intraoperative identification of the complex of the superior longitudinal and arcuate tracts.

The authors dataset is rather small and they should continue this important study; our recommendation would be to include patients with gliomas of the brain that involve other long association tracts.

This is the first work in the Russian literature on this particular topic and it will be useful for practicing neurosurgeons who treat patients with intracerebral brain tumors, which will improve the safety and effectiveness of surgical interventions.

V.L. Puchkov (Moscow, Russia)
Evaluation of Vascular Reactivity to Overcome the Limitations of Neurovascular Uncoupling in BOLD fMRI of Malignant Brain Tumors

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The sensitivity of fMRI in identification of eloquent cortical centers in the case of large infiltrative growing tumors and pronounced peritumoral edema may be reduced or significantly limited in some cases. The main cause is an attenuated Blood-Oxygen-Level-Dependent response (BOLD) caused by pathological vascular reactivity and subsequent neurovascular uncoupling of fMRI. In our study, we attempted to overcome these limitations and increase the sensitivity of this technique in identification of eloquent cortical areas adjacent to brain tumors by using vasoreactivity features of a breath-holding test and including these data in the BOLD analysis. Local vasoreactivity using a breath-holding paradigm with the same block design of both motor and speech tests was determined in 5 healthy volunteers and 3 patients in the preoperative period (two patients with high grade gliomas and one patient with single metastasis). Obtained coherence maps demonstrated clinically more significant activation zones that were not seen with standard methods of fMRI analysis. Thus, neurovascular uncoupling that is known to affect the accuracy of the BOLD fMRI response adjacent to brain tumors may be partially overcome by including an independent measurement of vasoreactivity using a breath-holding test in the BOLD analysis.

Keywords: BOLD fMRI, brain tumors, vascular reactivity, breath-holding, neurosurgery.

Neurosurgical resection remains one of the key methods used to treat malignant brain tumors. The degree of tumor resection ensuring minimal damage to eloquent brain structures has a significant impact on patients’ postoperative life span and quality of life. Preoperative identification of eloquent cortical areas using fMRI and identification of the essential white matter tracts using various MR tractography techniques, followed by their subsequent intraoperative neurophysiological verification, is currently considered the standard in brain tumor surgery [1, 2, 3, 4]. However, both of these methods are known to have their own limitations and disadvantages.

BOLD fMRI maps were shown to occasionally yield false-negative results if large invasive brain tumors that are located near the eloquent cortical areas [5—9]. BOLD fMRI is based on an assumption that there is functional correlation between neuronal activity and local blood flow. This method assesses vascular response rather than neuronal activity. Pathological vessels of malignant tumors are abnormal, both structurally and functionally [5], and are characterized by altered vascular reactivity [10—14]. In patients with malignant brain tumors, abnormal tumor vessels often do not respond to increased neuronal activity, resulting in reduction of BOLD signal intensity [15]. Peritumoral edema also alters vasoreactivity, thus complicating the construction of fMRI maps.

In a number of recent studies [9, 16—18], attempts have been made to reveal correlations between the anatomical localization of the neurovascular uncoupling area (determined by quantitative measurements of cerebrovascular reactivity) and the false-negative BOLD fMRI results.

The technique most commonly used for analyzing the fMRI data is based on the principle of invariance of the hemodynamic response function upon respective stimulation. This may lead to underestimation of the degree of activation or false-negative results in statistical parametric BOLD maps in cases when the tumor affects the adjacent eloquent cortical area.

A possible way to avoid these false-negative results caused by the pathological network of tumor vessels and neurovascular uncoupling is to measure vasoreactivity and include these data in BOLD fMRI analysis. One of the methods to evaluate vasoreactivity is breath holding. Breath holding leads to hypoxia and, potentially, hypercapnia, which normally results in the dilation of brain vessels [14, 17, 18]. Vasodilation can be assessed using the same procedure as the one employed to measure the BOLD fMRI responses under the standard paradigms. In such cases, it is assumed that the hemodynamic response function of the pathological vascular network deviates from normal conditions to the same extent regardless of the type of stimulation (breath-holding or motor/speech paradigms). If this assumption turns out to be correct, it will be possible to identify activation zones even in the areas of the pathological vascular network by assessing coherence between the hemodynamic response

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function during breath-holding and standard fMRI paradigms.

The aim of this pilot study is to apply coherent analysis that takes into account the altered hemodynamics for comparison of BOLD fMRI maps obtained during motor or speech tests and the breath-holding test.

Material and Methods

The study involved five healthy volunteers (3 males and 2 females; median age, 23.5 years) and three patients with brain tumors (two patients with high-grade gliomas, one patient with an anaplastic oligodendroglioma in the left fronto-temporo-insular region, one patient with a glioblastoma in the left posterior frontoparietal region, and one patient with a solitary lung cancer metastasis in the left fronto-temporo-insular region, one patient with a glioblastoma in the left posterior frontoparietal region, and one patient with a solitary lung cancer metastasis in the left parietal lobe).

MRI was performed on a 3.0 T MRI scanner using an 8-channel head coil. In all cases, routine T1-weighted, T2-weighted, and T2-FLAIR MR images, as well as 3D SPGR images (slice thickness of 1 mm) were acquired to obtain an anatomical model. Functional MRI during the breath-holding, speech and motor tests was conducted using the echo-planar imaging technique (TR = 3 s; TE = 30 s; flip angle = 60; matrix, 128×128; FOV=240 mm; slice thickness, 5 mm). The voxel size = 3 s; TE=30 s; flip angle=60; matrix, 128×128; FOV=240 mm; slice thickness, 5 mm). The voxel size was 1.88×1.88×5 mm3.

A total of 30 fMRI studies were conducted using standard block paradigms for mapping motor and speech zones in the volunteer group. Speech mapping was performed in the patient with anaplastic oligodendroglioma in the deep parts of the left temporal lobe. The patients with glioblastoma in the left posterior frontoparietal area and metastasis in the left parietal lobe underwent mapping of the motor cortex.

All subjects also underwent a breath-holding test, whose design was exactly the same as the motor and motion-related block paradigms.

An abdominal cuff was used to control breath holding during fMRI. In addition, oxygen saturation level was determined during the breath-holding test using a pulse oximeter; a 2% decline in blood oxygen level was detected in all volunteers and patients.

In all the tasks, a total of 112 volumes (8 times 14 volumes) were recorded during a 6-minute scan. An abdominal cuff was used to control respiratory movements to monitor breath holding.

Design of the standard fMRI consisted of eight blocks, with 14 volumes per block: six volumes for activity and eight volumes for rest (both when performing tasks and during breath holding). The tasks for activating the motor areas included simultaneous bimanual finger tapping and toe movement on both feet. Speech tasks consisted of three test variants: “letters”, “verbs” and “listening”. In the “letters” task, a volunteer or a patient mentally articulated the words beginning with a letter they saw on the screen. The “verbs” task consisted of mental articulation of verbs expressing actions related to an object shown on the screen. The “listening” task consisted of passive listening to the text without articulation.

The preliminary data processing included:
1) correction of movements and time shifts using the AFNI software;
2) MRI brain image segmentation based on thresholding using the FSL software;
3) voxel-wise removal of linear trends in time series using the AFNI software;
4) spatial smoothing using a Gaussian filter kernel with full width at half maximum (8×8×8 mm3) in the Matlab software.

Correlation and coherence analysis of all fMRI images was performed using the MATLAB v. 2017b software package [19].

Figure 1 presents the main concept of the proposed method. The parametric activation maps were constructed in accordance with the principle of correction of the effects of breath holding on vascular reactivity and the BOLD signal in healthy volunteers and study patients.

During the first stage of processing the data obtained from healthy volunteers and study patients, the fMRI map of vasoreactivity was constructed by calculating the correlation between the time series obtained during the breath-holding tests x(t) and the activation function I(t). I(t)=1 during breath holding (activity) and I(t)=0 during unrestrained breathing (rest).

The vasoreactivity function in the activation zone (green line) normally has the same shape as the function of an ideal hemodynamic response (black line) (see Fig. 1a). Parametric activation maps were obtained using the conventional analysis based on correlation coefficients. A positive correlation was considered statistically significant at p<0.05 (one-tailed test for the Pearson correlation coefficient with Bonferroni correction for multiple comparisons).

In patients with tumors, the shape of the activation function (shown in black in Fig. 1b) may differ from that of the vasoreactivity function (an ideal hemodynamic response, green curve). The vasoreactivity function for such cases was calculated by modified standard analysis based on coherence (see Fig. 1c).

The parametric activation maps in the presence of a tumor were obtained using the vasoreactivity function; modified analysis involved correction of pathological vascular reactivity based on coherence using the fMRI data during breath holding (see Fig. 1d). The coherence-based analysis uses the fMRI data during breath holding and suggests that the hemodynamic response depends on voxel localization because of the abnormal vasoreactivity of brain tissues adjacent to the tumor. In order to determine the activation zones by modified standard analysis based on coherence, the maximum coherence coh(y(t), I(t)) between the MR signal during the task y(t) and activation function I(t) was calculated for each voxel in the frequency range [0.006, 0.028] Hz. The coh_thr coher-
ence threshold value was chosen by the iterative method so that the number of voxels with \( \text{coh}(y(t),I(t)) > \text{coh\_thr} \) was equal to the number of activated voxels for the standard correlation-based analysis. Next, voxel-wise calculation of the maximum coherence \( \text{coh}(y(t),x(t)) \) between the signal obtained during the task \( y(t) \) and the signal obtained during breath holding \( x(t) \) was performed in the frequency range indicated above. The voxels were marked as activated if \( \text{coh}(y(t),x(t)) > \text{coh\_thr} \) for the threshold value obtained at the previous step.

**Results**

Analysis of the results involved evaluation of the relationship between neurovascular responses recorded during the breath-holding tests and when performing the paradigms for motor/speech activation. Furthermore, the results of the conventional and modified methods for constructing parametric maps for fMRI recorded during breath holding and motor/speech activation were compared.

*Figure 2* compares the time functions of response averaged with respect to the rest + activity periods and recorded by fMRI using the standard motor task \( Y(t) \) (blue line) and by fMRI during the breath-holding test \( X(t) \) (red line) for an individual voxel in the activation zone for the patient with an intracranial tumor. The \( Y(t) \) and \( X(t) \) graphs are opposite in phase for this voxel. The linear correlation between \( Y(t) \) and \( X(t) \) suggests that the coherence functions are similar for block motor/speech fMRI and fMRI during breath holding. It is shown for the same voxel (*Fig. 2b*). The blue line represents the coherence function for fMRI during the standard motor task, while the red line is that for fMRI during the breath-holding task.

**Comparison of fMRI results based on the correlation and coherence functions**

Since healthy volunteers have no vasoreactivity disturbances, similar activation maps were obtained using the conventional method for analyzing the fMRI and
coherence-based analysis, with allowance for the breath-holding data (Fig. 3).

Coherent analysis with allowance for the breath-holding data showed larger areas of activation zones when mapping eloquent cerebral cortex areas located in the immediate vicinity of the tumor (Figs. 4, 5).

Figure 4 presents the data for the patient with anaplastic oligodendroglioma in the left fronto-temporo-insular region. The conventional correlation method (Fig. 4a) visualized an activation area located in the medial frontal gyrus lateral to the tumor. Coherent analysis with allowance for the breath-holding data showed a more extensive activation zone in the pars triangularis of the left inferior frontal gyrus, with transition to the medial frontal gyrus (Fig. 4b).

We failed to map the Broca’s area via direct intraoperative cortical stimulation during tumor resection. Nevertheless, no speech disorders were detected during the postoperative period after resection of at least 70% of the tumor volume. The negative outcome of direct cortical electrostimulation can be attributed to the fact that the tumor displaced the inferior frontal gyrus (where fMRI analysis showed activation of speech zones during mapping) towards the superior edge of the trephination window. This speech zone turned out to be located outside the craniotomy.

Figure 5 shows activation maps of the motor zone of the right hand in a patient with a solitary lung cancer metastasis in the left parietal lobe. The standard method of

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Fig. 2. The results of fMRI data analysis for one voxel of the motor area in a patient with a tumor.
Blue lines represent the functions for fMRI during a standard motor task; red lines represent the functions for fMRI during the breath-holding test. a – time functions of response obtained by fMRI and averaged with respect to the rest + activity periods; b – the coherence function for fMRI.

Fig. 3. fMRI mapping of the motor zone controlling the right hand in a healthy volunteer (using different processing methods).
a – standard analysis; b – coherent analysis with allowance for breath-holding revealed no differences between the activation zones.
Fig. 4. fMRI mapping of the speech zones in a patient with anaplastic oligodendroglioma of the left frontal temporo-insular area using the verb generation test (activation maps).

a — the map obtained using the conventional correlation method shows a small activation area in the medial frontal gyrus; b — the map obtained using coherent analysis with allowance for the breath-holding data showed more extensive activation in the triangular part of the inferior frontal gyrus with transition to the medial frontal gyrus.

Fig. 5. fMRI mapping of the motor zone controlling the right hand in a patient with a metastasis in the left parietal lobe. Activation maps.

a — the map obtained using the conventional correlation method revealed a small activation area along the anterior contour of the tumor; b — the map obtained using coherent analysis with allowance for the breath-holding data shows a more extensive activation zone in the left precentral gyrus.

Fig. 6. a — The overall view of the surgical wound: trephination was performed; the dura mater was opened; the surgeon performs mapping of the right hand motor area with a bipolar electrode. An adapter of the Fiagon navigation system is attached to the bipolar electrode; b — a screenshot of the Fiagon navigation system. Coronary section: a tumor in the left parietal lobe is visualized; the activation zone of the right hand is visualized medially from it. The bipolar electrode sensor is located in this area. A neurophysiologist registered the M responses during bipolar stimulation (at current of 4.5 mA).
fMRI data analysis revealed a small activation zone along the anterior contour of the bulky lesion.

Coherent analysis with allowance for the breath-holding test data allowed visualization of a larger activation area in the deformed precentral gyrus.

Intraoperative mapping of the motor area controlling the right hand showed a 100% agreement between the fMRI data and direct cortical electrostimulation (Fig. 6).

Discussion

The vasodilating effect caused by an increase in CO2 concentration can be used to calibrate BOLD signal intensity and for better identification of activation areas in the peritumoral region during fMRI [7, 8, 11, 20—23]. The coherent analysis employed in the work was tested in functional studies on healthy volunteers and applied to three patients: two patients with high-grade gliomas and one patient with a metastasis. The proposed coherence method differs from the standard analysis of the fMRI data and assumes that there is linear dependence between vasoreactivity during breath holding and the BOLD response. We believe that a larger-scale study is needed because the pathological effect of a tumor on vascular response substantially varies. A larger sample size should be used in this study; furthermore, such factors as tumor localization and invasion, as well as the type of an eloquent cortical area, should be taken into account.

Effectiveness of the proposed coherence method largely depends on patient’s compliance during all the activation tasks, including breath holding. The breath-holding task can be quite difficult in a clinical setting depending on the severity of patient’s condition [3]. In our pilot study, both healthy volunteers and all three patients in the study group properly performed all the tasks and succeeded with the breath-holding test.

An adequate statistical threshold should be used for construction of statistical parametric maps of cerebral activation in preoperative fMRI planning, like in any other MRI study. However, in neuroradiological studies involving healthy volunteers, a fixed threshold value is often set for all the subjects included in group analysis. For patients with brain tumors, the adequate choice of threshold values requires a personalized approach. One of the reasons for this is that BOLD signal intensity is attenuated by the significantly altered hemodynamic response, as it has been demonstrated for a patient who had performed the motor activation task [9]. In clinical practice, the requirements to the threshold values are less stringent than in research in order to reduce the incidence of false-positive results. In this study, taking into account multiple comparisons, the threshold was p<0.05. We have chosen this rather conservative approach to have a basis for comparisons. It is quite possible that the differences between the standard maps and the vasoreactivity-based ones will become more apparent once the threshold values are set for each case individually. Our study is based on the well-known vasodilating effect of increased CO2 concentration and reduced O2 concentration. This effect can also be used for BOLD fMRI. We have taken the first steps towards understanding how vasoreactivity during breath holding can be used to improve fMRI imaging of the eloquent cortical areas in patients with brain tumors. We employed the relatively crude and insufficiently controlled method of breath holding to measure vasoreactivity in our study. An abdominal cuff was used to control breath holding during fMRI. The saturation level was also determined during the breath-holding test using a pulse oximeter. A 2% decrease in blood O2 saturation in all volunteers and study patients was revealed, which confirmed that the breath-holding test effectively induces hypoxia. In our opinion, the breath-holding test can be applied in the clinical studies without using additional equipment or medical staff. The direct methods for creating hypercapnia (e.g., by inhaling a gas mixture with a high CO2 content [23]) can be monitored better and provide better results in combination with fMRI studies. However, the risk of side effects of elevated CO2 concentrations in blood (such as increased intracranial pressure or epileptic seizures) rises in patients with brain tumors.

Conclusion

Pathological vascular reactivity attenuates the BOLD signal response from the motor/speech cortex in the peritumoral region and limits the informative value of preoperative fMRI. We suggest that these functional areas are identified by independent assessment of vasoreactivity using fMRI coupled with the breath-holding test. According to our preliminary data, coherent analysis including the fMRI data with the breath-holding paradigm can reveal clinically significant extended activation zones. The presented preliminary results demonstrate that neurovascular uncoupling, which is known for its impact on accuracy of BOLD fMRI in the peritumoral regions, can be at least partially overcome by supplementing the conventional BOLD analysis with independent assessment of vasoreactivity.

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Commentary

The article is devoted to an important problem of neuroimaging: improvement of mapping of the eloquent cortical areas during surgical planning. Vascular reactivity plays an important role not only in brain malignancies but also in other pathologies altering the function of the vascular system, and vascular diseases of the brain in particular. The presented data are obtained for a small sample of patients. However, fMRI coupled with breath-holding tests and coherent analysis (which is independent of signal amplitude) can improve visualization of the eloquent cortical areas in the tumor area and peritumoral edema region. It should be further studied whether or not the breath-holding test can be used for a larger sample of patients. The paper “Evaluation of Vascular Reactivity to Overcome the Limitations of Neurovascular Uncoupling in BOLD fMRI of Malignant Brain Tumors” is undoubtedly of interest for the audience.

R.N. Konovalov (Moscow, Russia)
Surgery of suprasellar meningiomas is a challenge and associated with a high risk of injury to the vascular-neural structures lying along the approach and surrounding the tumor. Currently, many foreign clinics and our Center have introduced a technique for resection of suprasellar meningiomas through the anterior extended transsphenoidal endoscopic endonasal approach.

Objective. The study objective was to evaluate the role of extended transsphenoidal endoscopic endonasal approaches in surgery of suprasellar meningiomas.

Material and methods. The present study is a retrospective analysis of surgical treatment outcomes in 45 patients (11 males and 34 females aged 23 to 70 years [median, 50 years]) with suprasellar meningiomas who underwent surgery for skull base tumors using the anterior extended transsphenoidal endoscopic endonasal approach in the Surgery Department of the Burdenko Neurosurgical Institute in the period from 2009 to 2017. In all cases, surgery was the primary method of treatment.

Results. Total tumor resection (the tumor was resected completely together with an infiltrated DM — Simpson 1) was achieved in 77.8% (35/45) of cases; subtotal resection (more than 80% of the tumor was removed) was in 17.8% (8/45) of cases; in 4.4% (2/45) of cases, resection was partial (less than 80% of the tumor was resected). Worsening or development of visual impairments immediately after surgery occurred in 13 (28%) of 45 patients. In 3 of them, vision was completely recovered on conservative treatment by the time of hospital discharge. In 4 patients, vision partially improved by the time of discharge. In 6 patients, vision was not recovered by discharge (in 2 of them, vision partially improved during follow-up). Therefore, by the time of hospital discharge, deterioration in vision occurred in 10 (22%) of 45 patients. In 7 (21.2%) out of 33 patients who had visual impairments before surgery, there was an improvement in vision in the postoperative period.

Conclusion. Analyzing the findings and generalizing our experience, we may say that, in surgery of suprasellar meningiomas, the anterior extended transsphenoidal endoscopic endonasal approach should be used for relatively small (up to 3 cm) and located symmetrical tumors that do not involve large vessels. The efficacy of this technique for tumors extending into the optic nerve canals requires additional analysis in a larger series of cases.

Keywords: suprasellar meningiomas, transsphenoidal endoscopic endonasal approach.

Meningiomas account for about 1/3 of all primary tumors of the central nervous system [1]. Suprasellar meningiomas whose site of initial growth is the limbus and planum sphenoidale, prechiasmatic groove, and tuberculum and diaphragma sellae account for 5—10% of all intracranial meningiomas [2—4]. Also, tumors originating from the meninges of the anterior clinoid processes [5, 6] are referred by some authors to suprasellar meningiomas.

Surgery of suprasellar meningiomas is particularly challenging and associated with a high risk of injury to the neurovascular structures surrounding the approach and the tumor [7]. Until recently, only transcranial approaches, such as subfrontal and pterional, were used for removal of suprasellar meningiomas [8—11]. However, the rapid development of endoscopic techniques and extended transsphenoidal endoscopic endonasal approaches in the last decade has led to dramatic changes in surgery of suprasellar tumors, including meningiomas [5, 12—16]. For example, at present, many foreign clinics and our Center actively use the anterior extended transsphenoidal endoscopic endonasal approach for resection of suprasellar meningiomas.

The extended transsphenoidal endoscopic endonasal approach has a number of indisputable advantages over transcranial approaches in surgery of suprasellar meningiomas. First, it avoids traction of the frontal and temporal lobes, which reduces the risk of postoperative epileptic seizures [5, 12]. Second, the use of 0º to 70º endoscopes improves viewing the surgical field and enables peering “round the corner”. Also, the transnasal approach facilitates complete removal of the infiltrated bone and DM that is the source of tumor growth [17]. Undoubtedly, the advantages of the endonasal approach include the absence of a cosmetic defect; however, the introduction of supraorbital keyhole approaches has eliminated the cosmetic outcome problem in transcranial approaches. The disadvantages of transsphenoidal approaches include primarily the complexity and often failure to remove asymmetric tumors (due to limited access to the lateral supracalvarial ICA) as well as the complexity of removing solid meningiomas involving the major ves-
sels. A high risk of postoperative nasal cerebrospinal fluid (CSF) leak and associated meningitis is no less important. Despite the fact that the rate of these complications decreased after the introduction of various reconstruction techniques (sandwich, nasoseptal flap), these problems have not been fully resolved [14—16, 18—20].

The issues of both transcranial and extended transsphenoidal surgery of suprasellar meningiomas have been widely covered in the international literature. There are also a number of publications comparing the outcomes of surgical treatment of suprasellar meningiomas using various surgical approaches. However, the authors of these studies indicate the incorrectness of this comparison because patient groups are actually incomparable: there are particular indications and contraindications for each approach, which complicates comparison of treatment outcomes for transcranial and transnasal approaches.

The objective of this study was to assess the role of extended transsphenoidal endoscopic endonasal approaches in surgery of suprasellar meningiomas. Should suprasellar meningiomas be removed through the nose? To answer this question, we analyzed our 9-year experience in surgical treatment of these tumors using the anterior extended transsphenoidal endoscopic endonasal approach.

Material and methods

We performed a retrospective analysis of surgical treatment outcomes in 45 patients (11 males and 34 females aged 23 to 70 years; the median age, 50 years) with suprasellar meningiomas who were operated on by the authors (P.L., D.V., M.A.) using the anterior extended transsphenoidal endoscopic endonasal approach at the Department of Skull Base Tumor Surgery of the Burdenko Neurosurgical Institute between 2009 and 2017. Surgery was the primary method of treatment in all cases.

For transsphenoidal removal, we selected predominantly symmetric suprasellar meningiomas of small or medium size, without massive extension of the tumor into the optic nerve canals. Also, the patient’s desire to be operated on using the transsphenoidal approach was taken into account. Our initial confidence in the histological diagnosis was not confirmed during surgery in one case only: suspecting a pituitary adenoma in a young patient, we found an exceptionally solid meningioma. The following indicators were analyzed: demographic data, location and size of the tumor, clinical symptoms and their changes in the postoperative period, features and amount of surgery, tumor histology, development of complications, recurrences, or continued tumor growth, and type of subsequent treatment.

All patients were examined according to a standard protocol that included clinical, laboratory, and neuroimaging examinations. Changes in the visual functions and neurological status were examined in each patient before and after surgery. All patients underwent a preoperative contrast-enhanced MRI study in different modes. On the first postoperative day, all patients underwent a control CT scan. During the follow-up period, a contrast-enhanced MRI examination was performed every 4—6 months after surgery.

The clinical picture was represented by chiasmal syndrome of varying severity in 25 (55.6%) of 45 patients, isolated visual impairment due to the tumor impact on the optic nerve in 8 (17.8%) of 45 patients, and cranial pain syndrome in 23 (51.1%) of 45 patients. In 4 patients, there were no clinical manifestations of the tumor. There were no preoperative endocrine-metabolic disorders.

Unilateral tumor invasion into the optic nerve canal was in 5 (11.1%) patients. There was no bilateral invasion in any case. The tumor diameter varied from 1.2 to 4.2 cm. In some cases, CT revealed local hyperostosis in the planum sphenoidale and tuberculum sellae area.

Surgical technique

Extended endoscopic endonasal surgery requires coordinated work with four hands of 2 surgeons through both halves of the nasal cavity. In all extended approaches, surgery begins with placement of an external lumbar drain. Its use after surgery reduces the risk of postoperative nasal CSF leak due to a decrease in ICP caused by external CSF drainage [15, 21]. The patient is lying on the operating table, with its head end being elevated by 20° and slightly bent backward. Surgery is always carried out through the bilateral endonasal approach using an endoscope as the only visualization tool.

Extended transsphenoidal endonasal surgery consists of several stages: nasal stage, sphenoidal stage, tumor removal, and plastic closure of the resulting skull base defects. At the nasal and sphenoidal stages, an approach to the sellar floor and planum sphenoidale is performed, which ends with trepanation of these bone structures. We will not dwell on the initial stages, they have been described in detail in numerous works on endonasal endoscopic surgery [14, 15, 22].

Removal of suprasellar meningiomas should begin with careful DM coagulation in the planum sphenoidale and prechiasmatic groove region where the tumor matrix is located, which enables tumor removal almost without blood loss. For this purpose, we use monopolar coagulation in a sparing mode. After coagulation of the matrix, the DM is opened anteroposteriorly and linearly in the planum sphenoidale area. A DM incision depends on the meningioma size; usually, the incision corresponds to the anteroposterior tumor diameter. Most often, meningiomas have a rather dense consistency; an US disintegrator operating at maximum power is used for their removal. Removal of the tumor is carried out gradually, from its center to its periphery. After removing the main central tumor part, the tumor is separated from the ICA, posterior communicating arteries, anterior cerebral arteries, basal chiasm surface, optic nerves, and pituitary stalk using various curettes and hooks (Fig. 1). Small vessels
feeding the optic nerves and chiasm should be spared as much as possible to avoid the development or worsening of visual defects. We use coagulation of vessels in the suprasellar space in extreme cases only, trying to stop minor bleeding with hemostatic gauze or hemostatic sponge.

Of particular complexity is removal of tumors deviating from the midline in the lateral direction and extending into the suprasellar ICA and optic nerve canals. The complexity of removing these tumors is associated with a lateral size of planum sphenoidale trepanation, which is limited by the ICA, and with failure to remove lateral tumor portions by direct US suction.

After removal of the tumor, both local and drug hemostasis is performed.

The stage of skull base defect closure is also very challenging because the most frequent and potentially life-threatening complications of extended transsphenoidal surgery (postoperative nasal CSF leak and meningitis associated with it) depend on the quality of performed plasty [19, 20]. The main materials that we have used for reconstruction of extensive postoperative defects associated with the transsphenoidal approach are autologous tissues, such as fat, a fascia lata flap, and a bone flap dissected from the posterior nasal septum and rostrum at the endonasal approach stage. The positive aspects of using autografts are their absolute biocompatibility, good closing effect, and ease of implantation [20].

We developed an original technique of multilayer sandwich plasty of a skull base defect using autologous materials in combination with a Foley catheter inflated in the nasal cavity (Fig. 2). We used this reconstruction technique in 21 (46.6%) patients. First, a central fascia lata fragment harvested through a small skin incision on the leg is intradurally put behind the bone defect edges, then, by using an autologous bone fragment dissected from the nasal septum, the fascia is closely and tightly fixed in the cranial cavity, so that the fascia edges are 1.0—1.5 cm within the sphenoid sinus cavity. This stage is very important; the autologous bone flap should be congruent to the skull base defect to enable a firm plasty base. Further, this layer is fixed with fibrin-thrombin glue, after which a second fascia layer is placed on the adhesive layer. Then, the fibrin-thrombin glue layer is repeatedly applied, after which the sphenoid sinus is packed with autologous fat also taken from the patient’s thigh. To prevent contact of the autologous fat with air, the procedure is supplemented with a hemostatic sponge layer. Also, sandwich plasty in 11 (24.4%) patients was supplemented with autologous tissues with preserved blood supply (middle nasal concha and a pedicled mucoperiosteal flap dissected from the nasal cavity septum and floor) [14, 20].

Reconstructive material layers are fixed, from the nasal cavity side, with an elastic tampon or a Foley catheter inflated with 7—10 mL of saline. The Foley catheter is left for 5—7 days and provides mechanical support for the material until the primary scar forms.

Both we and foreign surgeons have some doubts regarding the use of lumbar drainage in the postoperative period [23, 24]. There is no proven benefit of lumbar drainage in prevention of postoperative CSF leak in the case of extended transsphenoidal approaches, and the risk of infectious complications is significantly increased. Initially, we used lumbar drainage for 7 days after surgery, but now, we remove a lumbar drain 1—5 days after surgery. In any case, lumbar drainage should not be an obstacle to early verticalization of the patient, starting on the 2nd postoperative day.

Results

We evaluated the outcomes of surgical treatment of suprasellar meningiomas according to the following indicators: changes in the main clinical syndromes (neuroophthalmological symptoms, neurological and hormonal status), surgery radicalness, the rate and type of postoperative complications, and postoperative mortality.

Total tumor removal (the tumor was completely removed together with the infiltrated DM — Simpson 1) was achieved in 35 (77.8%) of 45 patients, subtotal removal (more than 80% of the tumor was removed) was achieved in 8 (17.8%) patients, and removal was partial (less than 80% of the tumor was removed) in 2 (4.4%) of 45 patients.

In all cases, subtotal and partial removal was associated with an increased tumor density, which, combined with the infiltrative growth pattern and, in some cases, with active intraoperative bleeding, prevented complete removal of meningiomas.

Figure 3 shows an example of a suprasellar meningioma totally removed through the anterior extended transsphenoidal endoscopic endonasal approach.

In all cases of subtotal and partial removal of suprasellar meningiomas, the tumors were characterized by a considerable density, an extensive matrix (often with the tumor extending into the optic nerve canals), and a tight relationship between meningiomas and the ACA, ACoA, and ICA, which increased the risk of injury to the neurovascular structures. Figure 4 presents images of a female patient with an anterior cranial fossa meningioma that could not be totally removed due to an exceptional density of the tumor.

In 13 (28%) of 45 patients, visual impairments worsened immediately after surgery or developed in the postoperative period. In 3 of these cases, vision fully restored under conservative treatment by discharge from the hospital. In 4 patients, vision partially improved by the time of discharge. In 6 patients, vision did not restore by discharge (vision partially improved in 2 of these during the follow-up period). In 7 (21.2%) of 33 patients who had visual impairment before surgery, vision improved in the postoperative period. Therefore, by the time of discharge from the hospital, visual impairment amounted to 22% (10/45) of the total number of patients; in 78% of cases,
visual function either improved or remained at the pre-operative level.

Out of 5 patients with the tumor spreading into the optic nerve canals, vision remained unchanged in 3 patients, worsened in 1 patient, and improved in 1 patient.

Cranial pain syndrome regressed in most patients after surgery.

Despite the fact that the pituitary stalk was not transected in any case, and the pituitary gland remained intact, 6 (13.3%) of 45 patients developed hypopituitary disorders of varying severity (diabetes insipidus, hypocorticism, hypothyroidism) after surgery, which required replacement hormone therapy. In all cases, the hypopituitary disorders regressed at various times after surgery.

Postoperative CSF leak occurred in 3 (6.7%) of 45 patients. In 2 cases, CSF leak developed after sandwich plasty. In 1 case, sandwich plasty was combined with a nasoseptal flap and a Foley catheter. In 2 patients, there was recurrent postoperative CSF leak; for this reason, repeated skull base defect reconstruction was accompanied by placement of a lumboperitoneal shunt. The combination of shunting surgery with endoscopic skull base defect reconstruction enabled stopping CSF leakage.

**Fig. 1.** Removal of a suprasellar meningioma through the anterior extended endoscopic endonasal approach (30° endoscope).

a — trepanation scheme (marked in black): 1 — trepanned sellar floor (posterior 1/3), 2 — anterior 2/3 of trepanation refers to the planum sphenoidale, 3 — bony prominences of the intracavernous ICA, 4 — opticocarotid recesses, 5 — bone of the left optic nerve canal. The tumor matrix is coagulated; b — removal of the central meningioma portion using US suction; c — removal of a suprasellar meningioma: 1 — left ACA, 2 — left frontopolar artery, 3 — chiasm, 4 — dorsum sellae, 5 — tumor; d — meningioma was removed. Exploration of the suprasellar space: 1 — pituitary stalk, 2 — chiasm, 3 — AComA, 4 — dorsum sellae.

**Fig. 2.** Diagram of sandwich plasty of a skull base defect.
The DM is shown in blue; a fascia lata fragment is shown in red; the yellow band denotes the autologous bone; fibrin-thrombin glue is marked in violet; the sinus cavity is filled with fat.
Fig. 3. Example of a suprasellar meningioma totally removed through the anterior extended transsphenoidal endoscopic endonasal approach.

a, b — preoperative MRI scans; c, d — postoperative MRI scans.

Fig. 4. Subtotal removal of an anterior cranial fossa meningioma.
Contrast-enhanced T1-weighted MRI scans: a — before surgery; b — after surgery.
Of other complications, it is necessary to note one intraoperative injury to the ACA branch during tumor removal, which caused active arterial bleeding stopped with a Tachocomb fragment and did not lead to neurological deficit in the postoperative period.

One patient died on the 25th postoperative day due to progressive multiple organ failure in the setting of sepsis and meningitis. In this patient, meningitis caused by Klebsiella and Acinetobacter developed late on the 6th postoperative day. It is worth noting the lack of postoperative CSF leak in this case. The total number of meningitis in our series of observations was 4.4% (2 patients).

The mean duration of hospital stay was 13.2 days (8—37 days). Twenty-eight patients have been followed-up. The median follow-up is 7 months (1 to 60 months). There was no case of tumor recurrence for totally removed tumors. Five patients with incompletely removed meningiomas underwent a course of stereotactic radiotherapy at various times after surgery.

Discussion

The goal of surgical treatment for suprasellar meningiomas is to preserve or restore lost visual functions [25, 26]. As suprasellar meningiomas grow, they compress the optic nerves and chiasm, which causes progressive loss of vision. Visual impairment after surgery develops primarily due to devascularization of the visual tracts upon removal of the tumor, because they often have common blood supply with the tumor [26—28]. In this regard, one of the most difficult tasks of surgical removal of suprasellar meningiomas is achieving total tumor removal without deterioration of the visual functions after surgery.

The subfrontal transcranial approach most widely used in suprasellar meningioma surgery has certain disadvantages: the need for traction of the frontal lobes to access the tumor, which is rare, but may provoke epileptic seizures in the postoperative period; transsection of the olfactory nerves with the development of anosmia; opening of the frontal sinus, which is associated with a risk of CSF leak and meningitis; cosmetic defects [7]. Also, in the case of short optic nerves, which occurs in 10% of cases, the subfrontal approach is poorly applicable for removal of the tumor due to an extremely narrow interneural gap.

In contrast, the extended transsphenoidal approach to suprasellar meningiomas has several advantages, which are related to the approach direction. The approach “from below” provides early tumor devascularization in the planum and tuberculum sellae area with total removal of the hyperostotic bone and infiltrated DM, which enables almost bloodless tumor removal [29]. The transsphenoidal approach, in contrast to the transcranial one, does not require frontal lobe traction. In addition, a number of authors believe [30, 31] that the transsphenoidal approach reduces the risk of visual impairment because the ICA—ACA complex provides blood supply to the optic nerves and chiasm, and removal of the tumor using the extended transsphenoidal approach is performed under direct view of these vessels and their branches.

However, the transsphenoidal approach has disadvantages that limit the indications for its use in suprasellar meningiomas. They primarily include complicated removal of large solid meningiomas whose lateral portion significantly deviates from the midline, falling behind the supraclinoid ICA, which is caused by a limited area of planum sphenoidale trepanation in the transverse direction.

The extent of suprasellar meningioma removal in the case of transcranial and transnasal approaches is often incomparable due to the use of different radicalness criteria and ambiguous assessment of the tumor removal extent (sometimes based solely on the surgeon’s own opinion) as well as the complexity of forming comparable groups of tumors in the case of different surgical approaches [26, 28, 32]. However, comparison of transcranial and endoscopic transsphenoidal removal of suprasellar meningiomas showed that the transcranial approach provided a slightly higher rate of total tumor removal (85%, on average, versus 74% for the transnasal approach) [12]. In our series, total tumor removal was achieved in 77.8% of cases. One of the limiting factors for total removal of suprasellar meningiomas using the endoscopic endonasal approach, in our opinion and according to foreign authors, is the tumor size exceeding 3 cm [29].

Despite the fact that a number of authors [29, 33] consider extension of the tumor into the optic nerve canal as an absolute indication for transnasal removal because the inferior, lateral, and medial walls of the canal can be trepanned simultaneously, our opinion in this case is not so categorical. Our previous results of transcranial decompression of the optic nerve canal indicate a high efficiency of the transcranial technique [34]. However, this is probably due to our small experience in transnasal decompression of the optic nerve canal (only 2 cases).

Unfortunately, we cannot boast of the same high rates of visual function recovery after transnasal surgery compared to those of our foreign colleagues who have sometimes achieved a 86% vision restoration efficacy (69%, on average, versus 58% for transcranial approaches) [13, 27, 35, 36]. An analysis of foreign publications reveals a low rate of visual impairment during transsphenoidal removal of meningiomas — no more than 5% (in Russia — 22% by the time of discharge) [29]. Here, it is important to note that, according to different authors [26, 32], the rate of visual impairment upon transcranial removal is 19—24.2% of cases. What is the cause for this high rate of visual impairment after surgery in Russian patients? Most likely, devascularization of the chiasm and optic nerves during tumor removal plays the main role in the genesis of visual impairment. Therefore,
it is extremely important to minimize the use of coagulation (especially monopolar) during removal of meningioma and its separation from the visual tracts. All patients with visual impairment in the postoperative period received vasodilator and hormone therapy.

Postoperative nasal CSF leak occurs in both transnasal and transcranial approaches (through the open frontal sinus). Undoubtedly, the rate of CSF leak after extended transsphenoidal surgery is significantly higher (up to 35%) than that for transcranial approaches (mean, 4.3%) [37, 38]. According to P. Gardner and co-authors [12] who have now the largest experience in transnasal removal of suprasellar meningiomas, the use of a vascularized nasoseptal flap for skull base defect reconstruction has drastically reduced the rate of nasal CSF leak from 69% in the early series of operations to 11.7% in the last series. In our series, postoperative CSF leak amounts to 6.7%, which is considered to be a very low value arguing for the used variant of sandwich plasty. According to the literature [21, 39, 40], the rate of infectious complications, primarily meningitis, after extended transsphenoidal surgery is 0.6—7.0%. In our series, meningitis occurred in 2 (4.4%) patients, but it was not accompanied by postoperative CSF leak in both cases. Unfortunately, meningitis was the cause of death in 1 patient.

Our experience of extended transsphenoidal surgery for suprasellar meningiomas is contradictory; there has been dizziness with success and bitter disappointments. Analyzing the obtained results and summarizing our experience, we may say that the anterior extended transsphenoidal endoscopic endonasal approach is advisable to use in surgery of suprasellar meningiomas for relatively small (up to 3 cm) symmetric midline tumors that do not involve the large vessels. The efficiency of this technique for tumors extending into the optic nerve canals requires additional analysis of a larger series of cases.

Authors declare no conflict of interest.

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On the basis of their findings, the authors quite rightly believe that the choice of this approach is possible, but has several limitations and should be very balanced, especially upon laterization of the tumor growth or extension of the tumor into the optic nerve canal. The importance and timing of optic canal exploration and decompression during endoscopic endonasal resection of tuberculum sellae and planum sphenoidale meningiomas. The influence of tumor size, duration of symptoms, and microsurgery on surgical outcome in 101 consecutive cases. J Neurosurg. 1984;61:633-641.


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Wound liquorhea is a serious and dangerous complication developing after neurosurgical interventions. The highest risk group includes patients operated on using approaches to the skull base. In pediatric neurosurgery, approaches to the posterior cranial fossa are some of the most common ones, with wound liquorhea amounting to 33%. Studies devoted to the wound liquorhea problem have been performed in heterogeneous patient groups, which complicates evaluation of the results and reduces their practical value.

Material and methods. The analysis included pediatric patients operated on by a single surgeon for posterior cranial fossa (PCF) tumors in the period from 2009 to 2016. There were 472 patients. Criteria for inclusion in the study were as follows: age under 18 years; predominant tumor location in the fourth ventricle; primary surgery. According to the inclusion criteria, the study involved 211 patients. A search for the key words “liquorrhea”, “pooling”, “meningocele”, “pseudomeningocele”, and “meningitis” was performed through electronic medical records of the involved patients. We analyzed the data on the total bed-day and the number of days spent in the critical care unit. Surgery protocols were the source of the following information: the presence of an external ventricular drain or ventriculoperitoneal shunt before tumor resection; information on DM closure; information on additional sealing of dura sutures. In addition, the patients were divided into two groups, the main difference between which was the use of additional sealing of dura sutures (Tachocomb, fibrin-thrombin glues, and their combination) to minimize the risk of wound liquorhea.

Results. A total of 211 patients were included in the study. Postoperative wound liquorhea occurred in 6 (2.8%) patients; another 5 (2.4%) patients had significant pseudomeningocele. Most children spent no more than 1 day in the critical care unit — totally 176 (83.4%) patients; the other 35 (16.6%) children spent more than 1 day in the critical care unit. A group of patients without sealing of dura sutures consisted of 144 (68.2%) patients. Liquorrhea occurred in 4 (2.8%) cases; in 3 (2.1%) cases, there was symptomatic pseudomeningocele without liquorhea. In a group of patients with the use of suture sealing (Tachocomb, fibrin-thrombin glue in various combinations — 67 (31.8%) patients), there was liquorhea in 2 (3%) cases and pseudomeningocele without liquorhea in 2 (3%) cases. On the basis of PSM algorithm application, 2 groups of 67 patients each were formed: the group with sealing (A) and the group without sealing (B) of the DM. Of the 67 cases of sealing, TachoComb was used in 64 (95.5%) patients, and fibrin-thrombin glue was applied in 33 (59.1%) patients. Differences between the groups in the rate of liquorhea (2.4% patients in group A and 6.0% patients in group B) and pseudomeningocele (3 (4.5%) patients in group A and 5 (7.5%) patients in group B) were statistically insignificant (p=0.68 and p=0.58, respectively).

Conclusion. Wound liquorhea has remained a topical issue in surgery for posterior cranial fossa tumors and, if develops, doubles the postoperative bed-day. Our strategy of perioperative management of patients proved its efficacy in reducing the rate of postoperative liquorhea up to 2.8%. A low percentage of liquorhea did not allow unambiguous evaluation of the effect of additional sealing of dura sutures (TachoComb and fibrin-thrombin glue).

Keywords: liquorhea, posterior cranial fossa, fourth ventricle, dura mater, duraplasty.

Abbreviations:
VPS – ventriculoperitoneal shunt
PCF – posterior cranial fossa
MRI – magnetic resonance imaging
DM – dura mater
PSM – propensity score matching

Wound liquorhea remains one of the most important and fundamentally preventable complications in neurosurgery [1]. This problem is often discussed in the context of extended approaches to the skull base [2, 3]. However, in pediatric neurosurgery, the incidence of wound liquorhea can reach 33% in the surgery of tumors of the posterior cranial fossa (PCF) and primarily of the fourth ventricle tumors [4]. Most of the studies of the last decade have focused on the use of additional means to improve the sealing of the dura mater (DM) sutures [5, 6]. Though some of them being of high methodological design and level of evidence (prospective, randomized), these studies did not provide any effective ways to prevent postoperative liquorhea. The analysis of the available literature data revealed several significant deficiencies affecting the results of those studies. The most significant issues of previously published studies on wound liquorhea in neurosurgery can be divided into two categories.

1) The first problem is the joint analysis of different surgeries with various potential risks of liquorhea in heterogeneous patient groups. In some cases, patients with supratentorial and infratentorial tumors are considered together; in other cases, both tumor and traumatic pathologies are studied.
2) The second problem that could affect the parameters under study is the large variability of “surgery techniques” due to sampling the data from several clinics or from single one but from different surgeons. For example, the joint assessment is made of patients with the basal and fourth ventricle tumors, or patients who underwent craniotomy and craniectomy, etc. To eliminate the influence of the above factors, the postoperative liquorhea prevention effectiveness should be studied on a large homogeneous group of patients operated on in a relatively short period of time by one surgeon whose surgical technique has already been established without any fundamental changes during that time. As the preliminary stage of the future study, we decided to perform a retrospective analysis of available data in the field of PCF tumor surgeries. The prospective study plan will be based on the results of this analysis.

Materials and Methods

The rate of wound liquorhea and the factors affecting its development in the most homogeneous, large and unselected retrospective series of pediatric patients, operated on from 2009 to 2016 by one surgeon was studied. The literature data and our empirical experience indicate that the risk of postoperative liquorhea is the highest for the PCF tumors [4, 7, 8]. Also, the PCF tumors are the most common neuro-oncological problem in the pediatric population [9]. The patients initially operated on for tumors of the fourth ventricle were chosen as a study group since they constitute up to 80% of all children with the PCF tumors. This choice was based on identical surgical approaches, wide opening of the cerebrospinal fluid paths during the surgery and the stereotypical postoperative period. The period from 2009 to 2016 was selected for the following reasons:

— the need to include a sufficient number of patients who, due to organizational reasons, did not undergo sealing of dura sutures (until mid-2012). This group will also allow evaluating the risk of liquorhea after resection of the fourth ventricle tumor;

— by 2009, the first author already had ten years of experience in pediatric neurosurgery (more than 3,500 surgeries), and his personal surgical technique was already established. In addition, no significant technological changes in surgery of the PCF tumors occurred during this period;

— the expected size of the study group was to be at least 200 patients with primary surgery to remove the fourth ventricle tumors.

Since 1999, the first author has prospectively kept a register of all operated patients with the records of surgery types. The identifiers of all patients operated on for any PCF tumors from 2009 to 2016 were selected from this database. All surgery protocols for these identifiers (472 cases) were subsequently retrieved from the medical information system of the Burdenko Neurosurgical Institute. After analyzing the surgery protocols, the patients were selected corresponding to the objectives of the study. The inclusion criteria were the following: age under 18 years; predominant tumor location in the fourth ventricle; primary surgery. Ultimately, the sample was reduced to 211 patients.

Then, the following data recorded as a part of routine clinical practice were retrieved from the medical information system of the Burdenko Neurosurgical Institute: statistics, diary entries, records of surgeries and manipulations. The following parameters were analyzed: number of bed-days in the intensive care unit, number of postoperative bed-days, repeated hospitalizations associated with complications, additional surgical interventions. For all diary entries, a contextual search was performed for keywords “liquorrhea”, “pooling”, “meningocele”, “pseudomeningocele”, “meningitis”. Then, the diaries with the keywords were analyzed by the operating surgeon. The following data were retrieved from surgery protocols:

— the presence of an external ventricular drain or ventriculoperitoneal shunt before tumor resection;

— the information on DM closure; primary sutures/plastic surgery (material);

— the information on additional sealing of dura surfaces (Tachocomb, glue, a combination of drugs).

All surgeries were performed with patients in the sitting position. In the case of overt hydrocephalus at the beginning of the surgery, external ventricular drainage was always installed to prevent tense pneumocephalus in the early postoperative period. A median suboccipital craniotomy was used in all cases. There were no cases of damage to the DM at the stage of craniotomy. The typical V-shaped or Y-shaped incision of the DM was used. The approach to and resection of the tumor were performed through the tumor-expanded Magendie’s foramen, which, if necessary, was expanded by dissecting a telovelochoroidal fissure. The objective of the surgery was always the radical resection of the tumor. In all cases, at the end of the surgery, the fourth ventricle, the cerebral aqueduct, and the communication with the spinal subarachnoid space were widely opened. Hemostasis was performed by bipolar coagulation and covering of the infiltration zones with Surgicel. The DM was stitched with PGA 4-0 (Resorba) multifilament suture. Depending on the specific situation, both nodal and continuous sutures were used. We have always tried to carry out the primary suturing without using DM substitutes. In rare cases, through-out sutting of a pronounced occipital sinus to achieve hemostasis made it impossible to suture the DM without strong tension or diastasis. Then, a patch of the DM substitute was inserted (fascia or Durepair matrix). Until mid-2012, no sealing of dura sutures was used. Since 2012, fibrin-thrombin glue (Tissucol or Evicel) and Tachocomb have been used with varying frequencies (depending on availability). The decision to use sealants in this group of patients was approved by the medical com-
mission of the Burdenko Neurosurgical Institute, given the need to prevent dangerous complications. During this period, we did not use “sandwich” technique of applying Tachocomb. Tachocomb plate was always placed on top of the dura suture area with an overlap of at least 5 mm. The bone flap was always put in place at the end of the surgery and fixed with 4 silk (3-0) sutures. The wound was completely sutured layer by layer. Immediately after the surgery, all patients were placed for one day in the neuro-resuscitation waking room. Extubation was performed on awakening in case of stable vital indicators. In case of sufficient level of wakefulness and regardless of local neurological symptoms, the patient was transferred to the general ward the next morning. The external ventricular drainage remained open during its installation in the patient’s body in order to resolve the pneumocephalus and for debridement of the cerebrospinal fluid in the early postoperative period, as well as to prevent possible increases in intracranial pressure. Usually, it was set at the level of +5 cm H2O. For the first 2–3 days after the surgery, all patients underwent the so-called relief lumbar punctures — usually the next day after the surgery and then once more every other day in case of persistent signs of pseudomeningitis. With a standard postoperative course, the drainage was removed on Day 4—5 after the surgery. In the patients with a prolonged stay in the intensive care unit, the drainage was kept for a longer period, until the patient reached the level of general activity, making it possible to clinically evaluate the increase in intracranial hypertension after the drainage removal.

It should be noted that over the period under study, the surgical technique, suture materials used and the principles of postoperative patient management remained unchanged. It makes it possible to consider the patient test group as the most homogeneous regarding possible “uncontrolled” factors affecting the reliability of the results of this retrospective study.

The main working hypothesis of our study was the possible effect of the sealing of dura sutures on the incidence of wound liquorhea and pseudomeningocele. To compare the incidence of liquorhea in cases of sealing and in cases without additional sealing, a sub-analysis was conducted using pseudorandomization technique (Propensity Score Matching, PSM) to select factor balanced subgroups potentially affecting the outcome and minimize systematic selection error. Statistical data analysis was performed in the environment for statistical programming R (version 3.3.2, www.r-project.org). The differences between groups were recognized as statistically significant at the level of significance of \( p<0.05 \).

**Results**

The retrospective analysis included the data from 211 patients. The main characteristics of the sample studied are presented in Table 1. The age and distribution of the rate of histological variants speak in favor of the representativeness of our series in comparison with the data in international literature [9]. Among the patients included in the present analysis, postoperative wound liquorhea was observed in six (2.8%) patients, with four of them also having pseudomeningocele of varying severity. Five (2.4%) other patients have developed a clinically significant subcutaneous accumulation of CSF in the early postoperative period. In total, these observations amounted to 5.2%. Liquorrhea developed within 6 to 17 days after the surgery. In all cases, liquorhea was relieved by lumbar punctures or by installing external lumbar drainage. One patient required implantation of a ventriculo-peritoneal shunt after the relief of meningitis. Another patient developed liquorhea on the 3rd week after the surgery (already after discharge from the clinic), accompanied by superficial abscess of soft tissues, which required re-hospitalization, drainage of the abscess and implantation of external lumbar drainage. In 5 patients with pseudomeningocele without liquorhea, subcutaneous accumulations of cerebrospinal fluid have been noted from 3 to 13 days after the surgery. In four cases, they were resolved after several lumbar punctures. In one case, pseudomeningocele was a symptom of development of aresorptive hydrocephalus and required ventriculoperitoneal shunting on the 13th day after the initial surgery.

It is known that the severity of the patient’s condition after the surgery, as well as the development of complications, including liquorhea, affect the number of postoperative bed-days. We used a stay in the intensive care unit for more than one day as an indicator of the patient’s severe postoperative condition. On this basis, we divided the patients into two groups: a standard postoperative course (no more than one bed-day in intensive care unit) and a complicated postoperative course (more than one bed-day in intensive care unit). The majority of patients (176 (83.4%)) spent no more than one day in intensive care. Among them, four (2.3%) patients had liquorhea. The mean number of postoperative bed-days for these patients was 17.0±6.2 whereas for patients without liquorhea it was 9.6±4.5. With a small number of observations, these differences were statistically significant (Mann — Whitney two-tailed test; \( p=0.008 \)). Thirty-five (16.6%) patients spent more than one day in intensive care and are regarded as patients with a complicated postoperative course. Two (5.7%) of them had liquorrea. The mean number of postoperative bed-day for these patients was 38.0±11.3, while for patients without liquorhea it was 24.1±16.1. These differences are statistically insignificant (Mann — Whitney two-tailed test; \( p=0.086 \)). The observed trend of higher rate of liquorhea among patients with a complicated postoperative course (5.7% versus 2.3%) was not confirmed by statistical analysis (Fisher’s exact test two-sided; \( p=0.260 \)), possibly due to the small number of events in the sample.

The group of patients without the use of the DM sealing consisted of 144 (68.2%) people. Liquorrhea occurred in four (2.8%) cases; in three (2.1%) cases, there
was symptomatic pseudomeningocele without liquor- 
rhea. In a group of patients with the use of suture sealing 
(Tachocomb, fibrin-thrombin glue in various combina-
tions — 67 (31.8%) patients), liquorrrhea was observed in 
two (3%) cases and pseudomeningocele without liquor-
rhea in two (3%) cases. There were no statistically sig-
nificant differences in the incidence of liquorrrhea and 
pseudomeningocele in these groups (Fisher’s exact test 
two-sided, \( p = 0.71 \)).

Among 35 patients with a complicated postoperative 
course, Tachocomb with fibrin-thrombin glue was used in 
13 cases, and liquorrrhea developed in one (7.7%) case. 
In 22 cases, no additional sealing was used, and liquor-
rhea also developed in one (4.5%) case, with no differ-
ences identified (Fisher’s exact test two-sided; \( p > 0.999 \)).

One patient with a complicated postoperative course 
died on the 8th day from a sudden decompensation of car-
diovascular activity, while being on artificial ventilation 
of the lungs in the neuro-intensive care unit. Twelve (6%) 
patients developed non-neurological complications as-
associated with the surgery. Table 2 gives the information 
on these complications. It should be emphasized that 
among the patients with problematic wound healing 
there were no patients who underwent the sealing of dura 
sutures. Also, there was not a single case of an allergic 
reaction to the preparations used. These facts support the 
safety of the DM sealants use in pediatric neurosurgical 
practice.

To test the hypothesis of differences in the incidence of 
postoperative liquorrrhea and pseudomeningocele 
depending on the use or non-use of the DM sealants, a 
sub-analysis was conducted in subgroups specially se-
lected using the PSM pseudo-randomization algorithm to 
minimize the systematic selection error. The age, sex, 
histological type of the tumor, intraoperative plasty of the 
DM and the number of bed-days from the moment of 
hospitalization to the surgery were considered as covari-
ants determining the probabilities of distribution in the 
studied groups.

As a result of applying the PSM algorithm, two 
groups of 67 patients each were formed: the group with 
sealing (A) and the group without sealing (B) of the 
DM. Of the 67 cases of sealing, Tachocomb was used in 
64 (95.5%) patients, and fibrin-thrombin glue was used in 
53 (59.1%) patients. There were no statistically signifi-
cant differences between the two selected groups by sex 
(\( p = 0.86 \)), age (average value in group A is 5.6±4.1, in 
group B, 5.6±3.8 years; \( p = 0.92 \)), histological diagnosis 
(\( p = 0.71 \)), frequency of use of the DM plasty (\( p = 0.37 \)), 
length of hospitalization before the surgery (2.1±2.1, 
2.3±1.8, respectively; \( p = 0.25 \)). The differences between 
the groups in the rate of liquorrrhea (2 (3.0%) patients in 
group A and 4 (6.0%) patients in group B) and pseudo-
meningocele (3 (4.5%) patients in group A and 5 (7.5%) 
patients in group B) were statistically insignificant 
(\( p = 0.68 \) and \( p = 0.58 \), respectively, see Figure).

### Discussion

The problem of postoperative liquorrrhea is still rele-
vent since this complication leads to additional suffering 
for patients and doubles the cost of treatment [1, 10]. In 
pediatric neurosurgical practice, patients with an in-
creased risk of postoperative liquorrrhea traditionally in-
clude all patients who undergo PCF surgeries [4, 11, 12]. 
In the literature, various modifications of surgical tech-
niques and application of sealants and materials to the 
dura suture are considered as methods to reduce the risk 
of liquorrrhea [5, 6, 11, 13, 14].

In our practice, the DM sealants (Tachocomb, fi-
brin-thrombin glue) have become sporadically available 
since 2012. Their use was not selective but based on their 
availability. It determined the features of the formation of 
compared sample sets with a certain degree of random-
ness in this process. However, due to potentially remain-
ing possibility of selection bias in this retrospective study, 
we used the pseudorandomization algorithm (PSM) to 
test the hypothesis of differences in the incidence of post-
operative liquorrrhea and pseudomeningocele with and 
without the use of sealing methods.

The rate of liquorrrhea in children with the PCF tu-
mors varies from 4 to 33% in different clinical se-
ries [4, 11]. Our data (2.8%) correspond to the minimum 
levels of the rate of postoperative liquorrrhea described in 
the literature. Such a low rate of liquorrrhea in our series 
can be attributed to several factors. The most important 
of them is most likely the methodology of recording the 
fact of liquorrrhea. Naturally, a retrospective analysis of 
medical records is likely to lead to an underestimation. 
Also, a number of works regarded all pseudomeningocele

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**Table 1. The main biological indicators of the patient series under study**

<table>
<thead>
<tr>
<th>Histological analysis</th>
<th>Age, years</th>
<th>The male/female ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medulloblastoma</td>
<td>6.9±3.6</td>
<td>1.8:1</td>
</tr>
<tr>
<td>Astrocytoma</td>
<td>7.7±4.6</td>
<td>1.9:1</td>
</tr>
<tr>
<td>Epindomima*</td>
<td>4.3±3.7</td>
<td>1.8:1</td>
</tr>
<tr>
<td>Others**</td>
<td>6.2±6.1</td>
<td>1.1:1</td>
</tr>
<tr>
<td>Entire series</td>
<td>6.4±4.2</td>
<td>1.7:1</td>
</tr>
</tbody>
</table>

* — including anaplastic variants; ** — ETANTR, ATRT — choroid papilloma, ganglioglioma, meningioma (all these tumors predominantly localized in the lumen of the fourth ventricle and were removed through the Magendie’s foramen).
(including asymptomatic and observed only on MRI) to be the complications described as liquorrhea, which we believe to be controversial [4]. Small pseudomeningocele without liquorrhea does not actually affect the clinical course of the disease, the timing of discharge from the hospital and the need for additional manipulations. Another important factor is the use of craniotomy, rather than a cranietomy for all patients in our series. It has been demonstrated that this technique reduces the rate of liquorrhea in pediatric neurosurgery from 27 to 4 [11]. In addition, this work had the lowest reported rate of liquorrhea in surgery for PCF tumors in children when performing a craniotomy. Other possible reasons for the low rate of liquorrhea in our series are the extensive use of external ventricular drainage in the perioperative period, lumbar relief punctures in all patients, i.e., a specific patient management algorithm aimed at the debridement of the cerebrospinal fluid and effective reduction of liquor pressure. The drainage of the cerebrospinal fluid through the external ventricular drainage and periodic lumbar punctures can lead to faster debridement of the cerebrospinal fluid, at the same time effectively reducing the cerebrospinal fluid pressure during the first 4—5 days after the surgery, ensuring natural sealing of the wound in the healing process. The works demonstrating that the issue of liquorrhea and pseudomeningocele is not a problem of the DM sealing, but rather a problem of liquorodynamics confirm our point of view [11, 15]. In this case, it is not surprising that we did not see an additional effect from the use of sealants (Tachocomb and fibrin-thrombin glue). Other works [5, 6, 16], including prospective randomized studies, also did not prove the effectiveness of the DM sealants. Although these studies have the formally high level of evidence (prospective and randomized), they are not without a significant number of shortcomings that make them uninformative for answering the question about the effectiveness of the prevention of postoperative liquorrhea. First of all, this refers to a very heterogeneous spectrum of surgeries with completely different risk of liquorrhea. Another problem is the multicenter nature of the studies which could include 200—300 patients from 50—60 surgeons in 20 clinics. In such cases, the surgical technique may play an important role.

When planning and performing this retrospective analysis, we tried to take into account the shortcomings of published works and eliminate or minimize them in our own research. In our work, the only fundamental disadvantage is its retrospective nature. On the one hand, a low rate of liquorrhea speaks in favor of our perioperative patient management strategy, but on the other, it does not allow us to statistically reliably assess the effect of the DM sealing. Research in this direction must be continued, taking into account the potentially preventable nature of the problem and its significance in the overall outcome of the treatment of neuro-oncological patients. Given the socioeconomic component of this problem, the cost of finding an effective approach will quickly pay off [1, 10].

### Conclusion

Wound liquorrhea remains an urgent problem in surgery of tumors of the posterior cranial fossa, and its onset doubles the number of the postoperative bed-days. Our strategy of perioperative management has proven its effectiveness in reducing the incidence of postoperative liquorrhea to 2.8%. A low rate of liquorrhea did not allow us to unequivocally determine the effect of the additional use of the DM sealing (Tachocomb and fibrin-thrombin glue), it is quite possible that in a clinic with a higher rate

### Table 2. Information on patients with “non-neurological” complications

<table>
<thead>
<tr>
<th>No.</th>
<th>Age, years</th>
<th>Histology</th>
<th>Bed–days in the intensive care unit</th>
<th>Bed–days after the surgery</th>
<th>Complication</th>
<th>Sealant</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.75</td>
<td>Anaplastic ependymoma</td>
<td>21</td>
<td>29</td>
<td>Bedsore in the upper 1/3 of the wound</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>13</td>
<td>Medulloblastoma</td>
<td>1</td>
<td>16</td>
<td>Hematoma in the tumor bed</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>Choroid papilloma</td>
<td>1</td>
<td>15</td>
<td>Epidural Hematoma of PCF</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>Medulloblastoma</td>
<td>2</td>
<td>16</td>
<td>Hematoma in the tumor bed</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>15</td>
<td>Pilocytic astrocytoma</td>
<td>39</td>
<td>85</td>
<td>Epidural hematoma outside the surgical area</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>0.67</td>
<td>Anaplastic ependymoma</td>
<td>23</td>
<td>42</td>
<td>Bedsore in the upper 1/3 of the wound</td>
<td>Tachocomb</td>
</tr>
<tr>
<td>7</td>
<td>5</td>
<td>Medulloblastoma</td>
<td>21</td>
<td>52</td>
<td>Hematoma in the tumor bed</td>
<td>Tachocomb</td>
</tr>
<tr>
<td>8</td>
<td>12</td>
<td>Medulloblastoma</td>
<td>1</td>
<td>17</td>
<td>Necrosis of the skin of the upper 1/3 of the wound</td>
<td>Tissucol</td>
</tr>
<tr>
<td>9</td>
<td>0.17</td>
<td>Anaplastic ependymoma</td>
<td>1</td>
<td>28</td>
<td>Subcutaneous abscess of the postoperative wound area</td>
<td>Tissucol</td>
</tr>
<tr>
<td>10</td>
<td>1.83</td>
<td>Medulloblastoma</td>
<td>1</td>
<td>8</td>
<td>Shunt infection</td>
<td>Tissucol</td>
</tr>
<tr>
<td>11</td>
<td>6</td>
<td>Anaplastic ependymoma</td>
<td>6</td>
<td>13</td>
<td>Hemorrhage into the tumor after the installation of EVD</td>
<td>None</td>
</tr>
<tr>
<td>12</td>
<td>9</td>
<td>Medulloblastoma</td>
<td>1</td>
<td>28</td>
<td>Shunt infection</td>
<td>Tissucol</td>
</tr>
</tbody>
</table>

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of complications this effect will be noticeable. On the other hand, our data confirm the safety of using both Tachocomb and fibrin-thrombin glue as the DM sealant in surgery of tumors of the posterior cranial fossa in children. The problem deserves further study in carefully planned research on adequately homogeneous groups of patients. It is also important to identify groups of patients with an increased risk of liquorrhea, for whom the additional use of the DM sealing may have a more pronounced clinical effect.

Authors declare no conflict of interest.

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Commentary

The problem of postoperative complications after the resection of the posterior cranial fossa tumors in children is relevant and remain primarily unsolved to date. These complications include an increase in the neurological deficit, postoperative hematomas, pneumocephalus, meningitis, posterior fossa syndrome, akinetic mutism, a progression of hydrocephalus, etc. Wound liquorrhea is not the most frequent and most dangerous of these com- ponents, but it significantly lengthens the postopera- tive period and often requires additional surgical inter- ventions, leading to the delayed onset of chemotherapy and radiation therapy. All of these make the paper by Yu.V. Kushel et al. extremely useful. The development of postoperative liquorrhea is only minimally associ- ated with the patient or the tumor but depends almost entirely on the surgical technique. Therefore, the rate of this complication is different for different surgeons and in different clinics. The most important factor affecting the development of liquorrhea in patients with the posterior cranial fossa tumors is the thoroughness of trepanation and closure of the postoperative defect. Particularly sig- nificant are the economical use of monopolar coagula- tion and prevention of charring of tissues, careful open- ing of the DM, osteoplastic rather than resection trepan- ning, radical resection of the tumor, hermetic closure of the DM, proper positioning of the bone flap, careful, layer-by-layer, suturing of muscles, subcutaneous fatty tissue and skin, elimination of cerebrospinal fluid hyper- tension. The article summarizes a large volume of mate- rial: 211 primary pediatric patients with the fourth ven- tricle tumors, operated on over eight years (2009—2016) by one surgeon. Liquorrhea was detected in six (2.8%) patients, and subcutaneous accumulation of cerebrospi- nal fluid (pseudomeningocele) in five (2.4%), a total of 11 (5.2%) cases. What do these numbers mean? First of all, the Burdenko Neurosurgical Institute has tradition- ally high level of surgical technique; during operations, great attention is paid to the stages of trepanning and stitching of the structures of the posterior cranial fossa. Indeed, osteoplastic trepanation of the scales of the oc- cipital bone has been used by pediatric departments of the Institute since the late 1990s. The tumor is usually completely resected, which allows unblocking the ce- rebrospinal fluid paths and stopping the progression of hydrocephalus. The thoroughness of the postoperative wound closure is also considered to be a critical task, and often this step of the surgery was not entrusted to novice surgeons. All the facts mentioned above contrib- uted to the low level of postoperative liquorrhea. With other works of the Burdenko Neurosurgical Institute (S.S. Ozerov, 1999 [1], O.A. Medvedeva, 2016 [2]) hav- ing demonstrated it recently, this article is a new example. However, such a small number of complications (eleven patients over eight years) does not allow the authors to analyze and reliably identify the cause of their occur- rence. One would hardly call it a drawback, but it is not possible to reliably estimate what factor was decisive in the development of liquorrhea with such a small sample. I would agree with authors consideration that the whole complex of surgical measures served as a guarantee of a good outcome. It was not possible to establish the role of additional agents for the DM sealing, such as Tachob- comb and fibrin-thrombin glue. However, their impor- tance for preventing liquorrhea has already been shown in surgery of the skull base (especially for transfenoidal interventions), as well as in other works on PCF surgeries.
(V.V. Shimanskiy [3]). The use of means to temporarily reduce the cerebrospinal fluid pressure, such as external ventricular drainage, also plays an vital role in the favorable course of the postoperative period. Prophylactic lumbar punctures after the surgery, even with an installed external ventricular drainage, are the author’s unique approach, however, taking into account the excellent results shown in the article, this method is also worth looking at. Thus, we do not know any single “magic remedy” to prevent wound liquorhea, but the attention paid to the most seemingly insignificant details of trepanning and closing of the postoperative wound can significantly reduce the level of postoperative complications.

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REFERENCES


Comparative Analysis of the Efficiency of Dura Mater Defect Repair in Cerebral Surgery

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Kirov Military Medical Academy, St. Petersburg, Russia

The need in replacement of a dura mater (DM) defect occurs in more than 40% of cerebral interventions. Various artificial DM substitutes facilitate solving this problem; however, their efficacy compared to that of patient autogenous tissues has been poorly understood.

Aim — we aimed to study the efficacy of various substitutes in repair of dura mater defects.

Material and methods. The study included patients with various intracranial pathologies who were operated on at the Neurosurgery Clinic of the Military Medical Academy in the period between 2010 and 2017, and who underwent repair of the DM during surgery. In surgery for the supratentorial structures, patient autogenous tissues, grafted non-resorbable materials, or applicable collagen matrices were used as substitutes. Depending on the type of substitute material, patients were divided into groups to assess the efficacy of DM closure by comparing the rate of postoperative liquorrhea. In surgery for the posterior cranial fossa (PCF), applicable dural substitutes were not used; in this cohort, the efficacy of autogenous tissues and synthetic materials was compared.

Results. In 232 patients, the total rate of liquorrhea was 23.7%. In supratentorial surgery (175 cases), the use of autogenous tissues (n=73), synthetic materials (n=42), and collagen matrices (n=60) was associated with CSF exfusion in 13 (17.8%), 13 (31.0%) and 16 (26.7%) cases, respectively; in statistical analysis, these results were comparable (p>0.05). In PCF surgery (57 cases), the use of autogenous tissues (n=34) significantly more effective (p=0.021) prevented liquorrhea compared to synthetic materials (n=23): complications occurred in 4 (11.8%) and 9 (39.1%) cases, respectively.

Conclusion. If a DM defect is located supratentorially, the choice of a dural substitute affects the rate of CSF exusion and related complications. The use of autogenous tissues in PCF surgery statistically significantly reduces the rate of liquorrhea compared to that of synthetic materials.

Keywords: dura mater, dural substitute, liquorrhea, pseudomeningocele.

Material and Methods

The study includes observation and treatment results of 232 patients operated on at the Neurosurgery Clinic of the Military Medical Academy in the period between 2010 and 2017. The study has been approved by the local independent ethics committee (extract from the minutes №156 of the meeting of the independent ethics committee of the Kirov Military Medical Academy on December 23, 2014).

The main inclusion criteria were:
1) open neurological intervention on the brain;
2) the patient is older than 18 years of age;
3) informed voluntary consent of the patient or his/her legal representatives to participate in the study;
4) formation of the DM defect during neurosurgical intervention by compared to the rate of postoperative liquorrhea. In surgery for the posterior cranial fossa (PCF), applicable dural substitutes were not used; in this cohort, the efficacy of autogenous tissues and synthetic materials was compared.

Results. In 232 patients, the total rate of liquorrhea was 23.7%. In supratentorial surgery (175 cases), the use of autogenous tissues (n=73), synthetic materials (n=42), and collagen matrices (n=60) was associated with CSF exusion in 13 (17.8%), 13 (31.0%) and 16 (26.7%) cases, respectively; in statistical analysis, these results were comparable (p>0.05). In PCF surgery (57 cases), the use of autogenous tissues (n=34) significantly more effective (p=0.021) prevented liquorrhea compared to synthetic materials (n=23): complications occurred in 4 (11.8%) and 9 (39.1%) cases, respectively.

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The main inclusion criteria were:
1) open neurological intervention on the brain;
2) the patient is older than 18 years of age;
3) informed voluntary consent of the patient or his/her legal representatives to participate in the study;
4) formation of the DM defect during neurosurgical intervention followed by plastic surgery;
5) the possibility of intraoperative monitoring and accounting by researchers of the DM defect repair method;
6) the possibility of postoperative monitoring and registration of wound healing (up to 42 days).

The main exclusion criteria were:
1) the refusal of the patient or his/her legal representatives to participate in the study;
2) the history of allergic reactions to any components of the suture materials or plastic materials;
3) death of the patient prior to wound healing;
4) the history of severe trauma-induced brain injury, stroke or intracranial tumor;
5) resection of the tumor-affected DM region;
6) duraplasty in the presence of Chiari type I malformation;
7) inadvertent damage to the DM with defect formation during craniotomy;
8) reduction of the area of DM grafts due to their drying, electrocoagulation, as well as mummification as a result of exposure to a powerful light source of the operating microscope.

Such patients require additional substitute materials for repair of the DM defect. Various artificial DM substitutes contribute to solving this problem, but their effectiveness is still poorly understood and questionable compared to that of patient autogenous tissues.

The aim of the work is to study the efficacy of various substitutes in repair of dura mater defects.

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4) impossibility of unbiased monitoring by the researcher of intraoperative and/or postoperative parameters.

A total of 232 patients (129 (55.6%) men and 103 (44.4%) women) were selected and included in the study based on the above-mentioned criteria. The patients’ age ranged from 18 to 79 years, the median age was 48 years (interquartile range, 33 to 57 years).

The choice of the method for DM defect repair was made depending on the intraoperative situation, availability of the required substitute material, personal preferences of the surgeon.

In 107 (46.1%) cases, patient autogenous tissues (fragments of the pericranium, aponeurosis, nuchal ligament, fascia lata, and subcutaneous fat) were used as plastic material. Plastic repair was performed by fixation of these materials to the edges of the dural defect using a continuous suture (Fig. 1a).

In 65 (28.0%) cases, replacement of the DM defect was carried out with the use of official non-resorbable synthetic polytetrafluoroethylene (Dura Preclude ( Gore)) or polysterurethane membranes (NeuroPatch (“BBraun”)) (see Fig. 1b). In all cases of plastic material suturing (both patient autologous tissues and synthetic DM substitutes), a 5/0 monofilament polypropylene material (Prolene), which was additionally sealed with Tachocomb plates (“Takeda”), was used.

In 60 (25.9%) patients, the defect closure was performed using free-lying collagen matrix (Duraform (Codman), Duragen (Integra) or Lyostypt (“BBraun”) without suture fixation, by application of the material to the defect (see Fig. 1c). At the same time, DM substitutes were layered both as a single fragment and in several parts with overlapping edges for closure of the defects exceeding the official materials in square size (“tile-like” plastic surgery), which allowed achieving compliance with the spheroid shape of the brain.

Further closure of the operating wound was carried out according to the standard method in all groups: if necessary, cranioplasty with autologous bone or titanium mesh was performed, aponeurosis and skin were sutured using Donati or intradermal suture techniques with resorbable or non-resorbable suture material.

The quality of DM defect sealing was assessed based on the detection of external CSF leak or pseudomeningocele. To identify differences between some specific groups, pairwise comparisons were additionally performed using the Pearson χ² test, and χ² test with Yeats correction or the Fisher’s exact test were used for small samples depending on the sample size, while odds ratio was used to quantify the differences. The Student’s t-test was used for comparison of the duration of the DM repair stages between the groups after verification of normal data distribution. The level of statistical significance was considered to be 0.05.

**Results**

The total incidence of CSF leak was 55 (23.7%) of 232 patients included in the study, including 23 (9.9%) cases of external CSF leak and 32 (13.8%) cases of occult CSF leak accompanied by pseudomeningocele.

The patient autogenous tissues, synthetic non-resorbable materials or the above-mentioned method utilizing collagen matrices were used for the DM defect repair in case of supratentorial localization of the dural defect (n=175) among the entire set of cases included in the study (n=232). In surgery for the PCF (n=57), applicable dural substitutes were not used (collagen matrices were used only for the purpose of additional sealing of the suture between the DM and graft). In this regard, the patients were divided into two groups depending on the DM defect location for further analysis of the study results.

The main clinical results of the use of various materials for supratentorial DM defect repair are presented in Table 1.

Analysis of the obtained results demonstrated absence of the sufficient evidence (p>0.05) in favor of the hypothesis on the impact of the type of substitute material on the incidence of liquorrhoea in the postoperative period upon closure of supratentorial DM defects.

It should be noted that the duration of the stage of the surgery with applicable collagen matrices (n=60) was significantly shorter than the time spent on graft fixation using manual suture (n=172) and comprised 7.7±3.5 min and 48.9±10.9 min, respectively (p<0.0001 according to Student’s t-test), i.e. it was reduced by more than 6 times.

The main results of using different materials for subtentorial DM defect repair in clinical practice are presented in Table 2.

Postoperative liquorrhoea was observed in 4 (11.8%) patients when using patient autogenous tissues for the repair of subtentorial DM defects; in case of using synthetic membranes, these complications occurred in 9 (39.1%) patients. Differences in the parameters estimated using Fisher’s exact test were statistically significant (p=0.024). The probability of liquorrhoea or pseudomeningocele when using synthetic materials was shown to be 4.8 times

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**Table 1**

<table>
<thead>
<tr>
<th>Material Type</th>
<th>Incidence of Liquorrhoea</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autologous Tissues</td>
<td>23 (9.9%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Synthetic Materials</td>
<td>32 (13.8%)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

**Table 2**

<table>
<thead>
<tr>
<th>Material Type</th>
<th>Duration of Surgery (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manual Suture</td>
<td>48.9±10.9</td>
</tr>
<tr>
<td>Collagen Matrices</td>
<td>7.7±3.5</td>
</tr>
</tbody>
</table>

---

**Figures**

Fig. 1a: Continuous suture technique for DM defect closure.

Fig. 1b: Plastic repair using synthetic materials.

Fig. 1c: Suture fixation without material layering.

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**References**

1. Donati or intradermal suture techniques with resorbable or non-resorbable suture material.

2. Plastic repair with overlapping edges.

3. Information on the type of substitute material on the incidence of liquorrhoea in the postoperative period.
higher than in case of using patient autogenous tissues (95% CI 1.27–18.37; p=0.021).

It should be noted that the incidence of external liquorrhea was not statistically significantly different (p=0.093), i.e. the worst results in the subgroup with the use of synthetic materials are due to the higher frequency of occult CSF leak.

The absence of significant differences in the incidence of nosocomial meningitis (p=0.184), the need for reoperations (p=0.093) and mortality (p=0.778) is explained by the small number of cases with these complications, which significantly reduced statistical efficiency and increased the probability of a type II error. At the same time, according to these parameters, the best results were observed in the subgroup with patient autogenous tissues. However, statistical confirmation of this hypothesis is possible only after increasing the number of observations.

**Discussion**

The need for the duraplasty, which is accompanied by the formation of dural defect both in emergency and planned surgeries, raises the question of the choice of the substitute material for a neurosurgeon. According to a number of authors, patient’s autologous tissues, namely, pericranium, fascia lata, fascia temporalis, and subcutaneous fat are optimal choice from the point of view of biological compatibility and economic efficiency [3]. However, obtaining these materials leads to additional

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Fig. 1. Intraoperative photographs.

Surgical trauma and increases the duration of surgery and, in some cases, entails the need for additional incision [4]. The use of cadaveric dura mater graft would seem to ensure the greatest compatibility between the structure of the plastic material and the patient’s DM. However, cases of iatrogenic Creutzfeld—Jakob disease caused by unintentional introduction of prions into the recipient’s body using cadaveric DM [5—8] have limited the use of such allografts.

With the appearance of a wide range of such plastic materials as synthetic ones [9—11] and materials derived from animal collagen [12—14], the possibilities of DM defect repair have expanded. However, there is still no unified concept of selection and definition of indications for the use of various methods for dural defect repair.

A rather high overall incidence of postoperative liquorrea (23.7%) in our study is due to the fact that both external and temporary occult CSF leak, including pseudomeningocele (which is often not considered as a complication by some authors), were referred to these complications. At the same time, the frequency of reoperations (5.6%) for the ongoing postoperative liquorrea does not exceed the data of the majority of the studies published on this topic.

Table 1. Clinical results of supratentorial dural defect repair (n=175)

<table>
<thead>
<tr>
<th>Complication</th>
<th>Substitute material</th>
<th>Pearson χ² value</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patient autogenous tissues (n=73), %</td>
<td>Synthetic materials (n=42), %</td>
<td>Collagen materials (n=60), %</td>
</tr>
<tr>
<td>Liquorrhea Total</td>
<td>13 (17.8)</td>
<td>13 (31.0)</td>
<td>16 (26.7)</td>
</tr>
<tr>
<td>External liquorrea</td>
<td>5 (6.8)</td>
<td>8 (19.0)</td>
<td>5 (8.3)</td>
</tr>
<tr>
<td>Meningitis</td>
<td>4 (5.5)</td>
<td>4 (9.5)</td>
<td>6 (10.0)</td>
</tr>
<tr>
<td>Reoperation</td>
<td>2 (2.7)</td>
<td>2 (4.8)</td>
<td>4 (6.7)</td>
</tr>
<tr>
<td>Mortality</td>
<td>4 (5.5)</td>
<td>1 (2.4)</td>
<td>3 (5.0)</td>
</tr>
</tbody>
</table>

Footnote. * — the level of statistical significance of differences in the analysis of contingency tables using Pearson χ² test for large-scale tables (the critical χ² value at a significance level of p<0.05 is 5.991).

Table 2. Clinical results of PCF dural defect repair (n=57)

<table>
<thead>
<tr>
<th>Complication</th>
<th>Substitute material</th>
<th>Fisher’s exact test value</th>
<th>OR (95% CI)</th>
<th>p for OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patient autogenous tissues (n=34), %</td>
<td>Synthetic materials (n=23), %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liquorrhea Total</td>
<td>4 (11.8)</td>
<td>9 (39.1)</td>
<td>0.0241</td>
<td>4.8 (1.3—18.4) 0.021</td>
</tr>
<tr>
<td>External liquorrea</td>
<td>1 (2.9)</td>
<td>4 (17.4)</td>
<td>0.1464</td>
<td>6.95 (0.7—66.8) 0.093</td>
</tr>
<tr>
<td>Meningitis</td>
<td>2 (5.9)</td>
<td>4 (17.4)</td>
<td>0.2083</td>
<td>3.37 (0.6—20.2) 0.184</td>
</tr>
<tr>
<td>Reoperation</td>
<td>1 (2.9)</td>
<td>4 (17.4)</td>
<td>0.1464</td>
<td>6.95 (0.7—66.8) 0.093</td>
</tr>
<tr>
<td>Mortality</td>
<td>1 (2.9)</td>
<td>1 (4.3)</td>
<td>1.0</td>
<td>1.5 (0.09—25.3) 0.778</td>
</tr>
</tbody>
</table>

Fig. 2. Scanning electron microscopy of the puncture sites of the Dura Preclude (Gore) material by monofilament suture materials.

a — Prolene 6-0 (Ethicon); b — Gore-Tex 6-0 (Gore).
The hypothesis that the type of plastic material affects the incidence of CSF leak in the postoperative period after supratentorial dural defect closure did not receive sufficient evidence in the study thus indicating the advisability of a series of previously described methods for DM defect repair and confirming the results of other studies [9, 10, 15, 16]. However, many artificial polymeric implants also require fine fixation with manual suture. From this point of view, collagen materials, which are made from animal connective tissue by special treatment including removal of all cellular elements and other antigenic components, are the most convenient ones [17].

The main advantages of such matrices of biological origin are high resorption ability, stimulation of reparative processes, no requirement for their fixation to the DM edges and experimental modeling.

Adverse effects of the use of collagen and synthetic dural substitutes include their impermeability to ultrasound (probably due to the material porosity and the presence of air microvesicles in the implant), in contrast to autogenous tissues, which makes it impossible to perform ultrasound examination of the brain through a trephine defect in the immediate postoperative period, and it should be taken into account when choosing a substitute material during planning such examinations.

During PCF surgeries, the worst results of evaluating DM tightness restored using synthetic substitutes are most likely due to the CSF leak through the microscopic defects occurring in the puncture area near rigid materials upon their fixation by manual suture. This hypothesis has been previously proposed by us when studying various materials for dural repair using a scanning electron microscope (Fig. 2) [22].

In addition, leak of the CSF through the intact implant surface was often noted in delayed and late re-interventions, probably due to the loss of the waterproofing properties of the synthetic membrane.

Moreover, the degree of adhesion of additional sealing materials and adhesive compositions to various plastic materials obviously varies and affects the surgery outcome. However, this hypothesis requires further research and experimental modeling.

Conclusion

The incidence of postoperative liquorhea after replacement of supratentorial dural defects does not depend on the type of dural substitute and the method of its fixation. The application method of supratentorial dura mater defect closure allows 6-fold reduction of the duration of this stage of surgery compared to fixation of implants with a manual suture. The risk of liquorhea in replacement of the dura mater defects in the posterior cranial fossa is 4.8 times higher with the use of synthetic implants than when using patient autogenous tissues.

Contribution of authors:
The concept and design of the study — A.D., S.D. Collection and processing of the material — A.D., A.E., S.D.

Text writing — A.D., A.E., S.D.

Editing — A.D., S.D.

Authors declare no conflict of interest.

REFERENCES


Commentary

The article is devoted to a comparative analysis of the efficacy of the dura mater (DM) defect repair in various brain surgeries when DM defect closure without the use of autologous tissues or artificial materials is impossible for various reasons. The urgency of the problem is beyond doubt. As the authors rightly point out, such a need arises in almost half of the cases (more than 40% of brain surgeries), and the risk of serious and even fatal complications in the development of external liquor rhoea enhances the need to approach the above-mentioned issue seriously. Recently, as a result of appearance of many synthetic artificial membranes (both based on non-resorbable synthetic membranes and collagen matrix), operating neurosurgeons face the need to decide which DM repair method is more advisable (in case if there are options). No doubt, autologous tissues are the most available option as the authors of the article confirm, patient autologous tissues provide the greatest tightness. However, the use of autografts largely requires an increase in surgery duration, additional invasion, which also affects the risks of complications in the postoperative period. In the current article, the authors quite clearly confirm that the use of various options of supratentorial DM defect repair does not affect the incidence of CSF leak and related complications. The use of synthetic materials in supratentorial approach significantly increases the risk of postoperative complications associated with DM repair leak. Although it is fair to note that the authors used collagen membranes in several cases, including TachoComb, for additional sealing of the suture on the DM when using autologous tissues, which could also play a role in a significant decrease in the incidence of CSF leak, but there is not much information on the role of additional sealing in the article. There is an article published in the journal “Voprosy neurochirurgii” No.5 in 2016 on the method of using double layers of the TachoComb collagen sponge for the posterior fossa defect repair with the 1.7%, incidence of liquor rhoea, which is almost 2 times lower than the authors observed when using autografts (2.9%) and 10 times lower than in case of using synthetic materials in the current study (17.4%). The use of an electron microscope for visualizing puncture sites for synthetic materials as well as the idea that it is the presence of such leaky sutures between patient’s and synthetic tissues that cause postoperative liquor rhoea are very rational. Thus, the authors demonstrated that the use of autologous tissues has a significant advantage compared to artificial synthetic materials. However, I suggest expanding the study of this issue with considering the above-mentioned comments. The work is of undoubted interest for practicing neurosurgeons who face the need of DM sealing during various types of brain surgery.

Sh. H. Gizatullin (Moscow, Russia)
Diagnosis and Interventional Treatment of Pain Syndromes after Surgery for Degenerative Lumbar Spine Diseases

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4Burdenko Neurosurgical Institute, Moscow, Russia

The purpose of this study was to investigate the structure of pain syndromes after surgery for degenerative lumbar spine diseases (DSDs). The epidemiologic data are contradictory; clinical and radiological diagnostics is often low efficient; capabilities of interventional diagnosis and treatment techniques are poorly understood.

Purpose — the study purpose was to investigate the structure of pain syndromes after surgery for DSDs of the lumbar spine, based on complex diagnostics, as well as to evaluate the capabilities of interventional treatment.

Material and methods. We examined 310 patients with postoperative pain syndromes. Patients with obvious indications for repeated surgery were excluded from the analysis; the remaining patients underwent selective diagnostic blockades followed by interventional (puncture) treatment. A positive outcome was defined as a reduction in pain by 50% on the numerical rating scale (NRS-11), by 20% in the Oswestry index (ODI), and by 8 points in the sciatica bothersomeness index (SBI), with the effect lasting for 12 months. Predictive factors for the risk of pain syndromes were analyzed.

Results. Out of 310 patients, 162 (52.6%) patients had no obvious indications for surgery. Radicular pain was detected in 56 (18.6%) of 310 patients; the positive treatment outcome was achieved in 38 (67.86%) of 56 patients. Facet pain was present in 29 (9.35%) patients; the positive treatment outcome was achieved in 23 (79.31%) patients. Discogenic pain was found in 12 (3.87%) patients; the positive treatment outcome was achieved in 5 (41.63%) patients. Sacroiliac joint (SIJ) pain was present in 42 (13.55%) patients; the positive treatment outcome was achieved in 23 (79.31%) patients. Myofascial and competing pain was detected in 12 (3.87%) patients; the causes were not identified in 11 (3.55%) cases. The main risk factors were sagittal balance parameters.

Conclusion. Complex diagnostics revealed postoperative pain not associated with surgical causes in 52.6% of cases; the origin of pain was identified in 49.95% of cases. Interventional treatment was effective in 64.81% of cases; failed back surgery syndrome was diagnosed in 16.13% of patients.

Keywords: failed back surgery syndrome, postoperative pain syndrome, facet pain, degenerative spine disease, interventional pain management, diagnostic blockade.

The prevalence of surgical interventions for degenerative-dystrophic spine diseases (DSD) is 50 per 100 thousand people per year. About 20% of patients report persistence of pain after a surgery and require further treatment [1—2], including another surgery; on average, ca.10% of previously operated on patients undergo repeated interventions, which is less than half occur within the first two years after the initial surgery [3—5]. The term ‘failed back surgery syndrome’ (FBSS) was introduced to describe persistent pain syndrome, which is resistant to therapy, in the absence of indications for re-operation [6]. The capabilities of clinical and radiological examination of such patients are limited [7, 8]. Selective blockades and discography have been shown to be effective in the diagnosis of certain types of spinal pain syndromes [9, 10], but their capabilities have not been adequately investigated. Most non-invasive treatments for spinal pain have weak evidence base and are supported by a limited number of papers only [11]. The results of using interventional methods of treating pain (puncture) are significantly better, and it is the absence of the effect of such treatments that is used as a criterion for the diagnosis of FBSS and is an indication for the use of neuromodulation methods [12].

The purpose of this study is to examine the structure of pain syndromes after DSD surgery at the lumbar level using complex diagnostics and to assess the capabilities of interventional pain treatment.

Materials and Methods

This prospective study included a group of patients who underwent DSD surgery at the lumbar level in the Department of Neurosurgery of Nikiforov All-Russian Center of Emergency and Radiation Medicine in 2012—2017. The scope of intervention included microdiscectomy, microsurgical decompression of the spinal canal, posterior and transforaminal interbody fusion with transpedicular fixation at level 1—2, fusion with extended fixation at the level 3 and more.

The inclusion criteria were: an axial and/or radicular pain syndrome that persists or appears within 2 years after surgical treatment and is resistant to conservative treatment; pain score of 4 points or more on the numeric rating scale (NRS-11) and/or 8 points or more on the sciatica bothersomeness index (SBI), and/or impairment of activity of 30% or more on Oswestry disability index (ODI).

The exclusion criteria were: obvious indications for repeated surgical intervention based on X-ray examination. In case of radicular pain syndrome, such indications include signs of compression of the nervous structures.
due to the relapse of the disease, pathology on the adjacent level. The degree of root compression of the spine and spinal canal stenosis was assessed according to classifications of C. Pfirrmann et al. [13], C. Schizas et al. [14], S. Lee et al. [15]. The perforation of the medial wall of the root of the arch and the protrusion of the screw into the canal should be more than 4 mm in accordance with standard recommendations [16]. In case of axial pain syndrome, indications included pseudoarthrosis with instability of the components of the fixation system, proximal junctional instability (PJI), signs of segmental instability in the form of sagittal translation of the vertebral bodies of more than 4 mm during functional spondylography, signs of pronounced disruption of sagittal balance based on the following parameters: sagittal vertical axis over 9.5 cm; pelvic tilt (PT) over 30°; pelvic tilt (PI) and lumbar lordosis (LL) over 20°.

In patients without obvious indications for a surgery, further diagnostic search was conducted to clarify the nature of the pain syndrome.

The following types were identified:

1. Facet pain syndrome. Confirmatory test was a blockade of the medial branch of the primary posterior branch of the spinal nerve at appropriate levels, subject to a reduction in pain by 50% compared to the baseline. In case of a positive outcome, radiofrequency denervation was performed.

2. Dysfunction of the sacroiliac joint (SIJ). Confirmatory test was an intra-articular blockade. In the case of efficacy, intra-articular glucocorticosteroids (GCS) and/or radiofrequency denervation were used.

3. Discogenic pain syndrome. Confirmatory tests included negative blockades of intervertebral joints (IVJ) and/or SIJ and positive blockade of the connecting branch of the sympathetic trunk at the level of LI vertebral. In case of confirmation, a radiofrequency annuloplasty of the intervertebral disk (IVD) was performed.

4. Myofascial pain syndrome. Confirmatory test and therapeutic interventions were blockades of the trigger zones with an anesthetic and GCS after exclusion of other types of pain syndrome.

5. The diagnosis of radicular pain syndrome was established on the basis of the characteristic clinical presentation. In cases of doubts, other types of test blockades were performed initially. Transforaminal epidural blockade with GCS and pulsed radiofrequency ablation of the spinal ganglion at an appropriate level were the methods of interventional treatment.

6. Competing pain syndromes. If there are significant signs of suffering in the peripheral nervous system, hip and knee joints, etc. appropriate neural, intra- and para-articular blockades were performed for the purpose of differential diagnosis.

Assessment of outcomes. An outcome was considered to be positive in case of a decrease in the NRS-11 index by 50% or by 4 points, or a decrease in the ODI index by 20%, or a decrease in the SBI index by 8 points compared to the baseline and persistence of the effect for 12 months after the surgery. Assessment of outcomes was conducted by a telephone survey, by e-mail or during an outpatient visit 12 months after the procedure. Additionally, a search for risk factors for the development of the diagnosed pain syndrome and prognostic factors for the outcome of an intervention was performed.

Statistical processing of data. Non-parametric methods of analysis were used. The assessment of the significance of differences between the groups was carried out using Mann-Whitney U-criterion and Pearson’s χ2 for quantitative and qualitative indicators, respectively; in case of a small number of expected values in the contingency table Fischer’s exact test was used. Correlation analysis was performed using the Spearman’s r-correlation coefficient to identify the statistical relationship between the indicators. Regression analysis was performed to identify predictors of outcomes and the odds ratio (OR) and 95% confidence interval (CI) were calculated.

Results

We examined 310 patients with postoperative pain syndromes. The X-ray examination revealed that 148 (47.74%) of them had obvious indications for repeated surgical treatment, and they were excluded from further analysis. Data on the distribution of patients based on the results of X-ray diagnosis are presented in Table 1. A total of 162 (52.26%) patients were included in the final analysis, their distribution by the prevailing pain syndrome is presented in Table 2.

A total of 91 (29.36%) out of 310 patients had pain in the lower limb without an obvious compression substrate. Test blockades used for the differential diagnosis, resulted in a relief of pain syndrome in 35 (38.46%) of these patients. The radicular symptoms were imitated by SIJ pathology in 15 (42.86%) patients out of 35 and by facet pain syndrome in 11 (31.43%) out of 35 patients. Transforaminal epidural blockade was performed in 34 patients with radicular pain syndrome, transforaminal epidural blockade in combination with pulsed radiofrequency ablation of spinal ganglia was performed in 22 patients. The positive effect was achieved, respectively, in 15 (44.12%) and 16 (72.73%) patients, the differences are significant (p=0.048). Ten patients with a short-term effect of the blockade subsequently underwent pulsed ablation with a positive effect in 7 cases. Risk factors for the development of postoperative radiculopathy included the duration of symptoms before the surgery of more than 4 months (p=0.045) and presence of motor deficit (p=0.018) before the surgery. The prognostic factors of negative outcomes of analgesic interventions were the presence of allodynia and/or hyperpathies with OR of 1.26 (95% CI, 1.115–1.361) for the blockade and OR of 1.23 (95% CIb 1.076–1.282) for pulsed ablation.

Facet syndrome was identified in 29 (9.35%) patients out of 310, radiofrequency denervation was effective in
23 (79.31%) patients. The risk of development of facet pain syndrome increased with an increase in PI \((p=0.037)\) and a lack of local lordosis in LIV—SI segments relative to the general lumbar lordosis \((\text{LL (LIV — SI)} < 2/3 \text{ LL (LI — SI)})\). Negative prognostic factors for effectiveness of denervation were the difference between the pelvic tilt and lumbar lordosis of more than 10° \((\text{PI — LL} > 10°)\) with OR of 1.59 (95% CI, 1.381-1.848).

SIJ dysfunction was identified in 42 (13.55%) out of 310 patients. Intra-articular steroids were effective in 36 (73.81%) of them. In 8 patients, the effect of the blockade was short-lived; they underwent repeated administration of steroids in combination with radiofrequency denervation of SIJ which was effective in 5 patients. The risk of developing SIJ dysfunction increased for pathological PT \((p=0.009)\). Negative prognostic factors for the effectiveness of interventional procedures were the difference in pelvic tilt and lumbar lordosis over 10° \((\text{PI—LL} > 10°)\) and PT value over 20°, with OR of 1.59 (95% CI, 1.381-1.848). Negative prognostic factors for the effectiveness of interventional procedures were the difference in pelvic tilt and lumbar lordosis over 10° \((\text{PI—LL} > 10°)\) and PT value over 20°, with OR of 1.59 (95% CI, 1.381-1.848).

Pseudarthrosis and fixation instability 23 7.42
PJF 17 5.48
Segmental instability 7 2.26
Pronounced sagittal balance disorders 13 4.19
Total 148 47.74

Footnote. * — of the total number of patients (n=310).

The distribution of patients based on the type of the prevailing pain syndrome and the effectiveness of interventional treatment

<table>
<thead>
<tr>
<th>Pain syndrome</th>
<th>Number</th>
<th>%*</th>
<th>Treatment effectiveness</th>
<th>Number</th>
<th>%**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radicular</td>
<td>56</td>
<td>18.06</td>
<td>38</td>
<td>67.86</td>
<td></td>
</tr>
<tr>
<td>Facet</td>
<td>29</td>
<td>9.35</td>
<td>23</td>
<td>79.31</td>
<td></td>
</tr>
<tr>
<td>SIJ</td>
<td>42</td>
<td>13.55</td>
<td>36</td>
<td>85.71</td>
<td></td>
</tr>
<tr>
<td>Discogenic</td>
<td>12</td>
<td>3.87</td>
<td>5</td>
<td>41.67</td>
<td></td>
</tr>
<tr>
<td>Myofascial</td>
<td>5</td>
<td>1.61</td>
<td>3</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>Competing</td>
<td>7</td>
<td>2.26</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>11</td>
<td>3.55</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>162</td>
<td>52.26</td>
<td>105</td>
<td>64.81</td>
<td></td>
</tr>
</tbody>
</table>

Footnote. * — of the total number of patients (n=310); ** — on the number of patients with this pain syndrome.

Myofascial pain syndrome was proven in 5 (1.61%) of 310 patients. In 3 cases, it presented as the piriform muscle syndrome; in all cases the positive effect was achieved by infiltration with a local anesthetic and GCS.

Competing pain syndromes were detected in 7 (2.26%) patients, a combination of pain syndromes of various etiologies, in 27 (8.71%) patients, and in 11 (3.55%) patients the etiology of pain syndrome was not established.

Discussion

The reasons for persistence or onset of pain after the surgery were surgically significant in almost 50% of cases in the study. In a number of studies [17–23] devoted to the same problem, the frequency of surgical etiology reaches 60–85% of the cases. In case of routine use of discography [20, 22], the incidence of discogenic pain syndrome is 17–21.5%. However, the use of discography is limited by its invasiveness and unavailability of apparatuses for measuring intradiscal pressure. In the present study, the discogenic nature of pain was established based on the exclusion of other sources of pain and positive blockade of the connecting branch of the sympathetic trunk at the level of LII vertebra; its incidence was significantly lower. The theoretical substantiation of the use the ramus communicans blockade, whose afferents are a part of the white connective branch at the LII level, for
diagnosis of back pain is primarily sympathetic innervation of IVD. The method shows good diagnostic efficacy; however, it requires further study [24]. The relatively low effectiveness of annuloplasty in this study may indicate a deficiency in diagnosis or may be related to the capabilities of this method [25].

The incidence of postoperative facet pain and SIJ dysfunction is also related to the chosen selection criteria: the use of controlled blockade with two anesthetics and establishment of a significant threshold for reducing pain [26]. In our study, a single test with a threshold of 50% was used, which is the most convenient for routine practice, however, the incidence of facet syndrome did not exceed 10%, which may be due to the inclusion of a large number of patients with spinal fixation (63.74%) in the analysis, including those with extended fixation (17.74%). In contrast, SIJ pathology is more common after spinal fusion [27] and it prevailed over other types of axial pain syndromes in our study as well. Facet syndrome was more common in conditions of general lumbar hyperlordosis (with high PI) or in conditions of compensatory segmental hyperlordosis if the sagittal profile (LL (LIV–SI)<2/3 LL (LI–SI) is unbalanced. SIJ dysfunction was more common for pelvic retroversion with an increase in PT (relative to the calculated one for a given PI) and in case of general balance disorders with PI—LL>10°. The effectiveness of the subsequent interventional treatment with the number of positive results of about 80% is an indirect confirmation of the correctness of the performed diagnosis.

Radicular pain syndrome (without obvious compression substrates) was the most common (18.6%) issue in the study group, even in comparison with other studies, where the incidence of neuropathic pain did not exceed 10% [17]. This is due to the classification and importance of epidural fibrosis: in most works, it is considered as an independent cause of radicular pain syndrome, and its incidence reaches 34%. The relationship between clinical outcomes of spinal interventions and the severity of fibrosis according to MRI data has not yet been proven, and neither is the impact of methods for its prevention [28], therefore the severity of the cicatrical process was not taken into account in this study. The effectiveness of the interventional treatment of radicular pain syndrome was almost 70%.

Diagnosis and subsequent treatment of myofascial pain syndrome are based on extremely subjective criteria [29]. In our study, there were 3 cases of the piriform muscle syndrome which were successfully treated. It was possible to prove the significance of pain in a competing pathology in 2.26% of cases on the basis of diagnostic blockades.

According to the results of the study, based on the formal criteria for the diagnosis of FBSS (no obvious cause of pain, ineffectiveness of conservative treatment), we can estimate the incidence of this syndrome as 50 (16.13%) out of 310 patients; in 18 (5.8%) of them, the pain syndrome is represented by radicular symptoms and there are potential indications for neuromodulation.

Conclusion

The onset or persistence of pain after surgical treatment of DSD requires a comprehensive diagnosis to establish the indications for a repeated intervention, and, if they are excluded, to determine the tactics of further treatment. The use of selective diagnostic blockades under the control of navigation makes it possible to prove the source of the pain syndrome and justify the use of puncture treatment methods that demonstrate greater efficacy compared with conservative treatment. The ineffectiveness of diagnostic and therapeutic interventions may be the basis for the diagnosis of “failed back surgery syndrome.”

Authors declare no conflict of interest.

REFERENCES


The article concerns an important topic. The design of the study is well chosen and corresponds to the goals and objectives of the work. Statistical processing of the data is adequate. The results obtained are interesting for neurosurgeons and orthopedic surgeons operating on the spine, as they highlight problems that arise in the postoperative period in intermediate and remote periods, and the authors also describe possible solutions. The article is fully consistent with the subject of the journal and its level. The given literature sources are modern and relevant.

I consider it expedient to publish this article in the journal “Questions of Neurosurgery”.

A.A. Grin (Moscow, Russia)
Persistence or worsening of pain after a surgery for degenerative-dystrophic diseases of the spine is a serious medical and social problem. Its relevance is due not only or primarily to the prevalence of "failed back surgery syndrome", but rather to the difficulties of its treatment. In more than half of the cases, conservative therapy is ineffective. On the other hand, repeated surgical interventions without properly elucidated indications for them not only fail to contribute to the elimination of the pain syndrome, but often result in its exacerbation and even further disability. The authors of the work rightly placed emphasis on minimally invasive intervention methods, which are not only very effective in controlling vertebral pain syndromes (including postoperative ones), but also have great diagnostic and prognostic potential. For example, a simple diagnostic blockade which brings anesthetic directly to the source of pain can provide much more information than complex expensive studies, the results of which do not always correlate with clinical data. Moreover, it is not at all clear why attempts are being made to pump a body with analgesics and psychotropic drugs in cases where pain can be ameliorated or relieved with the help of the same blockades or other minimally invasive treatment methods. After analyzing sufficiently representative material, the authors convincingly proved the effectiveness of the methods used, and additionally demonstrated their proper places in the diagnosis and treatment of this complex pain syndrome. The main disadvantage of almost all minimally invasive methods described in the work is the relatively short duration of their analgesic action, which requires their regular re-administration. Therefore, it would have been interesting to establish the subsequent status of the same patients not only 12, but also 36 or more months after the treatment. However, the positive, even if the short-lived effect of such treatment may serve as the basis for the use of more complex modern minimally invasive methods, such as neuromodulation methods. For example, the positive results of pulsed ablation of the roots can serve as a basis for chronic electrostimulation of the same roots or epidural stimulation of the spinal cord. The need to frequently repeat the radiofrequency destruction of the medial branches of the posterior branch of the spinal root can be the basis for its chronic stimulation using a completely new technique of extraspinal stimulation. Despite the high efficiency, minimal invasiveness and high safety profile of all the described methods, their use mostly remains the lot of neurosurgeons and individual enthusiasts among algologists, anesthesiologists and algologists-neurologists. The absence of a school of algology, clear standards and recommended protocols allows neurologists and rehabilitators to delay the timely use of highly effective minimally invasive methods of treatment of complex chronic pain syndromes. Therefore, I would like to re-emphasize the relevance of this work, which once again raises the question of the need for the timely use of simple and inexpensive minimally invasive and safe treatment methods that also have a high diagnostic value. There is a hope that an exponentially increasing number of such studies will finally lead to the standardization of methods in this field, and formation and strengthening of the Russian school of algology.

E.D. Isagulyan (Moscow, Russia)
The optimal treatment modality for patients with degenerative-dystrophic diseases of the cervical spine is a disputable issue. At the same time, the polymorphism of clinical manifestations of cervical spine lesions, as well as the socio-economic and organizational aspects of treatment of this category of patients remain an urgent problem of modern vertebrology [1, 3, 9].

Degenerative diseases of the cervical spine accompanied by clinical manifestations of myelopathy occur in the most socially active age groups [12]. At the same time, the problems of surgical treatment of the most serious cases with polysegmental lesions of the cervical spine accompanied by kyphotic deformity are still unresolved [11].

Therefore, current problems include selecting the optimal surgical approach, extent of operation, and phasing of surgical treatment of patients with polysegmental degenerative lesions of the cervical spine accompanied by its kyphotic deformity.

Material and methods

A total of 36 patients with polysegmental degenerative stenosis of the cervical spine accompanied by MRI signs of myelopathy and neurological deficit of varying severity were operated on at the Vreden Russian Research Institute of Traumatology and Orthopedics. The patients were divided into two groups based on MRI data: type A, loss of cervical lordosis (N-22) and type B, kyphosis (Cobb’s angle more than 10°) (N-14).

Surgical treatment was aimed at spinal cord decompression, as well as elimination of pathological (kyphotic) spinal deformity (in the case of type B) and stabilization of the spinal motion segments. Operations were performed from the anterior approach, and, in the case of two-stage treatment (3 patients), from the posterior and anterior approach with various types of decompressive management. Primary stabilization was performed using transpedicular systems, interbody implants. Particular attention was paid to autologous bone grafting aimed at formation of adequate spinal fusion. Depending on selected surgical approaches, interbody, interpedicular, and interosseous fusion, as well as arthrodesis or their combinations were formed.

The results of treatment were evaluated on the basis of regression of neurological manifestations and fixation stability. In the case of the follow up period of up to 5 years, the results were evaluated using the JOA scale (Japanese Orthopedic Association Scale). The SPSS 22 software package for Windows was used for statistical processing.

Results

The objectives of the operation were achieved in all cases. In one case, additional posterior transpedicular fixation of the spine was required in the early postoperative period. Follow-up examination in the long-term period showed that decompression and spinal fusion were achieved in all patients. No reoperations associated with instability or failed spinal fusion were carried out in the long-term period.

All patients who underwent correction of spinal deformity (type B) along with spinal cord decompression demonstrated good outcomes as assessed by the JOA scale, while in patients with loss of cervical lordosis (type A), where the deformity was not corrected, good outcome was achieved only in 1 patient; in other cases, treat-
ment outcome was rated as satisfactory based on the JOA scale (Fig. 1).

In summary, treatment outcomes were significantly better in the case of simultaneous decompression, correction of deformity, and stabilization of the spine (Fisher’s exact 2-tailed test — $p<0.000001$).

**Case 1**

Patient E., 63 years old, was admitted to the clinic with complaints of weakness and pain in the arms and legs and pain in the cervical spine. Medical history shows that the patient experienced idiopathic numbness and tingling in the right half of the body. The condition worsened, repeated conservative treatment was ineffective. On examination: limited range of motions in the cervical spine, raising and placing the hands behind the head is painful, there are sensory disorders in the form of hyposthesia in the arms, legs, and body, mainly in the distal part on the right, mixed tetraparesis up to 4 points, tendon reflexes in the hands are reduced, there are pathological reflexes in the legs.

X-ray and multispiral computed tomography (MSCT) images of the cervical spine showed kyphotic deformity and spinal instability; MRI showed signs of anterior compression and spinal cord deformity (Fig. 2).

The operation included discectomy C3—C4, C4—C5, C5—C6, C6—C7, corporectomy C5, C6, removal of the ossified posterior longitudinal ligament and ossified disc hernias, decompression of the spinal cord and roots at the level of C4—C6, correction of spinal deformity, C3—C4 corporodesis with cage and C4—C6 corporodesis using mesh-cage with plate fixation (Fig. 3).

In the early postoperative period, control X-ray images showed loss of correction and change in plate configuration. Considering insufficient bone density, which was detected intraoperatively, it was decided to use additional posterior fixation. Deformity was corrected using transpedicular fixation (Fig. 5).

The patient was operated on, including C3—C4, C4—C5, C5—C6 discectomy, C4, C5 corporectomy, removal of the ossified posterior longitudinal ligament and ossified disc hernias, decompression of the spinal cord and roots at the level of C3—C6, correction of spinal deformity, corporodesis of C3—C6 using mesh cage with plate fixation.

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The patient was operated on, including C3—C4, C4—C5, C5—C6 discectomy, C4, C5 corporectomy, removal of the ossified posterior longitudinal ligament and ossified disc hernias, decompression of the spinal cord and roots at the level of C3—C6, correction of spinal deformity, corporodesis of C3—C6 using mesh cage with plate fixation.

In the postoperative period, there was regression of pain, segmental and conductive disorders (good outcome as assessed by the JOA scale) was observed in the early postoperative period. Therefore, decompression and plate stabilization turned out to be effective in the case of adequate bone density and fixation with screws of the appropriate length at more than four points of support.

**Case 2**

Patient Kh., 62 years old, was admitted to the clinic with complaints of weakness and pain in the hands, weakness and awkwardness in the legs, mainly in the left one, pelvic dysfunction in the form of retention, pain in shoulder girdle, neck, and back of the head. Medical history shows that the patients suffered from numbness in the fingers for about 10 years. Worsening was observed within several years, neurological symptoms intensified for no apparent reason within 2 months before hospitalization. On examination: the patient virtually cannot walk because of weakness in the legs, actions associated with fine motor skills of the hands are impossible. Palpation of the spinous processes is painful. There is limited range of motion in the cervical spine. Raising and placing the left hand behind the head and back results in severe pain with spastic strictures, increased paresis and numbness in the hand. Sensory disorders in the form of hyposthesia in the hands up to anesthesia in the distal regions. Mixed tetraparesis up to 3 points in the hands and 4 points in the legs. Tendon reflexes in the hands are reduced. In the lower limbs, the reflexes are sharply increased up to foot clonus. Pathological reflexes in the lower limbs. Abdominal reflexes are symmetrically increased. Pelvic dysfunction, central type. Introscopic data (MRT, MSCT) are shown in Fig. 4.

The patient was operated on, including C3—C4, C4—C5, C5—C6 discectomy, C4, C5 corporectomy, removal of the ossified posterior longitudinal ligament and ossified disc hernias, decompression of the spinal cord and roots at the level of C3—C6, correction of spinal deformity, corporodesis of C3—C6 using mesh cage with plate fixation.

In the postoperative period, there was regression of segmental and conduction disorders, relief of radicular pain and pain in the neck. At the moment, fine motor skills of the hands, as well as social and professional activity are restored (the patient plays guitar and wind instruments) (good outcome as assessed by the JOA scale).

Therefore, fixation of corrected deformity along with extended decompression using plate on four screws was insufficient, which manifested in the form of instability and loss of correction in the near future. Transpedicular fixation of the cervical segments proved to be effective with respect to primary stabilization and retention of correction.
Case 3

Patient D, 54 years old, was admitted to the clinic with complaints of numbness in the hands, more pronounced in distal parts, weakness mostly in the right hand, weakness and numbness in the legs, more pronounced in the left leg. Medical history showed that the patient experienced pain and weakness in the right arm and pain in the cervical spine for about 20 years. In 1993, he met with an accident, no traumatic bone injury was observed. On 25.05.11, the patient operated on for degenerative disease of the cervical spine at another hospital. The patient underwent hemilaminectomy of C3—C5 on the right with insertion of a test electrode. Immediately after the operation, he experienced increase in weakness in his right hand and left leg. At the time of hospitalization, he could move only with assistance. Neck palpation was painless. Limited range of motion in the cervical spine was observed. Raising and placing hands behind is impossible.

There are sensory disorders in the form of hyposthesia from the level of C5 dermatome more pronounced in the distal regions of the right arm and left leg. Deep mixed tetraparesis (sluggish, up to 1 point, in the hands and spastic, up to 3 points, in the legs). Tendon reflexes in the arms (biceps, carporadial) are significantly weakened. There are increased reflexes in the lower limbs, more pronounced on the left. There are pathological reflexes in the legs. Abdominal reflexes are symmetrically increased. The data of instrumental studies are shown in Fig. 6.

The patient was operated on, including transpedicular fixation of C3—C4—C5—C6—C7, laminectomy of C4, C5, C6, resection of the arches of C3—C7, foraminotomy of C3—C4—C5—C6 on both sides, decompression of the spinal cord and roots at the level of C5—C6 (Fig. 7).

In the early postoperative period, moderate positive dynamics was observed in the form of increased leg strength.

Control examination in a year showed gait improvement and no significant positive dynamics in the upper limbs (satisfactory result as assessed by JOA scale).
Discussion

Kyphotic deformity associated with degenerative disease of the cervical spine is characterized by gradual increase over a long period of time accompanied by development of instability in new spinal motion segments [11]. After reaching a certain level, kyphosis can quickly progress causing increase in neurological deficit.

Different types of laminoplasty used in patients with polysegmental stenosis are often ineffective in the case of spinal deformity when used as the only surgical treatment, and clinical efficacy of increasing the posterior subarachnoid space with preserved anterior compression is often questioned [5]. At the same time, along with the need for proper decompression, special attention is paid to correction of deformity and stabilization of the spine [11].

It is known that the spinal cord is rigidly fixed in the cervical region with the odontoid ligaments [10]. Under conditions of degenerative changes in the spinal canal and kyphotic deformity resulting from bending of the cervical spine, the spinal cord, being additionally fixed by the roots in degeneratively changed intervertebral holes, stretches along the deformity curve [6]. In this situation, additional adverse factors (compression, deformation) may include ventral disc herniation, osteophytes, as well as spondylarthrosis and ossification of the posterior longitudinal ligament [7].

Therefore, along with conventionally considered vertebromedullary conflict, dynamic vertebromedullary disproportion and, as a result, excessive stretching of the spinal cord also plays significant role [8]. This results in combined compression-traction effect on the conductors and segmental apparatus of the spinal cord. It is charac-
Characteristic that the introscopic picture of myelopathy in this situation can also be observed with normal size of the spinal canal and posterior subarachnoid spaces.

The concept of distraction vertebromedullary conflict is usually considered in terms of the pathogenesis of fixed spinal cord syndrome in spinal dysraphia [2], which is treated using, among other things, corrective orthopedic interventions aimed at reducing the height of the spinal column [4]. In our study, treatment outcomes were significantly better in those cases, where, in addition to decompression and stabilization of the spine, spinal cord stretching was eliminated by reducing the relative length of the spinal canal when eliminating kyphotic spinal deformity.

In patients with loss of cervical lordosis, decompression and stabilization did not lead to similar dynamics of clinical manifestations. It is likely that the relative increase in the length of the spinal canal is also important for this category of patients, which must be considered when performing stabilization. When these methods are ineffective, interventions aimed at reducing the height of the spinal column can be considered as an alternative surgical treatment. However, this approach should be further discussed.

Authors declare no conflict of interest.
REFERENCES


Commentary

The article focuses on the treatment of cervical myelopathy caused by spinal cord stretching associated with kyphotic spinal deformity. It should be noted that, according to Lang, no lengthening of the spinal canal occurs in the case of kyphosis with underlying degenerative process, since degeneration is associated with shortening (breaking) of the anterior cortical layer due to natural aging (data of E. Benzel), which causes kyphosis in 90% of cases of degeneration in contrast to lordosis. The possibility of formation of cervical myelopathy associated with the development of kyphosis was observed in children with congenital or abnormal (non-degenerative) deformity of the spine, which is often not accompanied by formation of myelopathic lesions. Thus, it is rather ventral dynamic compression of the brain than lengthening associated with “fixed spinal cord syndrome”, as stated in the article. At the same time, this study is undoubtedly valuable since it is well-known that selection of decompression options (ventral, dorsal) and stabilization methods (anterior metal plate or posterior trans-articular helical (hook) fixation) is a challenging problem. The complexity of choice is in many respects due to insufficient understanding of the anatomy of formation of myelopathic lesions (sometimes at some distance from compression itself) due to the discrete entry of supplying vessels at the level of cervical thickening and formation of critical circulation areas in the spinal cord substance. When selecting the direction of decompression for stenosis of the cervical spinal canal, we are guided by the following principles:

— the presence of kyphosis determines mainly the ventral component of compression and necessitates decompression and stabilization from the anterior approach;

— in all cases, simultaneous correction of kyphotic deformity is required (this is also emphasized in this work), which improves the rate and degree of neurological recovery;

— laminoplasty is carried out in the absence of kyphosis and can be used in situations when there is no risk of developing postoperative instability;

— in doubtful cases of spine flattening (in the absence of obvious kyphosis), the nature and degree of decompression can be determined based on neurophysiological studies.

This work is undoubtedly valuable and the problem being discussed is of great importance. However, the nature of spinal cord fixation, especially bilateral one (the so-called pincer phenomenon) should be taken into account, which is most significant in terms of prognosis of decompression-stabilizing measures at the cervical spine.

A.O. Gushcha (Moscow, Russia)
Minimally Invasive Dorsal Decompression-Stabilization Surgery in Patients with Overweight and Obesity

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Spinal surgery in patients with overweight and obesity is associated with an increased risk of perioperative complications. Minimally invasive (MIS-TLIF) and traditional (O-TLIF) techniques of rigid stabilization are extensively used, but the advantages and disadvantages of MIS-TLIF in patients with an elevated body mass index (BMI) remain controversial.

Aim — the study aim was to assess the efficacy of a new low-invasive rigid fixation technique and traditional open spinal fusion in surgical treatment of degenerative lumbar spine diseases in patients with overweight and obesity.

Material and methods. The study included 73 patients (49 males and 24 females, aged 53 (42; 65) years) with a BMI of more than 25 kg/m². Two study groups were allocated: group I (MIS-TLIF, n=32) included patients operated on using an original technique of spinal canal reconstruction, interbody spinal fusion, and combined transpedicular stabilization; group II (O-TLIF, n=41) included patients who underwent single-level rigid stabilization through the median approach. The mean follow-up period was 34 months in group I and 40 months in group II. Comparative analysis assessed clinical parameters, intraoperative indicators, postoperative period specificity, instrumental data, and complications.

Results. Compared to the O-TLIF group, the MIS-TLIF group was characterized by a shorter time of surgery, X-ray exposure, activation, and hospital stay as well as by a smaller amount of blood loss. A comparative analysis of the pain severity (visual analogue scale) and performance status (ODI) in the follow-up period revealed significantly better results in group I, which was associated with smaller intraoperative injury to soft tissues. The total rate of postoperative complications was 9% in group I and 17% in group II (p=0.01). In this case, the interbody bone block formed in the long-term postoperative period in 86% of group I patients and in 81% of group II patients (p=0.15). According to the instrumental data, there was statistically significant greater muscular atrophy in the group after O-TLIF (p<0.001).

Conclusion. The original technique of minimally invasive rigid stabilization is safe and highly effective in surgical treatment of degenerative lumbar spine diseases in patients with overweight and obesity. MIS-TLIF has a number of significant advantages over O-TLIF in the dynamics of clinical parameters and a low number of perioperative complications, which is confirmed by smaller injury to paravertebral tissues and a better performance status in the long-term postoperative period.

Keywords: overweight, obesity, lumbar spine, degenerative diseases, transforaminal interbody fusion, transpedicular stabilization, minimally invasive spinal surgery.

Obesity represents a significant social problem among people of different ages. The body mass index (BMI) of 25—30 kg/m² corresponds to overweight, and of more than 30 kg/m², to obesity [1]. In 2008, the global prevalence of obesity was 9.8% among men and 13.0% among women, which is two times higher than in 1980 [2]; in 2016, the prevalence of obesity increased and amounted to 11% in the male population and 15% in the female [3].

According to the WHO [4], about 2.8 million people worldwide die annually due to overweight or obesity, and approximately 35.8 million (2.3%) people are dysfunctional or disabled due to the same causes [4].

Obese patients, in most cases, have comorbidities with varying degrees of compensation: cardiovascular, diabetes mellitus, systemic diseases of the musculo-ligamentous apparatus, osteoarthritis of the knee and hip joints, lumbosacral pain [5, 6]. The increase in the number of overweight and obese people in the population is bound to adversely affect the number of patients with clinically significant degeneration of the lumbar segments.

Surgical treatment of such patients is accompanied by technical difficulties during surgical approaches [5, 7]. The total rate of perioperative complications during spinal surgery in overweight people amount to 36.9% [8]. The main adverse outcomes in obesity are associated with an increase in the duration of surgery, larger amount of blood loss and higher risks of revision interventions and thromboembolic complications [9—11]. However, some researchers [8, 11] claim that there are no significant differences associated with spinal surgery in patients with different BMIs.

Studies [12—14] comparing the outcomes of surgical treatment of patients with and without obesity using traditional and minimally invasive spinal techniques have been conducted to confirm the existing risks of surgery in overweight patients. These studies have established that minimally invasive interbody fusion is comparable in efficacy and safety with open surgical techniques.

Since 2013 the Neurosurgical Center of the Railway Clinical Hospital at the Irkutsk-Passenger Station has been using an original minimally invasive method of reconstruction of the spinal canal [15] with subsequent
transforaminal interbody fusion and transcutaneous transpedicular stabilization. This work is devoted to the comparative assessment of the outcomes of the use of the new low-invasive method and traditional open methods of fusion.

The aim of the study was to assess the efficacy of a new low-invasive rigid fixation technique and traditional open spinal fusion in surgical treatment of degenerative lumbar spine diseases in overweight and obese patients.

Materials and Methods

A prospective, non-randomized, single-center study has been conducted. From 2010 to 2015, the Neurosurgical Center of the Railway Clinical Hospital at the Irkutsk-Passenger Station used rigid stabilization of the vertebral motor segment in degenerative diseases of the lumbar spine in 1432 cases.

The study included 73 patients (49 men and 24 women) with an average age of 53 (42–65) years with single-level degenerative lesion of the lumbar spine, who underwent reconstruction of the spinal canal, single-level interbody transforaminal fusion using a cage and transpedicular stabilization.

The inclusion criteria were:

— pain in the lower back and clinical symptoms of radicular pain;
— herniated intervertebral disc (IVD) or arthrosis of the facet joint, based on neuro-visualization data, narrowing of the intervertebral foramen or the vertebral canal at the level of LII - SI;
— failure of complex conservative therapy over 6—8 weeks;
— BMI >25 kg/m²;
— availability of information about patients during the long-term follow-up.

The exclusion criteria were:

— prior spinal surgeries;
— the presence of competing pathology in the lumbar spine (infectious-inflammatory diseases, tumors, traumatic injuries, etc.);
— any concomitant pathology in the stage of decompression;
— lack of informed patient consent to participate in the study.

Interventions were carried out by one surgical team with patients lying on the abdomen supported by stress-relief blocks under the conditions of artificial respiration and intravenous anesthesia. The Pentero 900 optical zoom (Carl Zeiss, Germany) and the specialized microtools (Aesculap, Germany) were used under the control of C-arm fluoroscopic cone beam (Philips, the Netherlands).

In Group I (MIS-TLIF, n=32), the decompression was performed from paramedian (4—6 cm from the midline) monolateral intermuscular approach employing the original technique [15] using the Quadrant retraction system (Medtronic, USA) minimally invasive retractor, Insight (Synthes, Switzerland), and ARAS (Zimmer, Germany); the scope of the surgery was unilateral partial facetectomy, unilateral reconstruction of the spinal canal using high-speed Anspach drill (USA) in case of monoradicular symptoms or bilateral reconstruction in case of bilateral symptoms. It was followed by discotomy and preparation of the interbody foramen using specialized tools for the maximum removal of the pulpal nucleus and fibrous ring and preservation of the end-plates. Then transforaminal spinal fusion was performed using T-pal (Synthes, Switzerland) or Capstone (Medtronic, USA) cage. Subsequently, transpedicular screw systems Viper II (Synthes, Switzerland) or U-centrum (Ulrich, Germany) (Fig. 1) were simultaneously installed using the ipsilateral open and contralateral percutaneous approach (individual skin incisions of 1.5 cm).

In Group II (O-TLIF, n=41), the median approach was used for bilateral incision of the thoracolumbar fascia and skeletalization of the paravertebral muscles, reconstruction of the spinal canal in the form of a laminectomy/hemilaminectomy with unilateral or bilateral partial or full facetectomy using high-speed Anspach drill (USA) and pistol cutters. Discectomy, preparation of interbody foramen, and transforaminal spinal fusion with a Pezo-T (Ulrich, Germany) or Capstone (Medtronic, USA) cage were performed similarly to the Group I. Later, a 4-screw open transpedicular stabilization was performed using Konmet system (Russia) (Fig. 2).

In the postoperative period, the following main indicators were monitored: clinical (level of pain in the lumbar spine and lower extremities was assessed by visual analogue scale (VAS), functional status by ODI, patient’s satisfaction with the surgery by Macnab scale) at discharge and in the late postoperative period; instrumental (formation of the bone block in the late postoperative period using functional spondylography and MSCT was assessed by a radiologist and an independent neurosurgeon; complete spinal fusion was confirmed in case of the presence of bone bridges and a segmental movement of less than 3° [16]); the degree of atrophy of the multifidus muscle was assessed by the change in its area on an axial MRI before and after the surgery [17]).

In addition, the following secondary parameters were evaluated: size of the skin incision, duration of the surgery, volume of blood loss during and after the surgery, duration of irradiation (intraoperatively); duration of hospitalization, time to activation, complications (in the postoperative period).

Statistical data processing was performed using Statistica for Windows software, version 6.0. Descriptive statistics are presented as median (Me) and interquartile range (25%; 75%). The level of significance was \( p < 0.05 \). To compare the obtained values, we used the Mann–Whitney U-test and the Wilcoxon test for non-parametric data, and the \( \chi^2 \) test for categorical variables.
Results

Summary data on patients in the study groups are presented in Table 1. There were no inter-group differences ($p>0.05$) in respect to the main criteria: gender, age, BMI, comorbidities. The rate of patients with obesity was 44% in Group I and 46% in Group II. All patients had preoperative neurological manifestations associated with spinal stenosis, spondylolisthesis and hernias of the IVD with segmental instability. Most often the pathological process was localized in the lower lumbar segments (over 85%). The mean follow-up period was 34 months in group I and 40 months in group II.

Description of intraoperative and postoperative indicators is presented in Table 2. There were no conversions of a minimally invasive surgery to an open one. The analysis revealed that the total skin incision in Group I was significantly smaller than in Group II ($p=0.003$). Group I also has shorter duration of the surgery and smaller amount of intra- and postoperative blood loss ($p<0.05$). When performing surgical approach, a significant size of paravertebral tissues was observed (median depth of more than 140 mm) in patients of both groups without a statistically significant differences ($p=0.47$). The duration of intraoperative irradiation in both groups was comparable and was achieved in patients operated on using MIS-technologies through simultaneous installation of screw structures ($p=0.16$). The patients in Group I became active faster and the total duration of hospital stay was shorter compared to Group II ($p<0.05$).

The analysis revealed changes in pain syndrome and positive dynamics was observed in both study groups. There were no differences in pain in the lumbar spine and lower extremities in the preoperative period according to VAS ($p>0.05$) (Figs. 3, 4). At discharge and in the late postoperative period (median follow-up of 34 months for Group I and 40 months for Group II), Group I reported significantly less pronounced pain in the lumbar region ($p<0.05$) and in the lower extremities ($p<0.05$), which was attributed to smaller injury to the soft tissues during surgical access.

Comparative assessment of the performance status using ODI (Fig. 5) revealed similar preoperative values in both study groups ($p>0.05$).

At discharge and in the late postoperative period (mean follow-up of 34 months for Group I and 40 months for Group II), significantly better ODI ($p<0.05$) scores were reported for Group I, which may be attributed to smaller injury to the musculo-ligamentous complex and lower rate of development of cicatricial intracranial changes.

The analysis of long-term outcomes of the treatment using the subjective Macnab satisfaction assessment scale, excellent and good results were reported in Group I in 11 (34%) and 17 (53%) cases, respectively, in Group II excellent and good results were reported in 29 (71%) and 13 (29%) cases, respectively; there were no unsatisfactory outcomes.

Postoperative complications amounted to 9% in Group I and 17% in Group II ($p=0.01$) (Table 3). Most of the reported complications did not have a significant effect on recovery of the patients. A prolonged course of antibiotic was prescribed in the event of infection in the area of the surgery, intermuscular hematoma was treated by drainage, damage to dura mater was sutured with 6-0 prolen with additional application of fibrin glue to ensure reliable sealing, without liquororrhea in the postoperative period. In case of diagnosed deep vein thrombosis, anticoagulant therapy and physiotherapy treatment were conducted with mandatory dynamic ultrasound control to prevent thromboembolic complications. In case of clinically significant disease of the adjacent segment and pseudoarthrosis and the ineffectiveness of con-
servative treatment, repeated decompressive-stabilizing interventions were performed.

The follow-up observation using functional spondylograms and MSCT did not identify dislocation and migration of implants in patients of both groups. Full spinal fusion in the late postoperative period was observed in 88% of patients in the Group I and in 83% in Group II (p=0.15).

Assessment of the area of the multifidus muscle using MRI of the lumbar spine (Figs. 6, 7) before the surgery and in the late postoperative period (average follow-up of 34 months for Group I and 40 months for Group II) revealed significant muscular atrophy in Group II: from 6.3 (5.4; 7.2) to 3.1 (2.3; 3.9) cm² (on average over 50%), while in Group I it changed from 7.1 (6.1; 8.0) to 6.6 (5.8; 7.3) cm² (on average no more than 20%). Clinically significant degeneration at the level adjacent to the operated one was identified in 1 (3%) patient of Group I and in 2 (5%) patients of Group II.

Discussion

The widely used surgical techniques of minimally invasive and open transforaminal interbody fusion with rigid stabilization have ambiguous long-term functional outcomes [12, 18—21]. A number of studies have established high efficiency of MIS techniques in spinal surgery [16, 22]. However, there are also published work with comparable radiological [23] and clinical [24] outcomes of minimally invasive and open dorsal rigid stabilizations.

The development of tubular retractor systems allowed to reduce the degree of injury to the paravertebral tissues [13, 20]. The main goals of minimally invasive interventions are to minimize injury to the paravertebral tissues, reduce the risks of perioperative complications and shorten the duration of inpatient treatment [12, 25—27]. Currently, the issue of achieving the above outcomes in patients with obesity remains open, since a deep anatomical corridor, longer duration of surgery and higher risks of adverse consequences (infection of a postoperative wound, thromboembolic complications) contribute to a decrease in the performance status of patients in the late postoperative period [28—31]. For example, some authors [32] indicate a greater number of unsatisfactory clinical outcomes in patients with obesity when performing spinal interventions, others [12, 30, 33, 34]

Table 1. Summary of baseline characteristics of patients in the study groups

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Group I (n=32)</th>
<th>Group II (n=41)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, year (Me (25%; 75%))</td>
<td>52 (43; 64)</td>
<td>49.5 (41; 62)</td>
<td>0.52</td>
</tr>
<tr>
<td>Male, abs., %</td>
<td>21 (66%)</td>
<td>28 (68%)</td>
<td>0.34</td>
</tr>
<tr>
<td>Body Mass Index, kg/m² (Me — 25%; 75%)</td>
<td>30.5 (28.7; 31.3)</td>
<td>29.5 (28.2; 31.5)</td>
<td>0.26</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25‒30</td>
<td>18 (56)</td>
<td>22 (54)</td>
<td>0.18</td>
</tr>
<tr>
<td>&gt;30</td>
<td>14 (44)</td>
<td>19 (46)</td>
<td></td>
</tr>
<tr>
<td>Preoperative diagnosis, abs., %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>spinal canal stenosis</td>
<td>11 (34)</td>
<td>15 (36)</td>
<td></td>
</tr>
<tr>
<td>spondylolisthesis</td>
<td>16 (50)</td>
<td>23 (56)</td>
<td>0.41</td>
</tr>
<tr>
<td>IVD hernia, instability</td>
<td>5 (16)</td>
<td>3 (8)</td>
<td></td>
</tr>
<tr>
<td>Level of surgical intervention, abs.,%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LIII—LIV</td>
<td>4 (12)</td>
<td>6 (15)</td>
<td>0.78</td>
</tr>
<tr>
<td>LIV—LV</td>
<td>13 (41)</td>
<td>17 (41)</td>
<td></td>
</tr>
<tr>
<td>LV—SI</td>
<td>15 (47)</td>
<td>18 (44)</td>
<td></td>
</tr>
<tr>
<td>Concomitant pathology, abs.,%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>diabetes mellitus</td>
<td>4 (12)</td>
<td>5 (12)</td>
<td>0.94</td>
</tr>
<tr>
<td>arterial hypertension</td>
<td>8 (25)</td>
<td>6 (15)</td>
<td>0.18</td>
</tr>
<tr>
<td>kidney disease</td>
<td>3 (9)</td>
<td>3 (7)</td>
<td>0.87</td>
</tr>
<tr>
<td>smoking</td>
<td>9 (28)</td>
<td>8 (20)</td>
<td>0.11</td>
</tr>
<tr>
<td>Follow-up period, Me (min—max)</td>
<td>34 (12—48)</td>
<td>40 (15;50)</td>
<td>0.66</td>
</tr>
</tbody>
</table>
Table 2. Comparative assessment of the parameters in the intraoperative and postoperative periods

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Group I (n=32)</th>
<th>Group II (n=41)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total skin incision, mm</td>
<td>56 (48; 60)</td>
<td>90 (84; 102)</td>
<td>0.003</td>
</tr>
<tr>
<td>Duration of the surgery, min</td>
<td>105 (95; 120)</td>
<td>145 (130; 165)</td>
<td>0.02</td>
</tr>
<tr>
<td>Intraoperative blood loss, ml</td>
<td>130 (90; 150)</td>
<td>490 (380; 610)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Post-operative blood loss, ml</td>
<td>45 (20; 60)</td>
<td>180 (150; 240)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of irradiation, s</td>
<td>30 (25; 42)</td>
<td>27 (23; 39)</td>
<td>0.16</td>
</tr>
<tr>
<td>Size of paravertebral tissues for surgical approach (wound depth), mm</td>
<td>145 (126; 169)</td>
<td>141 (119; 163)</td>
<td>0.47</td>
</tr>
<tr>
<td>Time to activation, days</td>
<td>1 (1; 2)</td>
<td>3 (2; 4)</td>
<td>0.01</td>
</tr>
<tr>
<td>Duration of hospitalization, days</td>
<td>9 (8; 10)</td>
<td>13 (11; 14)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Table 3. Characterization of complications in patients of the study groups

<table>
<thead>
<tr>
<th>Type of complication</th>
<th>Group I (n=32)</th>
<th>Group II (n=41)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number</td>
<td>3 (9)</td>
<td>7 (17)</td>
<td>0.01</td>
</tr>
<tr>
<td>Infection in the field of surgical intervention, abs.,%</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Intermuscular hematoma, abs.,%</td>
<td>—</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Damage to dural matter of the dural bag/root, abs.,% (n/N)</td>
<td>—</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolism, abs.,%</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Deep vein thrombosis, abs.,%</td>
<td>—</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Disease of the adjacent segment, abs.,%</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pseudarthrosis, abs.,%</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 3. The dynamics of pain syndrome in the lumbar spine in patients of the study groups according to VAS.
Fig. 4. The dynamics of pain syndrome in the lower extremities in patients of the study groups according to VAS.

Fig. 5. The dynamics of functional state in patients of the study groups according to ODI.
Fig. 6. Clinical case: Patient Y., 33 years old, Group I (reconstruction of the spinal canal using the original technique on the left, transforaminal interbody fusion LV — SI, ipsilateral open and contralateral transcutaneous transpedicular stabilization).

a — postoperative spondylogram in direct projection; b, c — preoperative axial MRI and calculation technique (area (S) of the multifidus muscle on the right is 8.42 cm², on the left, 82 cm²); d, e — postoperative axial MRI and counting technique (area (S) of the multifidus muscle on the right is 7.51 cm², atrophy is 11%, on the left, 7.14 cm², atrophy is 19%).
Fig. 7. Clinical case: Patient B., 41 years old, Group II (reconstruction of the spinal canal to the right from the median approach, transformaminal interbody fusion LV — SI, open transpedicular stabilization).

- a — postoperative spondylogram in direct projection;
- b, c — preoperative axial MRI and calculation technique (area ($S$) of the multifidus muscle on the right is 6.22 cm², on the left 5.94 cm²);
- d, e — postoperative axial MRI and counting technique (area ($S$) of the multifidus muscle on the right is 2.31 cm², atrophy 63%, on the left 2.28 cm², atrophy 61%).
indicate comparable outcomes of minimally invasive and open surgical techniques in respect to performance status, and the third group [11] identified the advantage of MIS-techniques over traditional methods in reducing blood loss, duration of surgery and irradiation. Some authors [14, 16, 35] point to longer duration of EOP navigation, however in our series we used simultaneous installation of the transpedicular stabilization, which allowed us to use of intraoperative fluoroscopy for the optimal period of time.

Most researchers tend to believe that the outcomes of MIS-TLIF and O-TLIF are comparable. For example, M. Djurasovic et al. [36] noted comparable improvement in performance status in the minimal postoperative period of 2 years (an average of 15 points for ODI). J. Wang et al. [14] found lower level of pain using VAS scale during the first 2 days after the surgery in the MIS-TLIF group, but the results on VAS and ODI scales were comparable in the 3-year follow-up period. When conducting randomized studies J. Wang et al. [37] indicate better performance status on ODI scale in the first 6 months of the postoperative period; there were no statistically significant differences on VAS. In a study by F. Shunwu et al. [38], a comparative analysis revealed better outcomes in the group of minimally invasive spinal fusion in terms of pain syndrome, performance status, and duration of hospital stay and intraoperative fluoroscopy. At the same time, according to N. Tian et al. [24], O-TLIF has advantage over MIS-TLIF in terms of duration of X-ray radiation (on average by 41 s), and minimally invasive interventions are better than traditional ones in terms of blood loss (less by 219 ml) and duration of hospital stay (shorter by 2.7 days).

A number of studies [7, 8] confirm more significant risks of development of postoperative complications in overweight patients when performing traditional rigid stabilization. The frequency of detection of postoperative complications in obese patients is higher than in patients with normal BMI [39]. P. Park et al. [13] did not found any relationships in development of complications in overweight patients who underwent minimally invasive decompression-stabilizing interventions. Some authors [11, 12] point to the comparability of the risks of postoperative complications (the frequency of damage to the spinal roots, repeated surgeries, degeneration of the adjacent segment) in overweight patients after MIS-TLIF and O-TLIF.

The lack of consensus about the benefits of minimally invasive surgical techniques over open traditional ones is due to the fact that most studies lack clear patient selection criteria and the presence of large number of anatomical, instrumental and technical factors that influence the long-term clinical and functional outcomes. In addition, the absolute advantage of using MIS techniques is associated with the ability to perform both radical decompression and stabilization without increasing the incision length and preventing significant injury to the paravertebral muscles.

The present study established the advantages of the original minimally invasive surgical intervention over the traditional one in terms of intraoperative indicators (length of surgical incision, duration of surgery, volume of blood loss, duration of X-ray irradiation) and the postoperative period specificity (time to activation, duration of hospital stay, number of complications). In addition, persistent positive clinical and functional outcome has been achieved in the late postoperative period, which was significantly better in the group operated on using the author’s rigid stabilization technique; its minimally invasive effect was confirmed by less pronounced atrophy of the paravertebral muscles.

**Conclusion**

The original technique of minimally invasive rigid stabilization is safe and highly effective in the treatment of degenerative diseases of the lumbar segments in overweight and obese patients. MIS-TLIF has some significant advantages over O-TLIF in the dynamics of clinical parameters and low rate of perioperative complications, as evidenced by smaller injury to the paravertebral tissues and the better performance status in the late postoperative period.

Authors declare no conflict of interest.
Commentary

The paper describes a generally accepted algorithm for choosing a method for decompressive-stabilizing operations in patients with degenerative stenoses of the lumbosacral level. The authors analyze the outcomes of surgical treatment of patients with obesity, comparing the methods of open and minimally invasive surgeries. The article proves the advantage of minimally invasive access in overweight patients. Of course, the differences between open and minimally invasive accesses will be more pronounced due to the less traumatic penetration through soft tissues in the second case. In general, the novelty of the research is questionable, given the generally accepted status of the minimally invasive approach, which is designated in the article as the original technique. The article may be useful for practicing surgeons, given the prevalence of overweight people in the national population of patients.

A.O. Guscha (Moscow, Russia)
Delayed facial palsy is a complication developing 3 or more days after surgery. The etiology and pathogenesis of this condition has not been fully explored, and there are no treatment standards for it. As in the case of Bell's paralysis, glucocorticosteroids (GCSs) are currently used to treat delayed facial palsy. However, patients with contraindications to GCSs need new therapy modalities.

**Aim** — we aimed to evaluate the efficacy and safety of botulinum therapy in patients with delayed facial palsy after neurosurgical interventions.

**Material and methods.** We examined 33 patients with delayed facial palsy who developed 3 or more days after resection of vestibular schwannoma. The main group included 18 patients with contraindications to GCSs who received injections of botulinum toxin A (BTA) into the facial muscles of the healthy side for muscle relaxation. The comparison group consisted of 15 patients who received a course of prednisolone (1 mg/kg/day) for 5—7 days. The efficacy of treatment was assessed using the House—Brackmann scale and Clinical Global Impression Scale. The follow-up period after therapy was 3 months.

**Results.** Delayed facial palsy was more common in the following cases: the facial nerve was located near the antero-inferior tumor pole; the tumor was adherent to the facial nerve; the tumor extended in the oral direction; the tumor had unclear borders and was 11 to 30 mm in size. In most patients of both groups, facial muscle palsy developed more than 11 days after surgery. Treatment both in the main and control groups resulted in a significant improvement: complete regression of the facial asymmetry in patients of the main group and comparison groups 3 months after treatment onset was 83.3 and 93.3% (House—Brackmann scale), respectively.

**Conclusion.** Botulinum therapy may be recommended for patients with delayed facial palsy developed after vestibular schwannoma resection, who have contraindications to GCSs.

**Keywords:** vestibular schwannoma, delayed facial palsy, botulinum toxin A.
that among these patients there were no cases of neuropathy developing after 48 hours, and that in all patients delayed facial palsy occurred 3 days or more after the resection of vestibular schwannomas. The age of patients ranged from 32 years to 61 years (mean age 45.31±6.82 years). The main group included: 18 patients: 10 (55.6%) men and 8 (44.4%) women; the control group consisted of 15 patients: 8 (53.3%) men and 7 (46.7%) women.

Patients in the main group did not receive GCS therapy because they had gastric ulcer and duodenal ulcer (n=3; 16.7%), severe chronic heart failure (n=5; 27.8%), type 2 diabetes mellitus (n=4; 22.2%) and arterial hypertension of III degree (n=8; 44.4%). They received injections of BTA (Incobotulotoxin A) in the face muscles on a healthy side with the aim of reducing the increased muscle tone, which defines the degree of pulling of the mimic muscles towards the healthy side, and thus restoring the relative symmetry of the face. The following facial muscles were injected successively: m. frontalis (4 points 3 units each), m. corrugator supercilii (2 points 2 and 4 units), m. levator labii superior alaeque nasi (1 point 2 units), m. zygomaticus minor and major (1 point 2 units each), m. levator labii superior (1 point 2 units), m. levator anguli oris (1 point 2 units), m. orbicularis oris (2 points above the upper lip 1 unit each), m. depressor labii inferior (2 points 1—2 units each ), m. nasalis (1 point 3 units), m. buccinator (2 points 2—3 units), m. mentalis (1 point 2 units), m. platysma (4 points 4—5 units each) (Fig. 1). The total dose of BTA was 40—50 units, the number of injection points varied from 10 to 15.

Patients in the comparison group received a course of prednisone 1 mg/kg/day for 5—7 days, followed by rapid withdrawal within 3—4 days.

W. Koos et al. classification scheme of 1976 [13] was used to classify the tumor sizes.

The efficacy of treatment was evaluated clinically; the severity of the facial nerve dysfunction was evaluated according to the House—Brackmann scale (1 point - normal; 2 points - mild dysfunction; 3 points - moderate dysfunction; 4 points - moderately severe dysfunction; 5 points - severe dysfunction). After 3 months, patients self-completed the Clinical Global Impression Scale.

Statistical processing of the results was carried out using Microsoft Excel and the statistical software Biostat (Praktika Publishing House, 2006), SPSS 15.0 and Statistica 8.0 for Windows (StatSoft Inc., USA). Differences were considered statistically significant at an error level of p<0.05.

Results

When analyzing the topographic-anatomical features of the tumor and its size in patients with delayed facial palsy, it was found that in 20 (60.6%) patients the tumor sizes were within 15—30 mm, while sizes<15 mm and >30 mm were observed less frequently: in 12 (36.4%) and 1 (3.0%) patients, respectively. In 26 (78.8%) patients, the facial nerve was located along the anterior lower pole of the tumor and in 24 (72.7%) patients it was fused to the tumor, and in 14 (42.4%) patients the nerve could not be visually identified due to its significant thinning or stretching. A total of 21 (63.6%) patients had predominantly oral spread of the tumor; the boundaries between it and the soft shell were fuzzy in most cases (in 24 (72.7%) patients). Radical removal of the tumor was performed in 17 (51.5%) patients. This was accompanied by more active surgical manipulations in the area of the facial nerve and, therefore, greater trauma. There were no differences in topographic-anatomical features between the main group and the control group (Table 2).

Delayed facial palsy most often developed after 11 days or more after the surgery (n=15; 45.5%), less often, on Day 6—10 (n=11; 33.3%) and on Day 3—5 (n=7; 21.2%). There were no differences between the groups in terms of the time to onset of delayed palsy (Table 3).

Prior to the start of the treatment, 17 (51.5%) patients scored 2 points for the facial nerve damage, 11 (33.3%) scored 3 points and 5 (15.2%) scored 4 points on the House—Brackmann scale. Three months after the treatment, positive dynamics was observed in both groups: the complete regression of the face asymmetry was observed

| Table 1. The prevalence of delayed facial palsy based on the literature data |
| Author, year | Prevalence, % | The severity of the facial nerve dysfunction |
| M. Arriaga, 1993 [8] | 13.0 | Deterioration of the facial nerve function from acceptable (I—IV degree on a House—Brackmann scale) to unsatisfactory (V—VI degree) |
| G. Gianoli, 1996 [9] | 15.0 | Any degree of deterioration of the facial nerve function relatively to the initially normal one |
| A. Mandpe, 1998 [10] | 20.0 | The deterioration of the facial nerve function by one degree according to the House—Brackmann scale starting from 1 day after the surgery to the time of discharge from the hospital |
| R. Morton, 2011 [4] | 25.0 | Deterioration of the facial nerve function in the period from 1 to 30 days compared to the initially normal one before the surgery and after the surgery, |
| P. Kunert, 2015 [11] | 5.0 | Impairment of the facial nerve function according to the House—Brackmann scale up to grade I—IV three days after the surgery, |
| L. Carlström, 2016 [3] | 16.3 | Impairment of the facial nerve function by at least 2 degrees on the House—Brackmann scale in the period from 5 to 15 days after surgery |
in the majority of patients in both the main and control groups ($n=29; 87.9\%$) (Table 4).

Recovery of the facial muscles function was observed within the first month of therapy, starting from 8–12 days, in all patients with a predominant lesion of the upper half of the face (5 (27.8\%) in the main group and 4 (26.7\%) in the control group).

Patients in both groups were satisfied with the results of the treatment, most of them noted a pronounced improvement in the facial muscles function. Only 1 patient in the main group reported only slight improvement in mimic muscles, which after 3 months of treatment had changed to moderate from the initially moderately severe degree of facial nerve dysfunction (Fig. 2).

**Discussion**

Delayed facial palsy is a complication after the resection of posterior cranial fossa tumors and the risk of its development is higher in patients with a large tumor volume. This is confirmed by the results of the study: 97.0\% of patients in our group had the tumor size corresponding to grade II–III on the Koos scale.

In contrast to the idiopathic lesion of the facial nerve (Bell’s palsy), whose main pathogenesis mechanisms involve infectious-inflammatory, ischemic and compression-ischemic factors, the pathophysiology of delayed facial palsy in the postoperative period remains unclear. It is assumed that the facial nerve dysfunction is a result of a combination of several factors: perineural edema, vascular spasm and activation of viral infection [14—16]. Among them, vascular spasm and local perineural edema, developing during the first few days after the intervention, are the most likely causes of these disorders. It should be noted that the severity of symptoms in delayed postoperative facial palsy is significantly greater than in idiopathic neuritis, due to the close anatomical interaction of the acoustic-facial nerve group, the mass lesion and, as a result, the operative trauma during the tumor removal [17].

There is also evidence of elevated antibody titer to Herpes simplex viruses of the 1\textsuperscript{st} and 2\textsuperscript{nd} types, as well as to the Herpes zoster virus after the surgery in this category of patients [9, 15]. Currently, the algorithms of preoperative preparation of patients for surgical intervention do not include routine prevention of activation of a viral infection.

The evidence that the features of the surgical approaches used to remove the vestibular schwannoma are a risk factor for the development of delayed facial palsy are contradictory. For example, several small studies failed to establish a correlation between different types of surgical approaches and the occurrence of delayed palsy [4, 18]. A number of other studies [3, 19] demonstrated an increase in the risk of the facial nerve dysfunction by a factor of 3 when using retrosigmoid access to a tumor. It has also been suggested that the dispersion of bone dust due to insufficient irrigation when grinding the pyramid of the temporal bone and the internal auditory canal during translabyrinthal and retrosigmoid access can lead to excessive local inflammatory reaction and, as a consequence, delayed facial palsy [20]. It is assumed that the greater is the extent of decompression of the facial nerve during transamineral access, the lower is the potential for development of postoperative nerve edema. However, the available data are rarely taken into account when choosing a surgical access, since it is assumed that in almost 100\% of cases the function of the facial nerve is restored to I–II degree according to the House — Brackmann scale [5].

Additional risk factors for the development of delayed facial palsy include neuropathy with early onset (within the first 48 hours after the surgery), a large tumor (stage III — IV by Koos), nerve localization in relation to the tumor, and tumor structure. It is likely that larger amount of resection provokes a more pronounced swelling of the surrounding tissue and also increases the likelihood of activating a viral infection in the postoperative period [14].

There are studies [21—23] analyzing the outcomes in respect to the facial nerve function, depending on the topography of the neuroma. For example, V.N. Shimansky et al. [21] when analyzing the operations performed on 186 patients with vestibular schwannomas, found that the
incidence and severity of the facial nerve lesion in the early and delayed postoperative period increase with increasing size of the extracanal part of the tumor. In case of the oral direction of neuroma growth, the outcomes in relation to the facial nerve function in the early postoperative and delayed periods were significantly worse than in case of the caudal direction of tumor growth. In our study, patients with delayed facial palsy had predominantly oral direction of tumor growth.

In 2016 a group of Italian neurosurgeons presented a paper that analyzed the correlation between the postoperative function of the facial nerve and the location of the nerve relative to the tumor in 100 patients operated on for vestibular schwannomas. Four options for the localization of the facial nerve on the capsule of the tumor were identified: in the anterior, anterior superior, anterior inferior and posterior poles of the tumor. Functional outcomes were better in patients with anterior superior and anterior inferior facial nerve localization. The authors also indicate that in case of tumors that were larger than 3 cm, a significant spreading of the nerve along the tumor capsule and its stretching was observed intraoperatively, and, therefore, in these cases, the facial nerve dysfunction was observed more frequently in the postoperative period [22], which was also confirmed by the results of the study.

In addition to studies that analyze the functional state of the facial nerve depending on the size of the tumor and its topography, there are studies indicating an increased risk of injury to the facial nerve in case of cystic structure of the neuroma [23—26]. The authors report that the main problem and cause of facial nerve injury is the absence of the arachnoid plane of the dissection when it is separated from the capsule of cystic neuroma due to pronounced adhesions [24].

With timely treatment, the prognosis of the restoration of the function of the facial nerve in case of delayed palsy is favorable. Usually there is a complete or almost complete functional recovery within 1—2 months after the onset of a lesion with promptly initiated treatment. The data obtained in the study is consistent with the data of international literature [25]: most patients showed complete recovery of the lost functions.

Table 2. Topographic anatomical features of the facial nerve course and tumor sizes

<table>
<thead>
<tr>
<th>Topographic anatomical feature</th>
<th>Main Group (n=18), %</th>
<th>Control Group (n=15), %</th>
<th>Total (n=33), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>The location of the nerve in the anterior lower pole of the tumor</td>
<td>14 (77.8)</td>
<td>11 (73.3)</td>
<td>26 (78.8)</td>
</tr>
<tr>
<td>Impossibility of visual identification of the nerve</td>
<td>8 (44.4)</td>
<td>6 (40.0)</td>
<td>14 (42.4)</td>
</tr>
<tr>
<td>The fusion of the tumor with the facial nerve</td>
<td>13 (72.2)</td>
<td>11 (73.3)</td>
<td>24 (72.7)</td>
</tr>
<tr>
<td>Oral tumor spread relative to the normal axis of the facial nerve</td>
<td>11 (61.1)</td>
<td>10 (66.7)</td>
<td>21 (63.6)</td>
</tr>
<tr>
<td>Arachnoid dissection plane fuzzy or absent</td>
<td>13 (72.2)</td>
<td>11 (73.3)</td>
<td>24 (72.7)</td>
</tr>
<tr>
<td>Radical tumor removal</td>
<td>9 (50.0)</td>
<td>8 (53.3)</td>
<td>17 (51.5)</td>
</tr>
<tr>
<td>Tumor size, mm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11—20 (Koos II)</td>
<td>6 (33.3)</td>
<td>6 (40.0)</td>
<td>12 (36.4)</td>
</tr>
<tr>
<td>21—30 (Koos III)</td>
<td>11 (61.1)</td>
<td>9 (60.0)</td>
<td>20 (60.6)</td>
</tr>
<tr>
<td>&gt;30 (Koos IV)</td>
<td>1 (5.6)</td>
<td>—</td>
<td>1 (3.0)</td>
</tr>
</tbody>
</table>

Table 3. The time to onset of delayed facial palsy after surgery

<table>
<thead>
<tr>
<th>Time, days</th>
<th>Main Group (n=18), %</th>
<th>Control Group (n=15), %</th>
<th>Total (n=33), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>3—5</td>
<td>4 (22.3)</td>
<td>3 (20.0)</td>
<td>7 (21.2)</td>
</tr>
<tr>
<td>6—10</td>
<td>6 (33.3)</td>
<td>5 (33.3)</td>
<td>11 (33.3)</td>
</tr>
<tr>
<td>&gt;11</td>
<td>8 (44.4)</td>
<td>7 (46.7)</td>
<td>15 (45.5)</td>
</tr>
</tbody>
</table>

Table 4. The dynamics of the degree of face asymmetry using the House — Brackmann scale

<table>
<thead>
<tr>
<th>House—Brackmann score</th>
<th>Prior to the treatment</th>
<th>1 month after the treatment</th>
<th>3 months after the treatment</th>
<th>Prior to the treatment</th>
<th>1 month after the treatment</th>
<th>3 months after the treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>—</td>
<td>12 (66.7)</td>
<td>15 (83.3)</td>
<td>—</td>
<td>9 (60.0)</td>
<td>14 (93.3)</td>
</tr>
<tr>
<td>2</td>
<td>9 (50.0)</td>
<td>5 (27.8)</td>
<td>2 (11.1)</td>
<td>8 (53.3)</td>
<td>5 (33.3)</td>
<td>1 (6.7)</td>
</tr>
<tr>
<td>3</td>
<td>6 (33.3)</td>
<td>1 (5.5)</td>
<td>1 (5.6)</td>
<td>5 (33.3)</td>
<td>1 (6.7)</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>3 (16.7)</td>
<td>—</td>
<td>—</td>
<td>2 (13.4)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Median score</td>
<td>3.34±1.18</td>
<td>1.19±0.73*</td>
<td>1.06±0.57**</td>
<td>3.29±1.39</td>
<td>1.35±1.04*</td>
<td>1.13±0.42**</td>
</tr>
</tbody>
</table>

Footnote. * — p<0.05 — significant differences in the degree on the House—Brackmann scale before the treatment and 1 month after the start of the treatment; ** — p<0.05 — significant differences in the degree on the House—Brackmann scale before the treatment and 3 months after the start of the treatment.
The use of GCS therapy in facial palsy, which developed as a result of the removal of the vestibular schwannoma, is justified as anti-inflammatory therapy, but in many patients the use of this type of treatment is limited or impossible due to the large number of adverse events, especially in patients with contraindications due to comorbidities.

Botulinum therapy is an effective method for correcting the functions of the facial muscles and has been successfully used for facial nerve neuropathy of various etiologies [2, 26]. Based on the results of studies conducted by us earlier which involved patients with acute neuropathy, we suggested that BTA injections into the muscles of the relatively healthy side will also be effective in these patients. The effect is based on the prolonged relaxation of the facial muscles due to the weakening of the antagonistic action of the healthy side muscles, which reduces the over-stretching and traumatic effect on the paretic muscles of the affected side [27]. This proves that not only tone-less denervated muscles of the affected side, but also functionally hyperactive mimic muscles of the healthy side are involved in the development of the asymmetry.

The results of the study demonstrated the effectiveness of the administration of BTA, which manifested as reduced asymmetry of the face, ensuring better interaction between the affected and relatively healthy parts. In terms of outcomes, treatment with BTA is comparable to treatment with glucocorticosteroids.

Conclusions

The results of the study demonstrated for the first time that BTA injections are an effective and safe method of treating patients with delayed facial palsy, which arose after the removal of the vestibular schwannoma. BTA injections can be recommended for the treatment of patients with delayed facial palsy in order to reduce facial asymmetry and functional recovery if standard therapy is limited or contraindicated.

Authors declare no conflict of interest.

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The authors demonstrated that botulinum therapy is effective in better recovery of the facial muscles function. Glucocorticosteroids do not affect the facial symmetry, an important consideration, etc.). In addition, treatment with glucocorticosteroids has a large number of contraindications, which limits the use of the drugs (gastric ulcer and duodenal ulcer, severe ischemic heart disease, diabetes, hypertension, etc.). The data obtained in the course of the study can be successfully used to further study these undoubtedly complex and relevant scientific issues.

The work was done at a high scientific level, the material is well illustrated by figures and tables, which greatly facilitates the perception and understanding of the significance of the results obtained by the authors.

The article "The Efficacy of Botulinum Therapy in Treatment of Delayed Facial Palsy after Resection of Vestibular Schwannoma" is a completed scientific work.

A.I. Nerobeev (Moscow, Russia)
Technical Features and Complications of Cranioplasty in Patients after Decompressive Craniectomy in the Acute Period of Subarachnoid Hemorrhage

AN.N. KONOVALOV, YU.V. PILIPENKO, SH.SH. ELIAVA

Burdenko Neurosurgical Institute, Moscow, Russia

Decompressive craniectomy (DC) is used for arresting hypertension-dislocation syndrome developing in severe patients in the acute period of subarachnoid hemorrhage [1, 2]. After stabilization of the patient’s neurological and somatic status, cranioplasty is performed for protective, cosmetic, and therapeutic purposes.

The most common surgery in these patients is skull repair using an autologous bone graft. Before cranioplasty, the patient’s bone is preserved in two ways: cryopreservation or subcutaneous implantation to the anterior abdominal wall area. Recently, there have been numerous reports of early and delayed complications of cranioplasty with autologous bone grafts. The use of artificial grafts may reduce the risk of postoperative complications compared to an autologous bone graft. Previously, «freely» or «manually» simulated biopolymers were used. At present, they are rarely used for repair of extensive defects due to a poor cosmetic result. However, the advent of stereolithographic modeling and computer modeling of artificial grafts has improved the cosmetic result of this surgery.

The purpose of this study is to assess the risk of postoperative complications of cranioplasty as well as to define the criteria for choosing a cranioplasty technique.

Keywords: SAH, decompressive craniectomy, cranioplasty.

Materials and methods

The retrospective study included 61 patients who underwent preventive or delayed DC following microsurgical exclusion of the aneurysm in the acute period of aneurysmal SAH in the period from 2010 to 2016. Cranioplasty was performed in all patients after stabilization. The exclusion criteria were infancy, DC performed at another hospital, and bilateral DC. Gender, age, severity of the patient at the time of the primary surgery and during cranioplasty, graft fragmentation during primary surgery, duration of cranioplasty, material for cranioplasty, the frequency rate of ventriculoperitoneal shunting (VPS), complications and interventions after cranioplasty, and duration of the follow-up period were considered in the study.

Sample features

The sample included 61 patients (21 males and 26 females; mean age, 45.2±9.4 years). All patients underwent cranioplasty with autologous or artificial grafts after DC. Cranioplasty was performed in combination with VPS in 8 cases. A total of 36 (60%) patients were followed up in the period ranging from 6 months to 7 years (mean follow-up period, 3.6±1.8 years). Patient data are presented in Table 1.

*Method of patient’s bone preservation
Surgically isolated skull fragment was cleaned from blood, soft tissues and bone chips under sterile conditions, covered by dry sterile surgical material and stored in the freezer at a temperature of −10 to −30 °C. Prior to cranioplasty, the autologous graft was removed from the freezer, thawed and sterilized. Sterilization of models is

Abbreviations:

VPS — ventriculoperitoneal shunting
DC — decompressive craniectomy
CT — computed tomography
MSCT — multispiral computed tomography
SAH — subarachnoid hemorrhage
DM — dura mater

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Table 1. Characteristics of the studied group of patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Autogenous bone graft</th>
<th>Artificial bone graft</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients</td>
<td>47</td>
<td>14</td>
</tr>
<tr>
<td>Mean age, years</td>
<td>46.2±9.4</td>
<td>42.1±9.6</td>
</tr>
<tr>
<td>Male/female ratio</td>
<td>21:26</td>
<td>4:10</td>
</tr>
<tr>
<td>Duration, months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1—3</td>
<td>30 (65)</td>
<td>8 (57)</td>
</tr>
<tr>
<td>4—6 months</td>
<td>14 (30)</td>
<td>3 (21.5)</td>
</tr>
<tr>
<td>more than 6 months</td>
<td>2 (45)</td>
<td>3 (21.5)</td>
</tr>
<tr>
<td>Fragmented bone graft, abs. (%)</td>
<td>12 (25.5)</td>
<td>—</td>
</tr>
<tr>
<td>VPS, abs. (%)</td>
<td>6 (12.7)</td>
<td>2 (14)</td>
</tr>
<tr>
<td>Average follow-up period</td>
<td>4.2±1.85</td>
<td>2.3±1.86</td>
</tr>
</tbody>
</table>

Table 2. The incidence of complications after cranioplasty

<table>
<thead>
<tr>
<th>Type of graft — Number of patients</th>
<th>Graft autolysis, abs. (%)</th>
<th>Infectious Complications (fistulas, osteomyelitis), abs (%)</th>
<th>Epilepsy syndrome, abs (%)</th>
<th>Frontal sinus defect pneumocephalus, abs (%)</th>
<th>Total, abs (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autogenous bone graft — 47</td>
<td>7 (14.8)</td>
<td>6 (12.7)</td>
<td>2 (4.2)</td>
<td>1 (2.1)</td>
<td>16 (34)</td>
</tr>
<tr>
<td>Artificial bone graft — 14</td>
<td>0</td>
<td>0</td>
<td>3 (21.4)</td>
<td>1 (7.1)</td>
<td>4 (28.5)</td>
</tr>
</tbody>
</table>

Fig. 1. Cranioplasty using stereolithographic model of bone cement graft (Palacos)

a, b — prior to cranioplasty; c, d — after cranioplasty.
carried out by the gas method (using ethylene oxide) [13]. The method of subcutaneous implantation to the anterior abdominal wall area is not used at Burdenko Neurosurgical Institute.

**The method of cranioplasty**

The incision is made in the area of an old scar. Aponurotic graft is dissected from the temporal muscle and the dura mater predominantly by the method of blunt dissection. If necessary, a monopolar coagulator or blunt-pointed scissors can be used. The atrophied temporal muscle is carefully separated from the dura mater to prevent its damage, which can lead to liquorhea. If the DM has been injured during isolation step, it is sutured or repaired with a fragment of the periosteum. In case of protrusion in the area of the trephination defect, which does not allow implant placement and fixation, a bolus injection of a hyperosmolar solution (20% mannitol, 200 ml), short hyperventilation or temporary ventriculostomy of the anterior horn of the lateral ventricle can be

![Fig. 2. Bone graft autolysis 11 months after cranioplast.](image)

a — 3D reconstruction of MSCT data; b — intraoperative view of bone graft resorption; c — demonstration of graft lysis on the 3D model of the patient’s skull.

![Fig. 3. Pneumocephalus developed after cranioplasty. Arrow indicates defect of the frontal sinus.](image)
If autogenous bone is used as a graft, it is placed on the defect area and fixed by loop ligatures or cranial clips. In case of using a previously prepared sterile grafts or molds for intraoperative modeling, overlapping of the holes for suturing the temporal muscle is performed. The temporal muscle is fixed to the graft. Soft tissue are sutured in layers. An important point is to provide high-quality hemostasis prior to suturing soft tissues in order to prevent hemorrhagic complications. After suturing of soft tissues, a compressive aseptic dressing is applied. Removal of skin sutures is performed not earlier than 8 days after surgery.

**Results**

Autologous bone graft implantation has been carried out in 47 patients (21 males and 26 females, mean age, 46.2±9.4 years). In 12 cases, the graft was composed of several fragments. There were 6 cases of cranioplasty in combination with one-staged \((n=4)\) or delayed \((n=2)\) VPS. Late and early complications were noted in 16 (34%) patients. Two patients had epileptic seizures in the delayed period (after 2 and 6 months, respectively). Seizures were arrested by anticonvulsants. Two (4.2%) patients died from the causes not related to the intervention a few years after discharge in the follow-up period.

Artificial grafts were implanted in 14 patients. Complications were noted in 4 (28.5%) of these patients. They were mostly presented by delayed manifestation of the epilepsy syndrome (3 (21.4%) patients), which can be arrested by anticonvulsant drugs. It should be noted that these patients have not had seizures prior to cranioplasty and did not receive anticonvulsant treatment. One patient developed frontal sinus defect associated with pneumocephalus after cranioplasty, which required reoperation for defect repair. There were no deaths.

Data on complications of cranioplasty are presented in Table 2.

**Reoperations after cranioplasty**

A total of 11 patients, most of whom were autologous graft patients, required reoperation. Due to infectious complications (osteomyelitis of the graft), surgery was required in 6 (12.7%) patients. The average duration of manifestation of infectious complications was 3.7 months (range, 2 weeks to 6 months). In all cases, wound debridement and removal of osteomyelitis defect of the graft were performed. Subsequently, 4 patients underwent plastic surgery with an artificial graft after 4—6 months. In 2 patients, repeated cranioplasty was not performed due to contraindications for surgery. Bone lysis was noted in 7 (14.8%) cases (Fig. 1). It’s worth mentioning that 5 (71%) patients underwent cranioplasty with fragmented bone graft. In 2 cases, reoperations were performed for cosmetic and protective purposes: resection of partially lysed bones and cranioplasty with an artificial graft.

In 2 (2.1%) cases, pneumocephalus associated with the frontal sinus defect on the intervention side developed after cranioplasty (in one of the cases, it developed after implantation of an artificial graft) (Fig. 2). Plastic surgery was performed under general anesthesia using transbrow approach to the lateral parts of the frontal sinus with defect tamponading with a fragment of the periosteum, TachoComb and fibrin-thrombin glue. No cases
of recurred pneumocephalus were noted after these interventions. **Complication risk factors**

Material analysis allowed us to establish the risk factors for the development of infectious complications: patient’s age older than 60 years and graft fragmentation (5 patients out of 7 had a fragmented graft). Unfortunately, it is impossible to statistically confirm this assumption due to the small sample of patients.

We did not manage to identify factors associated with manifestation of epilepsy syndrome or hydrocephalus in the postoperative period.

**Discussion**

The aim of cranioplasty is not only cosmetic but also therapeutic issue: cranioplasty improves neurological status in the postoperative period as demonstrated by numerous studies [3, 5, 6, 14, 15]. Despite the fact that the surgery is quite easy technically, there is a risk of complications, which can reach 18—36.5% according to the literature [16—18]. Aseptic resorption of the bone graft occurs in 24—50% of patients. Elderly age, graft fragmentation, hydrocephalus, and VPS dependence were assumed as possible risk factors for bone resorption. However, the exact reasons have not been determined yet [6, 11, 15, 19—21].

It is possible that one of the factors affecting bone graft lysis is its storage and/or sterilization technique. For instance, one study has demonstrated that grafts with subcutaneous preservation in the anterior abdominal wall area become less autologous after cranioplasty [22]. In our opinion, this technique is not advantageous due to increased injuries (double invasion in the anterior abdominal wall). It was also shown that a graft can be lysed subcutaneously by macrophages [9].

To date, there are many artificial biopolymer- or titanium-based simulated grafts (Fig. 3), which have been shown to provide a good cosmetic effect with a low risk of complications [12, 22, 23]. At the same time, some grafts or preoperative computer simulating can be quite expensive, and there is a risk of a response to the allograft as a foreign body in rare cases [13].

In our opinion, complication in the form of manifestation of epileptic syndrome in the delayed period after cranioplasty is underestimated. According to the literature data [18, 23], the risk of this complication reaches 14.8%, its association with a type of graft is not confirmed. In our work, such a complication was noted in 5 (8.1%) patients. In all cases, the epileptic syndrome was of moderate severity with a frequency rate of 1 to 6 per year. There were no seizures observed in patients receiving anticonvulsant therapy.

Choosing a proper method of surgery in liquor-dynamic disorders (hygromas, ventriculomegaly, hydrocephalus) in patients who underwent DC remains to be a controversial issue. There is no consensus regarding the duration and order of shunt surgeries and cranioplasty. According to the study by Junyoung et al., which included 51 patients, shunt placement and cranioplasty were performed in one step in 32 (62.7%) cases. The risk of postoperative complications constituted 43%. Thus, the authors do not recommend conducting shunt surgery in one step with cranioplasty. Recently, we also started considering that these surgeries should be performed separately. Most patients can develop liquor-dynamic disorders in the form of hygromas and ventriculomegaly, which do not result in neurological disorders, after DC. According to the theory of cerebrospinal fluid (CSF) absorption proposed by Davson et al. in 1970, CSF is absorbed into the superior sagittal sinus (SSD) in the presence of a pressure gradient between them. A gradient of 3—5 mm Hg is required for normal absorption of CSF. In the long-term period, when integrity of the skull is disturbed (after DC), ICP becomes equal to the atmospheric pressure, which can lead to a decrease in the gradient (ICP/SSD) thereby causing CSF hypoabsorption, which manifests itself in the form of liquor-dynamic disorders. Studies demonstrate that these disorders can regress upon restoration of skull integrity (cranioplasty). In our study, cranioplasty was combined with simultaneous VPS in 3 cases only, 2 patients underwent VPS prior to cranioplasty, and 2 patients underwent VPS after cranioplasty. We were not able to determine the relationship between the terms of VPS and postoperative complications. In order to avoid unjustified interventions, we recommend skull defect repair as the first step of surgery followed by examination for possible indications for shunt placement. This issue requires a detailed analysis on a larger sample of patients and is not the main goal of our study.

Infectious and cosmetic complications were the reason for revising the indications for DC and limiting its unjustified use. We also decided not to use autologous grafts for cranioplasty of fragmented grafts [10, 11, 19, 20].

We noted that there is a lower risk of postoperative complications in case of using an artificial graft. We have not observed any cases with reaction to foreign material or infectious complications. In this work, we were not able to confirm the effect of the terms of cranioplasty on the risk of postoperative complications, since the authors of other studies do not observe such a relationship as well [23].

Based on our experience and the results presented in this paper, we believe that cranioplasty with simulated polymethyl-methacrylate (Palacos) grafts is more advantageous in elderly patients or patients with bone fragmentation during DC (Fig. 4). In our opinion, cranioplasty has a significant risk of postoperative complications, which reaches 18%. The tactics of extensive aggressive application of DC without strict indications in the acute period of aneurysmal SAH can lead to complications such as DC and cranioplasty.
Conclusion
Cranioplasty in patients after aneurysm clipping is associated with the risk of postoperative complications mainly including local infectious processes and bone graft resorption. Elderly age, bone graft fragmentation can increase the risk of postoperative complications and requirement for reoperation.

Authors declare no conflict of interest.
The current study presents analysis of complications and technical features of delayed cranioplasty performed in 61 patients who underwent decompressive craniotomy and intracranial aneurysm clipping for subarachnoid hemorrhage. Cranioplasty was performed using autologous bone in 47 patients and cement bone allograft in 14 cases. The authors reviewed the basic principles of cranioplasty with various materials and also presented relevant literature data. Relevance of the issue and its practical significance are demonstrated in the article.

**Commentary**

The article subject and design of the study are fully consistent with journal profile and requirements. The following types of cranioplasty-associated complications were identified: graft autolysis, infectious complications (fistulas, osteomyelitis), epilepsy syndrome, frontal sinus defect, and pneumocephalus. A comparative assessment of the incidence rate and nature of these complications in using autologous bone graft and allograft is presented. The authors convincingly demonstrated the advantages of using allograft.

In general, the work deserves appreciation and is of interest to readers of the journal.

*A.S. Saribekyan (Moscow, Russia)*
Lateral Extended Transsphenoidal Endoscopic Approach through the Pterygopalatine Fossa in Surgery for Meningoencephalocele of the Lateral Sphenoid Recess

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Meningoencephalocele is a hernial protrusion of the medulla and meninges through a defect in the skull bones. Due to poor accessibility of meningoencephalocele located in the lateral sphenoid recess region, modern surgical treatment of this pathology prefers to use endoscopic transsphenoidal approaches.

Material and methods. The study included 4 patients with meningoencephalocele of the lateral recess of the sphenoid sinus (1 male and 3 females; mean age, 46.8 years). All patients underwent resection of meningoencephalocele and repair of a skull base defect using the lateral extended transsphenoidal endoscopic approach through the pterygopalatine fossa (transpterygoid approach).

Results. In all patients, meningoencephalocele was resected to the bone defect level. There was no postoperative liquorrhea. Complications included bacterial meningitis (1 case), asymptomatic imbibition of the temporal lobe pole (1 case), and temporary numbness in the V2 innervation area of the trigeminal nerve (1 case).

Conclusion. The paper describes and demonstrates advantages of the lateral extended transsphenoidal endoscopic approach through the pterygopalatine fossa (transpterygoid approach) for surgical treatment of patients with meningoencephalocele of the lateral sphenoid recess.

Keywords: transpterygoid endoscopic approach, meningoencephalocele, endoscopic transsphenoidal approach, nasal liquorrhea.

Abbreviations:
ICA — internal carotid artery
SCT — spiral computed tomography
TMO — dura mater
MCF — middle cranial fossa

Meningoencephalocele is a hernial protrusion of the medulla and meninges through a skull bone defect. Basal meningoencephalocele (at the skull base) occurs in 1 out of 35 thousand people and it is classified into transethmoidal, sphenoethmoidal, transsphenoidal, and frontosphenoidal/sphenoorbital. Transsphenoidal spread of hernial protrusion is observed only in 5% of all cases of basal meningoencephalocele [1].

The lateral recess (lateral pocket) of the sphenoid sinus is formed as a result of pneumatization of the pterygoid process and/or the greater wing of the sphenoid bone [2].

Formation of the bone defect in the lateral recess of the sphenoid sinus is attributed to abnormal ossification of the sphenoid sinus and is usually accompanied by spontaneous nasal liquorrhea [3, 4]. In the neonatal period, the cartilage tissue of the sphenoid sinus is not replaced by osseous tissue, which leads to formation of the lateral craniopharyngeal canal (Sternberg’s canal) followed by formation of meningoencephalocele of the lateral recess of the sphenoid sinus through this canal [3—6]. However, in recent years, it is believed that defect formation in the lateral part of the sphenoid sinus with spontaneous nasal liquorrhea is caused by increased intracranial pressure in the case of large sphenoid sinus due to hyperpneumatized pterygoid process [7].

Bone defects in the lateral recess of the sphenoid sinus accompanied by formation of meningoencephalocele are among the most inaccessible areas for surgical reconstruction due to their complex anatomy [4, 8, 9].

External transcranial neurosurgical approaches and Le Fort I approach are associated with high mortality and prolonged hospitalization. External approaches (pterygoid, subtemporal) include large incision of the frontotemporal soft tissues associated with the risk of temporal muscle hypotrophy and injury to the temporal branch of the facial nerve, as well as the need for intraoperative traction of the temporal lobe. Furthermore, recurrent postoperative nasal liquorrhea and increased incidence of epileptic seizures (when patients has history of seizures) are often observed [10, 11].

Endoscopic endonasal approach is currently widely used for the treatment of basal meningoencephalocele with a minimum number of postoperative complications [4, 12—14]. In 2008, Cappabianca et al. [15] reported results of surgical treatment of 3 patients with menin-
goencephalocele through the lateral extended transsphenoidal endoscopic approach. Simultaneously, J. Socher et al. [16] published the paper where they reported successful endoscopic plastic repair of meningoencephalocele in 9 patients.

Here we report the use of lateral extended transsphenoidal endoscopic approach through the pterygopalatine fossa (transpterygoid approach) for surgical treatment of patients with meningoencephalocele of the lateral sphenoid recess.

Material and methods

The study included 4 patients with meningoencephalocele of the lateral recess of the sphenoid sinus. Patient records are shown in Table 1.

Before surgery, the disease in all cases presented with nasal liquorrea (usually unilateral). Discharge of clear fluid from the nose intensified during forward flexion of the head and the Valsalva test.

In 1 case, nasal liquorrea (due to post-traumatic meningoencephalocele) was preoperatively complicated by bacterial meningitis. In 1 patient, hernial protrusion of the medial part of the temporal lobe manifested in the form of absence seizures (Table 1).

All patients underwent preoperative CT cisternography in order to determine the location of the cerebrospinal fluid fistula, which enabled visualization of the outflow of contrast material from the cranial cavity through the bone defect at the area of meningoencephalocele.

In all patients, meningoencephalocele was located at the area of the lateral recess of the sphenoid bone, lateral to the V2 branch of the trigeminal nerve.

All patients underwent removal of meningoencephalocele and plastic repair of the skull base defect through the lateral extended transsphenoidal (transpterygoid) approach. In all cases, an elastic tampon was placed at the level of the entrance to the sphenoid sinus and external lumbar drainage was used after surgery. Drainage of cerebrospinal fluid was carried out for 5—6 days followed by removal of the lumbar drainage. The tampon was also removed from the nasal cavity on day 5—6 after the operation. No cases of nasal liquorrea were observed in the postoperative period.

Perioperative antibiotic prophylaxis was carried out: intravenous bolus injection of Amoxiclav 1.2 g 30 minutes before the operation. in 2 patients, postoperative antibiotic prophylaxis was extended for the entire period of external lumbar drainage (Amoxiclav 1.2 g intravenously, TID).

The technique of lateral extended transsphenoidal endoscopic endonasal approach through the pterygopalatine fossa (transpterygoid approach)

Endonasal approach to the anterior wall of the sphenoid sinus was performed under the control of 0° endoscope. The main anatomical landmarks are visualized in the nasal cavity, which determine the median line, as well as the apertures of the maxillary and sphenoid sinuses (Fig. 1).

The entrance to the sphenoid sinus is located between the nasal septum and the middle turbinate bone, about 1.5 cm above the choana. The entrance to the maxillary sinus is located behind the uncinate process. The cavernous sinus is projected behind the bulla ethmoidalis and posterior cells of the ethmoid bone located lateral to the middle turbinate bone. The middle turbinate bone can be resected (partially or fully) at the nasal stage of the operation on the side of approach in order to extend the operative approach.

Resection of the uncinate process of the medial wall of the maxillary sinus and posterior ethmoidal cells enable visualization of the anterior wall of the pterygopalatine fossa formed by the posterior wall of the maxillary sinus, as well as the lateral portions of the posterior wall of the sphenoid sinus and the medial wall of the orbit (Fig. 2).

Removal of the posterior wall of the maxillary sinus enables visualization of the contents of the pterygopalatine fossa: pterygopalatine ganglion, maxillary nerve, Vidian nerve and artery, palatine nerve and descending palatine artery, maxillary artery (Fig. 3).

Lateral displacement of the contents of the pterygopalatine fossa enables visualization the base of the pterygoid process, which is removed under the control of a 30° endoscope (Fig. 4).

Resection of the medial portions of the greater wing of sphenoid bone provides approach to the dura mater of

<p>| Table 1. Preoperative data of patients with meningoencephalocele of the lateral recess of the sphenoid bone |
|---------------------------------------------------------------|------------|-----------------|---------------------------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Patient number (sex, age)</th>
<th>Pneumatized pterygoid process</th>
<th>Etiology</th>
<th>Location of meningoencephalocele</th>
<th>Nasal liquorrea</th>
<th>History of meningitis</th>
<th>Epilepsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. F, 46 years old</td>
<td>Yes</td>
<td>Spontaneous</td>
<td>Lateral recess on the left sphenoid sinus</td>
<td>Yes</td>
<td>None</td>
<td>Yes</td>
</tr>
<tr>
<td>2. M, 29 years old</td>
<td>Yes</td>
<td>Posttraumatic</td>
<td>Lateral recess on the right sphenoid sinus</td>
<td>Yes</td>
<td>Yes</td>
<td>None</td>
</tr>
<tr>
<td>3. F, 48 years old</td>
<td>Yes</td>
<td>Spontaneous</td>
<td>Lateral recess on the left sphenoid sinus</td>
<td>Yes</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>4. F, 64 years old</td>
<td>Yes</td>
<td>Spontaneous</td>
<td>Lateral recess on the left sphenoid sinus</td>
<td>Yes</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>
the middle cranial fossa (Fig. 5). The Meckel's cavity, which contains the trigeminal ganglion, is bounded from below and medially by the ICA, laterally by the second branch of the trigeminal nerve, and from above by the abducent nerve. The sympathetic plexus of the ICA indicates the location of the abducent nerve.

**Results**

The lateral extended transsphenoidal endoscopic approach through the pterygopalatine fossa enables direct approach to the hernial protrusion and clear visualization of the defect at the area of the greater wing of the sphenoid bone in all cases.
The results of surgical treatment are shown in Table 2.

In all patients, meningoencephalocele was resected to the level of the bone defect and complex multilayered plastic reconstruction was carried out using autologous material and allomaterial, as well as pedicled mucoperiosteal flap [17, 18].

One patient (case 1) postoperatively developed numbness in the innervation zone of the maxillary nerve (V2), which regressed within 4 months. In one case (case 4), postoperative CT scan of the brain showed blood soaking of the pole of the left temporal lobe, which was accompanied by neurological symptoms.

Despite the preoperative antibiotic prophylaxis, 1 patient (case 2) with post-traumatic meningoencephalocele developed bacterial meningitis (Pseudomonas aeruginosa) on day 1 after skull base defect reconstruction,
which was successfully cured using antibiotic therapy with Doripenem 1.0 g TID for 14 days (complete purification of the cerebrospinal fluid was observed on day 7 of treatment).

The average follow-up was 13 months. No cases of recurrence of meningoencephalocoele and nasal liquorhea were observed during follow-up.

**Case study**

Patient T, 48 years old, complained of discharge of clear colorless fluid from the nose for 3 years. There were two unsuccessful attempts of endoscopic transphenoidal reconstruction of the cerebrospinal fluid fistula at the place of residence (2016). MRI of the brain showed meningoencephalocoele of the lateral recess of the sphenoid bone on the left (Fig. 6).
Meningoencephalocele was resected through the transpterygoid approach. The hernial sac containing brain tissue was excised. Reconstruction of the skull base defect was carried out in several layers: the first layer of fascia was fixed at the edges of the bone defect, fascia was covered from above with fat and another layer of fascia. Multilayered plasty was additionally covered with a mucoperiosteal flap fixed with fibrin-thrombin glue and an elastic tampon placed into the nasal cavity.

There was no negative postoperative dynamics of neurological status; nasal liquorrhea stopped. The patient was discharged in satisfactory condition on day 10 after the operation. Control MRI of the brain 4 months after surgery showed no evidence of recurrence of meningoencephalocele (Fig. 7). ENT examination showed no nasal liquorrhea.

**Discussion**

Surgical treatment of liquorrhea includes adequate approach to the area of the skull base defect, isolation of the osseous edges of the fistula, and adequate closure of the defect [4, 11, 19].

Surgical approaches to the lateral sphenoid recess include traditional microsurgical transcranial external approach, microsurgical transseptal transsphenoidal approach, Le Fort I osteotomy [20], and endoscopic endonasal approach.

In our opinion, effective closure of the skull base defect and plastic repair of the CSF fistula in patients with meningoencephalocele is impossible without resection of the hernial sac and the edges of the bone defect of the skull base (1 — bottom of the sella turcica; 2 — protrusion of the internal carotid artery; 3 — meningoencephalocele resected to the level of the skull base defect).

**Table 2. The results of surgical treatment of patients with meningoencephalocele of the lateral recess of the sphenoid bone**

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Postoperative nasal liquorrhea</th>
<th>Epilepsy</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
<td>None</td>
<td>Transient hypoesthesia of V2</td>
</tr>
<tr>
<td>2</td>
<td>None</td>
<td>None</td>
<td>Meningitis</td>
</tr>
<tr>
<td>3</td>
<td>None</td>
<td>None</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>None</td>
<td>None</td>
<td>Imbibition of the temporal lobe pole with blood</td>
</tr>
</tbody>
</table>

**Fig. 8. Endoscopic approach to the lateral recess of the sphenoid sinus on the left (visualization using a 30° endoscope).**

a — standard endoscopic approach to the recess of the sphenoid sinus, which allows partial visualization of the meningoencephalocele (1 — the bottom of the sella turcica; 2 — the cupula of the meningoencephalocele; 3 — posterior nasal septum); b — transpterygoid approach allowing visualization of the entire hernial sac and the edges of the bone defect of the skull base (1 — bottom of the sella turcica; 2 — protrusion of the internal carotid artery; 3 — meningoencephalocele resected to the level of the skull base defect).
bone defect itself and its adequate reconstruction are not accessible (Fig. 8).

Our surgical experience has shown that good visibility of the operative wound and wide anatomical corridor formed using the transpterygoid approach enable clear visualization of all the margins of the bone defect, as well as comfortable and effective multilayered reconstruction of the skull base defect under the control of 0° optics.

Preliminary anatomical study [21, 22] showed that, when closing skull base defects of the lateral sphenoid recess, it should be kept in mind that pituitary gland, optic nerve, cavernous sinus, pterygoid nerve, internal carotid artery, as well as III, IV, IV, and also V1 and V2 branches of cranial nerves, maxillary artery, and sphenopalatine artery are located in close vicinity to the sphenoid sinus.

Gradual wide resection of the bones of the anterior wall of the sphenoid sinus with a high-speed diamond bur during the transpterygoid approach enables correct identification of the mentioned structures, minimizing the likelihood of their damage.

Conclusions

Lateral extended transsphenoidal endoscopic approach through the pterygopalatine fossa is a necessary and effective supplementary measure to standard sphenoidotomy, which provides adequate visualization of the meningoencephalocele formation area, which is a prerequisite of reliable and safe plastic repair of the skull base defect.

Authors declare no conflict of interest.
Commentary

The article focuses on the topical problem of treatment of the skull base meningoencephalocele located in the lateral part of the excessively pneumatized sphenoid sinus, which is difficult to access. The authors reported 4 cases of this rare disease, which was treated using endoscopic transsphenoidal/transpterygoid approach and analyzed the results of the operations.

This study confirms the effectiveness and safety of endoscopic approach in the surgical treatment of meningoencephalocele. The authors provide original rationale for surgical approach to the lateral recess of the sphenoid sinus based on the anatomical preparations dissected by the authors.

The study is useful for specialists dealing with these problems.

A.S. Lopatin (Moscow, Russia)
Radicality and Complications of Reoperations for Malignant Neuroepithelial Tumors of the Posterior Cranial Fossa in Children

B.Z. CHEL’DIEV, Y.U.V. KUSHEL’, M.O. DEMIN

Burdenko Neurosurgical Institute, Moscow, Russia

Treatment of primary malignant neuroepithelial tumors of the posterior cranial fossa (PCF) in childhood includes surgical resection, radiation therapy (RT), and chemotherapy (CT). The radicalness of surgery is one of the most important prognostic factors of survival. Despite the significant advances in treatment, many of these tumors recur. Today, oncologists are increasingly recommending repeated surgery for recurrent malignant neuroepithelial tumors of the PCF to achieve gross total resection (GTR). Patients undergo this surgery after RT and palliative CT, which may increase surgical risks.

Objective — the study objective was to assess the resection extent of recurrent malignant neuroepithelial tumors of the PCF in children as well as the risk and structure of postoperative complications.

Material and methods. The prospective study included 50 patients under the age of 18 who underwent surgery for recurrent malignant neuroepithelial tumors of the PCF at the Neurosurgical Institute (NSI) in the period between 2002 and June 2015. Anaplastic ependymomas were present in 37 patients, and medulloblastomas were detected in 13 patients. A total of 58 repeated surgeries were performed.

Results. GTR was achieved in 53 (91.4%) cases, near total resection (NTR) was achieved in 2 (3.4%) cases, and subtotal resection (STR) was achieved in 3 (5.2%) cases. The mean bed-day after surgery was 12 (4―47) days, and the mean critical care stay was 3.2 (0―23) days. Seven patients required tracheostomy; meningitis developed in 3 patients; liquorheea occurred in 2 cases. Ventriculoperitoneal shunting was used in 8 (13.8%) cases. One (1.7%) patient died in the early postoperative period.

Conclusion. Our results demonstrate that resection of recurrent malignant neuroepithelial tumors in children can be performed with high radicalness (90%) and acceptable risks.

Keywords: posterior cranial fossa tumors, medulloblastoma, anaplastic ependymoma, neuroepithelial tumors, tumor recurrence, repeated surgical resection, tumor resection extent, surgical complications.

Abbreviations:
PCF — posterior cranial fossa
RT — radiotherapy
MRI — magnetic resonance imaging
PCT — polychemotherapy
CT — chemotherapy
GTR — gross total resection

Tumors of the central nervous system are the second most common among childhood cancers and rank first among solid tumors in children. The incidence of neoplasms of the central nervous system in children aged 0―19 years is 3.5―4.0 per 100 thousand children [1—3]. Annually, 1,000―1,200 new cases of brain tumors are detected in the Russian Federation [4]. Of these, 60―70% are infratentorial [5]. The following three most common histological variants are distinguished in children with PCF tumors: medulloblastoma (40%), astrocytoma (20―35%), and ependymoma (10%) [4, 6].

Treatment of newly detected malignant neuroepithelial tumors of the PCF in children has been studied for a long time. Currently, there are many different treatment protocols for these tumors, which lead to significant positive results. Surgical resection as the first stage is one of the main treatments for primary malignant tumors of the PCF. The radicality of this operation is an important prognostic factor [6—8].

Despite the progress in the treatment of malignant neuroepithelial tumors, many of them are recurrent. Thus, the 5-year and 10-year relapse-free survival rates for children with medulloblastomas are 81±2 and 75.8±2.3 months, respectively; overall survival — 87±1.8 and 81.3±2.1 months, respectively [9]; in the case of anaplastic ependymomas, the average period without progression is 66.2 months (11 days to 23 years) [10]. Pediatric neuro-oncologists suggest that maximum possible radical removal of local recurrences of malignant neuroepithelial tumors of the PCF improves the overall prognosis, improves the effectiveness of the use of additional adjuvant treatment regimens, and is the only effective option in the case of ependymomas.

The problem of surgical treatment of children with recurrent malignant neuroepithelial tumors of the PCF is poorly covered in the literature. In particular, there are no answers to the questions: what is the probability of successful radical resection, what early and late complications are associated with this operation?

This study is aimed at assessing the radicality of removal of recurrent malignant neuroepithelial tumors of the PCF in children, as well as the likelihood of development and pattern of postoperative complications.

Material and methods

The study is based on the results of analysis of a prospective group of pediatric patients, who were operated...
on at the Burdenko Neurosurgical Institute for recurrent malignant neuroepithelial tumors of the PCF from 2002 to June 2015. A total of 50 children (30 boys and 20 girls) were operated on by the same surgeon. The age of patients at the time of reoperation ranged from 1.4 to 14.6 years (median 5.8 years). All children underwent complex treatment by oncologists and were sent to the Burdenko Neurosurgical Institute when tumor recurrence was detected in order to make decision regarding reoperation. The operation was offered only in those cases, where radical removal of the tumor was possible as suggested by the expert opinion of a surgeon with extensive experience in these operations based on MRI and clinical presentation. Reoperation was denied in about one of five children (about 20%), who were sent for consultation. In most cases, these children received various options of radiation therapy.

Radicality of tumor resection was determined according to the following criteria: gross total resection (GTR) — there is no residual tumor on the control contrast-enhanced MRI, no evidence of tumor infiltration of surrounding tissues in the protocol of the operation; near total resection (NTR) — there is no residual tumor on control contrast-enhanced MRI, but there is clear evidence of tumor infiltration area in the brain stem or invasion of the cranial nerve roots; subtotal resection (STR) — there is residual tumor of any volume on the control contrast-enhanced MRI.

The following parameters were analyzed to assess postoperative complications: preoperative and postoperative neurological status, general surgical complications, duration of stay at the intensive care unit, duration of hospital stay, need for additional operations.

**Results**

The analyzed series included significantly more anaplastic ependymomas than medulloblastomas, 37 (74%) and 13 (26%), respectively. This is due to the fact that adjuvant therapy of anaplastic ependymomas is limited to radiation therapy, which is often ineffective. In this regard, oncologists often send children with recurrent anaplastic ependymomas for reoperation. It should be noted that some patients underwent many reoperations, so the calculation included the number of operations. A total of 58 reoperations were carried out. Of these, grand total resection was achieved in 53 (91.4%) cases, subtotal — in 3 (5.2%) cases, and nearly total resection — in 2 (3.4%) cases.

The average duration of inpatient treatment was 15.7 bed-days (from 6 to 51 days), the average number of bed-days after surgery was 12 (4—47 days), the average duration of stay at the intensive care unit was 3.2 (0—23 days).

We divided the patients into 4 groups in order to assess the postoperative neurological status. Group 1 included 35 (60.4%) children who had no significant postoperative disorders. Group 2 included 9 (15.5%) children who had postoperative increase in neurological deficit, which regressed at the time of discharge. Group 3 included 13 (22.4%) children who were discharged with persistent neurological deficit. One child (1.7%) with fatal neurological deficit was not included in these groups. This child was one of three children who underwent subtotal tumor resection.

Patients of the first two groups had no postoperative neurological complications after grand total tumor resection, and therefore the result was assessed as very good. When analyzing postoperative status in group 3 patients, bulbar syndrome was the most common neurological disorder, which was the only manifestation of pathology in the vast majority of cases (11 cases out of 13). Seven of these patients required tracheostomy. Oculomotor disorders were detected in 2 cases, 1 of these patients additionally developed cerebellar mutism. One patient had pyramidal insufficiency, another one had deficit of VII and VIII nerves. Several patients developed postoperative infectious complications and liquorrhea. Meningitis developed in 3 patients, 2 of them were in group 1. Liquorrhea was observed in 2 cases. The incidence of liquorrhea and meningitis did not exceed the incidence of these complications in patients with primary PCF surgery.

Eight (13.8%) patients required bypass surgery within 1 month after tumor resection. Ventriculoperitoneal shunting was performed in all cases.

**Case reports**

**Case 1**

Patient A, 14 years old, was admitted on 16.06.15. Diagnosis: medulloblastoma of the vermis and left cerebellar hemisphere. Condition after subtotal tumor resection on 17.05.10, insertion of the Ommaya reservoir, RT and PCT. Tumor recurrence (Fig. 1a).

Neurological status at admission: cerebellar symptoms (instability in the Romberg’s test without difference between left and right sides, correct finger-to-nose test with pronounced intention, ataxic gait).

The patient underwent surgery on 16.06.2015: removal of recurrent medulloblastoma at the middle cerebellar peduncle (MCP). The child was followed at the intensive care unit during the night after surgery. There was no negative dynamics of neurological status. Independent breathing through the natural respiratory tract. Independent eating. The patient was discharged on day 6. Control MRI scan of the brain was performed in 1.5 months after tumor resection: there were no signs of residual tumor (Fig. 1b).

**Case 2**

Patient B, 4 years old, was admitted on 12.05.15. Diagnosis: anaplastic ependymoma of the fourth ventricle. Condition after tumor removal on 18.07.12. Ventriculoperitoneal shunting on 06.08.13. Condition after PCT and RT. Tumor recurrence (Fig. 2a).
Neurological status at admission: cerebellar symptoms (instability in the Romberg’s test, finger-to-nose test with mild intention on both sides, ataxic gait).

Surgery was carried out on 12.05.2015: removal of the parastem ganglion of recurrent ependymoma of the PCF on the right under monitoring of motor evoked potentials (MEP).

The patient was followed at the intensive care unit for several hours after surgery. Neurological status: mild paresis of the sixth nerve on the right and persisting cerebellar symptoms. The girl was discharged from the hospital on day 6. In one month, there were no MRI signs of tumor (Fig. 2b).

**Case 3**

Patient D, 4 years old, was admitted to the Burdenko Neurosurgical Institute on 15.09.14. Diagnosis: relapse of anaplastic ependymoma of the stem and the fourth ventricle. Occlusive hydrocephalus. Condition after tumor resection on 20.06.12. Condition after RT and PCT (Fig. 3).

Neurological status at admission: paresis of the VI, VII nerves on the left, left hypoacusia, bulbar syndrome (no pharyngeal reflex on both sides, frequent food choking), cerebellar symptoms (instability in the Romberg’s test, ataxic gait). Surgery was carried out on...
17.09.14: removal of recurrent parastem ependymoma of the PCF (GTR).

After surgery, the patient stayed at the intensive care unit. Neurological status: there was increase in bulbar syndrome and therefore puncture-dilation tracheostomy was performed in 6 days after the operation. The child was transferred from the intensive care unit on day 8. On day 14 after the operation, the patient developed signs of
intracranial hypertension in the form of pronounced sympathetic reaction (tachycardia over 140 bpm, tachypnea of more than 22 breaths per minute, dilated pupils) followed by short-term apnea. MRI images 16 days after surgery are shown in Fig. 4. On day 21 after the operation, the child was implanted with a right ventriculoperitoneal shunt (Medtronic Delta 1.5). She was discharged on day 28 from the date of admission. Neurological status at the time of discharge: partial regression of the bulbar syndrome. Independent breathing through the tracheostomy tube, mixed food intake (independent and through the enteric feeding tube).

Discussion

Surgical treatment of recurrent malignant neuroepithelial tumors of the PCF in children is poorly covered in the literature. We found no publications with clearly substantiated and formulated indications for reoperation. Moreover, neurosurgeons believe that reoperations for malignant tumors of the PCF are more dangerous. Search through the database of medical periodical literature PubMed found only one article [11], addressing the issue of surgical treatment of recurrent intracranial ependyma. The article reports a retrospective analysis of medical histories of 22 children with recurrent intracranial ependyma, 18 of them initially had an infiltrating tumor. The study showed that the overall survival time was significantly improved due to reoperations (mainly GTR) and further adjuvant therapy. The questions about the risks and possible complications of surgical treatment, as well as indications and contraindications for surgical resection of recurrent tumors, are still unanswered. Nevertheless, according to current recommendations, in particular recommendations of the National Cancer Institute (USA), surgical treatment is indicated for all recurrent malignant neuroepithelial tumors of the PCF in children.

The results we obtained in the group of patients with recurrent anaplastic ependyma and medulloblastoma of the PCF argue for active surgical tactics in some clinical situations. Unfortunately, it is unlikely that any standardization of indications for surgery is possible. Surgeon's opinion whether radical resection in possible with acceptable risks was the main criterion for selection of patients in our series. Obviously, these indications will be different in clinical practice of each surgeon. Our experience shows that many local recurrent malignant neuroepithelial tumors of the PCF are fairly good “marginalized” from the surrounding neurovascular structures. Obviously, there is very high chance of successful radical removal in this situation. In this regard, further research aimed at discovering MRI signs of infiltration rate of recurrent tumors can be very helpful.

Conclusion

Analysis of our series showed that total removal of clearly circumscribed recurrent malignant neuroepithelial tumors of the PCF can be achieved in more than 91% of pediatric patients. It is important that this surgery is accompanied by acceptable risks: 1 child died in the early postoperative period (death rate was 1.7%), persistent neurological deficit developed only in 13 cases, which is 22.4% of the total group of patients, and hydrocephalus was the only complication developed in the long-term postoperative period, which can be completely stopped by shunting operations.

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Treatment modality in patients with recurrent medulloblastoma and ependymoma is an open question in neuro-oncology.

The results of treatment of children with ependymoma are still unsatisfactory, and the 5-year event-free survival rate does not exceed 70% [1]. The tumor recurs in more than 1/3 of patients despite the combination or complex treatment. Radical removal of ependymomas and radiation therapy significantly improve the results of treatment, while the effectiveness of chemotherapy is still discussed in the literature [1, 2].

The situation with treatment of children with medulloblastomas is somewhat different. The tumor responds well to radiation and chemotherapy. This reduces the role of the radicality of the operation as evidenced by the results of treatment. There are studies aimed at identifying the groups of patients where intensity of therapy can be reduced or even minimized. Therefore, despite the fact that medulloblastoma is formally more malignant than ependymoma, the results of treatment of patients with medulloblastoma are better (more than 80—85% of 5-year event-free survival).

A similar situation is observed in the treatment of patients with recurrent tumors: radical resection with repeated radiotherapy is indicated in patients with ependymoma, when possible [1], and active use of chemotherapy is indicated in patients with medulloblastoma.

This article addresses the important and complicated issues of radicality and complications of reoperations for malignant neuroepithelial tumors of the posterior cranial fossa (PCF) in children, and therefore it is highly relevant. Extensive clinical material (50 patients) was used to demonstrate that removal of recurrent tumor (medulloblastoma or ependymoma) of the PCF is possible with high degree of radicality and low level of postoperative complications. Thus, total or nearly total removal was achieved in 95% of cases, which is a very good result.

Unfortunately, the article does not provide the criteria to select patients for surgery. It was only noted that they were subjective and should not be considered as “clinical guidelines”. However, even the subjective opinion of an experienced surgeon may be of great interest to his/her colleagues.

Postoperative complications, including development of hydrocephalus, were observed in more than 20% of patients. On the one hand, this fact shows that these operations are quite feasible and do not belong to high-risk interventions, but, on the other hand, possible complications should also be taken into account, when deciding whether to remove residual tumor or its recurrence.

In the future, I would like to follow the long-term results of treatment of these patients: what kind of postoperative therapy they received, what are the overall and event-free survival rates, the more so since there was enough time for follow-up. Of course, it would be interesting to compare the outcomes in operated and non-operated patients to make sure that the efforts made to remove the tumor were not in vain.

In general, the data show that radical removal of a circumscribed tumor is a relatively safe and feasible treatment in children with recurrent malignant PCF tumors.

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Anterior Stabilization of the C1—C3 Vertebrae After Transoral Removal of an Aggressive Aneurysmal Bone Cyst of the C2 Vertebra (a Case Report and Literature Review)

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Treatment of patients with atlantoaxial instability caused by various diseases of the skull base and craniovertebral junction combined with ventral compression of the brainstem is a complex issue that is ambiguously resolved in different ways. We present a case of stepped treatment, the most important component of which was successful transoral removal of an aggressive aneurysmal bone cyst of the CII vertebra with anterior CI—CIII segment stabilization using an individual system, which was performed through the same approach.

 Clinical case. A 31-year-old male patient presented with destruction of the CII body and odontoid process affected by an aggressive aneurysmal bone cyst causing disintegration of the CII posterior wall and odontoid process, which clinically manifested by constricted motion and pain in the cervical spine.

 Results. Three-step surgical treatment was performed. First, we performed a puncture biopsy of the CII body through the submandibular approach as well as posterior occipitospondylodesis with metal instrumentation from the occipital bone level to the CIV vertebra. Two months later, the patient underwent transoral removal of the CII body and odontoid process lesion and anterior CI—CIII segment stabilization using an individual cover metal system through the same approach. Two weeks after the second intervention, the occipitospondylodesis was transformed to a posterior CI—CIII stabilization system. Control CT 8 months after surgery showed the correct position of both stabilization systems.

 Conclusion. The use of individual instrumentation for anterior stabilization of the CI—CIII vertebrae in various diseases of the craniovertebral junction area is an effective and promising technique.

Keywords: transoral approach, anterior CI—CIII segment stabilization, aggressive aneurysmal cyst.

Aneurysmal bone cysts account for approximately 2.5% of all primary bone tumors [1]. These are foci of cystic lytic bone lesions consisting of blood-filled lacunae separated by connective tissue septa. In 30% of cases, aneurysmal bone cysts are secondary and develop in the setting of preexisting bone lesions, such as chondroblastoma, giant cell tumor, fibrous dysplasia, chondromyxoid fibroma, and osteosarcoma; in 70% of cases, they are primary lesions [1—3].

Surgical treatment of aneurysmal bone cysts is the method of choice in the case of spinal instability and neurological symptoms. The optimal treatment in this case is complete resection of the cyst followed by stabilization [4—6]. Also, there are simple spinal bone cysts that are extremely rare pathology. In the literature, only single cases of simple cysts of the clivus and axis have been reported [7].

However, treatment of patients with atlantoaxial instability caused by various diseases of the skull base and craniovertebral junction combined with ventral compression of the brainstem is a complex issue that is ambiguously resolved in different ways. [8—13].

In the past, the use of a transoral approach for surgical treatment of various pathologies of the craniovertebral junction was accompanied by a rather high rate of severe complications such as cerebrospinal fluid (CSF) fistula, meningitis, deterioration of the neurological status, and prolonged healing of the posterior pharyngeal wall [14, 15]; at present, the use of a microscope, improvement of the approach procedure, and optimization of the microsurgical technique for manipulations within the lesion have reduced the rate of these complications from 6—8% to 3% [16, 17]. In addition, previously used posterior decompression is now less effective than anterior decompression [16, 18—20].

We demonstrate a surgical treatment approach for an aggressive aneurysmal cyst of the C2 vertebra, which includes three stages: a puncture biopsy and occipitospondylodesis (1st surgery); transoral removal of the cyst with simultaneous anterior stabilization of the C1—C3 spinal segment with an individual system (2nd surgery); remodeling of the occipitospondylodesis (C0—C4) system into the C1—C3 posterior stabilization system (3rd surgery).

Clinical case

A 31-year-old male patient M. Clinical diagnosis: an aggressive aneurysmal bone cyst of the C2 vertebra. The patient presented to the Priorov National Medical Research Center of Traumatology and Orthopedics (NMRCCTO) with complaints of local pain in the neck
and restricted motion in the cervical spine for surgical treatment.

In November 2015, after falling from a height of his height (during skating), the patient developed pain in the cervical spine.

An examination revealed restricted motion and pain in the cervical spine. There were no motor and sensory disorders in the extremities; pelvic functions were preserved.

Spiral computed tomography (SCT) and magnetic resonance imaging revealed destruction of the C2 body and odontoid process, which corresponded to an aneurysmal bone cyst, as well as disruption of the C2 posterior body wall and odontoid process (Fig. 1).

Given an extremely high risk of a C2 pathological fracture associated with gross neurological deficit and threatening to the patient’s life, he underwent (18.02.2016) a puncture biopsy of the C2 body through the submandibular approach as well as posterior occipitocervical spondylodesis with metal instrumentation from the occipital bone level to the C4 vertebra (Fig. 2).

An examination of the biopsy material, including that obtained later during the second operation, revealed a histological picture of an aggressive aneurysmal bone cyst: a fibrous stroma containing blood-filled cavities, highly mitotic fibroblasts, histiocytes, siderophages, and single osteoclast-like multinucleated giant cells. There were cavities of various configurations and sizes, which were lacking the endothelial lining. Stromal cells were monomorphic; atypical mitoses were not found. There were signs of reactive osteogenesis as well as connective tissue septa separating cavernous cavities (Fig. 3).

The postoperative period was uneventful. Given the clinical and radiographic picture as well as the histological opinion after the puncture biopsy, a decision was made to perform the second stage of surgery: transoral removal of the odontoid process and C2 body lesion and anterior stabilization of the C1—C3 spinal segment using a personalized stabilization system [21] containing an additional supporting element (Fig. 4).

The second stage of surgical intervention was performed on April 6, 2016.

**Description of surgery:** the patient was in the prone position. Tracheostomy was performed. Endotracheal anesthesia was used. A mouth gag was placed. Further, all surgical stages were performed under a microscope. A linear paramedian incision of the soft palate and a linear median incision of the posterior oropharyngeal wall were performed. The anterior C1 arch and anterior parts of the C2—C3 segment were skeletonized. The C2 body was trepanned, and the C2 body and odontoid process lesion was resected. A personalized stabilization system was placed on the anterior parts of the C1—C3 vertebrae, with upper and lower parts of the plate being placed on the anterior surface of the C1 vertebra and on the C3 body, respectively. An additional supporting element was placed on the inferior surface of the C1 vertebra and the superior surface of the C3 vertebra. Then, the personalized stabilization system was fixed by two screws inserted into the C1 lateral masses and two screws inserted into the C3 body (Fig. 5). Intraoperative X-ray control showed the correct positioning of metal instrumentation (Fig. 6a). The operative wound was sutured in layers. The total duration of surgery was 4.5 h. After surgery, control X-ray and SCT were performed (Fig. 6b, c, d).

Given the stability of C1—C3 fixation, a decision was made to shorten the posterior metal fixation device to increase the range of active motions in the cervical spine. On 21.04.2016, the system enabling occipitocervical spondylodesis was removed, and a system for posterior stabilization of the C1—C3 cervical spine segment was placed.

Control X-ray in a lateral projection and SCT with 3D reconstruction in a sagittal projection revealed the correct positioning of devices for anterior and posterior stabilization of the C1—C3 vertebrae (Fig. 7).

The postoperative period was uneventful. A follow-up CT examination 8 months after surgery demonstrated...
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the correct positioning of systems for anterior and posterior stabilization of the C1—C3 vertebrae (Fig. 8).

Discussion

An aneurysmal bone cyst is a benign destructive bone lesion characterized by reactive growth of connective tissue containing blood-filled cavities [22, 23]. It develops at any age, but mainly in the bones of the immature skeleton. Up to 80% of patients with aneurysmal bone cysts are children and adolescents under the age of 20 years [1]. The disease can affect any bone but most often involves the metaphysis of long bones: the distal femur and proximal tibia and humerus as well as posterior elements of the vertebral bodies [3, 23]. The disease occurs more often in males. About 70% of aneurysmal bone cysts are located in the thoracolumbar spine, and less than 25% of lesions occur in the cervical spine [24].

If an aneurysmal bone cyst is suspected, it is desirable to perform an open biopsy to verify the pathological process because a core needle puncture biopsy does not always identify specific signs necessary for the diagnosis of an aneurysmal bone cyst [25]. However, the puncture biopsy results in the presented case were quite informative and provided indications for the second operation.

The diagnosis of an aneurysmal bone cyst is primarily differentiated from telangiectatic osteosarcoma, giant cell tumor of bone, low-grade osteosarcoma containing a secondary aneurysmal bone cyst, solitary bone cyst, and hemangioma [1, 22].

The most common approach for treating various diseases accompanied by atlantoaxial instability and anterior compression of the brainstem and upper cervical spine segments is transoral decompression followed by posterior stabilization of the upper cervical spine or the reverse sequence of steps of this operation — posterior stabilization followed by transoral removal of the lesion [9, 14, 26—30]. However, an increasing number of authors have paid attention to the possibility of anterior stabilization of the atlantoaxial junction, which enables one stage surgery without intraoperative turning of the patient [8, 31—35].

J. Štulík and co-authors [36] described a case of total spondylectomy of the C1 vertebra in solitary metastasis of thyroid adenocarcinoma. Posterior fixation of the C1—C4 was performed at the first step; then, resection of the C2 body with the lesion and simultaneous C1—
C3 fusion with a mesh cage were performed through the anterior transmandibular approach (with dissection of the mandible). It is necessary to note that their approach was much more traumatic compared to our technique [21].

At present, treatment of a C2 aneurysmal cyst usually involves transoral removal of the cyst followed by posterior stabilization — occipitopondylodesis [37] or the reverse sequence (1st stage — occipitopondylodesis, 2nd stage — transoral removal of the lesion) [7].

In the literature [38―40], there are data on the use of puncture vertebroplasty in lytic processes in the C2 body using both submandibular and transoral approaches. In our case, the use of this technique would be associated with a high risk of cement leakage towards the spinal canal with compression of the dural sac due to a bone defect in the C2 posterior wall.

Anterior stabilization of the atlantoaxial junction was first described by R. Schmelzle and co-authors [41]. On the basis of biomechanical and clinical studies, many authors [15, 16, 42, 43] have demonstrated that anterior stabilization is a good alternative to posterior fixation of the atlantoaxial junction; however, there are disadvantages of the Harms plate, which are associated with its design [42]. In addition, a high rate of screw loosening has been noted [15, 43]. To eliminate these disadvantages, F. Kandziara and co-authors [42] combined anterior stabilization using the Harms plate with additional posterior stabilization using wire, as described earlier by A. Brooks and E. Jenkins [44]. The use of this combined stabilization improved the biomechanical and clinical results [15, 42], but the need for an additional approach was an obvious disadvantage.

There is screw transarticular stabilization of the C1—C2 vertebrae, which has demonstrated good results in treatment of patients with various pathologies of the craniovertebral junction [45]. For odontoid process fractures, Y. Hu and co-workers [46] suggested using an anterior odontoid screw plate for C1—C3 internal fixation. N. Xu and co-authors [47] proposed to use personalized 3D-printed vertebral bodies for reconstruction of the upper cervical spine.

The developed transoral anterior reduction plate (TARP) system has shown good results in biomechanical and clinical trials [8, 33, 48―50]. The authors marked the TARP advantages such as the versatility and capability of fusion of the C1—C2 segment [8]. Zhang Baochen and co-authors [51] suggested using a transoral atlantoaxial anchored cage system that demonstrated promising results in biomechanical studies.

We have developed a system for anterior stabilization of the C1—C3 vertebrae [21], the adjoining surface of which is completely congruent to the anterior surface of the C1—C3 spinal segment in a particular patient. The system has a supporting element with additional points of support on the inferior articular surface of the C1 and the
superior part of the C3 body and also includes locking elements that prevent screw loosening. The stabilization system is manufactured using mathematical modeling of the craniovertebral segment in a particular patient (Fig. 4a). This mathematical model is used to prepare a stereolithographic model of the craniovertebral segment from special plastic (Fig. 4b, c) and an anterior stabilization system from a titanium alloy (Fig. 4d, e). We also conducted a study comparing the biomechanical efficiency of anterior and posterior stabilization devices, which demonstrated the superiority of anterior stabilization of the atlantoaxial junction [52].

The presented clinical case demonstrates the effectiveness of C1—C3 anterior stabilization. The device for C1—C3 anterior stabilization was included in the joint scientific project of the Burdenko Neurosurgical Institute and Priorov National Medical Research Center of Traumatology and Orthopedics “The technology of craniovertebral junction reconstructive surgery with personalized stabilizing devices” (authors: A.N. Shkarubo,

**Fig. 5. Intraoperative image.**
The correct positioning of a system for anterior stabilization of the C1—C3 vertebrae.

**Fig. 6.** a — intraoperative control. The correct positioning of the anterior stabilization system of the C1—C3 vertebrae; b — control postoperative radiograph in the lateral projection — the correct positioning of the system for anterior stabilization of the C1—C3 vertebrae; c — postoperative SCT with 3D reconstruction (sagittal projection); d — postoperative SCT with 3D reconstruction (frontal projection): the correct positioning of the device for anterior stabilization of the C1—C3 vertebrae.

**Fig. 7. Correct positioning of devices for anterior and posterior stabilization of the C1—C3 vertebrae.**
a — X-ray in the lateral projection; b — SCT scan with 3D reconstruction.
A.A. Kuleshov, D.V. Tetyukhin, M.S. Vetrile, I.V. Chernov (that was presented at the World exhibition on inventions, research, and new technologies “Innova Barcelona 2017” (May 4–6, 2017, Barcelona, Spain) and was awarded the Gold medal with mention and the special prize Premio a la mejor innovacion.

Authors declare no conflict of interest.

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This work is devoted to a new surgical technology of transoral cervical stabilization in pathological processes at the C1—C2 level. The authors analyzed a single case of surgery for an aneurysmal bone cyst of the C2 body. The uniqueness of this case is associated with one-stage transoral removal of the lesion and transoral anterior fixation of the vertebrae with an personalized implant—a plate connecting the C1 body and the C3 body. This technology, despite available reports (Crocard, Harms), is unique primarily due to the personalized production of such systems, which ensures full complementarity between the system surface and the surface of the patient’s spine. The technique developed by the authors is very interesting and promising.

A.O. Gushcha (Moscow, Russia)
Brain arteriovenous malformations (AVMs) are the most common congenital developmental cerebrovascular anomaly that manifests clinically. The first disease symptoms usually develop at a young age [1—5]. AVMs account for a small fraction of all neurosurgical diseases, but given the fact that the most frequent disease manifestation is hemorrhage, often with extensive intracerebral hematomas and an unfavorable course, the problem of AVM treatment still remains topical.

To date, the indications for surgical and other treatments of AVM manifesting as intracranial hemorrhage are defined quite clearly [6]. At the same time, the approach to treatment of unruptured AVMs remains a matter of debate. The approach is usually based on comparison of the risk of surgical treatment and that of spontaneous hemorrhage from AVM [7, 8]. This task requires a more accurate evaluation of the rate and clinical significance of these risks. In addition to microsurgical treatment, it is necessary to consider, in the same terms, other existing AVM treatments: endovascular, radiosurgical, and combined.

In recent years, there has been growing interest in treating unruptured AVMs, which is reflected in a number of publications discussing this problem. An analysis of these publications is of great interest because treatment of cerebral AVMs is one of the main activities of the Vascular Department of the Burdenko Neurosurgical Institute and several other neurosurgical clinics in Russia. Below, we present the results of major studies.

A randomized multicenter clinical trial of unruptured brain AVMs (ARUBA)

In 2013, the ARUBA trial results [9] were published. This was the first prospective randomized trial that compared the results of conservative and interventional treatment of unruptured cerebral AVMs using statistical data analysis. A total of 223 patients were randomized. The most frequent AVM manifestations were headache and epileptic seizures, but also a large fraction (42%) of patients had asymptomatic AVMs. The patients were randomized into two approximately same size groups: a conservative treatment group (109 patients) and a group (114 patients) of interventional treatments, including embolization, radiosurgery, microsurgical resection, or combination of these techniques. During 33-month follow-up, stroke or death occurred in 30.7% of patients in the interventional treatment group and in 10.1% of patients in the conservative treatment group. The disability outcome (modified Rankin scale (mRs)) score of 2 or more was present in 46.2% of patients in the interventional treatment group. In the conservative treatment group, there were 15.1% of similar patients. Given the findings, the authors concluded that the conservative management (in fact, observation) of unruptured AVMs was more preferable than surgical and other interventional treatments. It should be noted that during the trial, the authors [10—12] encountered difficulties in recruiting patients, and, therefore, the study was completed earlier than planned, which raised questions about generalization of the results.

A Scottish audit of intracranial vascular malformations (SAIVMs) trial

The results similar to those of the ARUBA trial were obtained in a population-based prospective cohort study, SAIVMs, that compared conservative and intervention treatment groups. Unlike the ARUBA trial, the groups were not randomized. The trial was conducted in two stages: in 1999—2003 and in 2006—2010. The trial used the database of the National Health Service of Scotland. The trial included 204 adult patients with the diagnosis of unruptured AVM aged 16 years and over [13].

Criticism of ARUBA and SAIVMs

Publication of the ARUBA and SAIVMs trial results in journals Lancet and JAMA caused garnered criticism

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by neurosurgeons around the world. According to many researchers, the trials had a number of significant limitations that influenced the reliability of their findings.

Criticisms were reduced to the following provisions.

— In the ARUBA trial, out of 1,740 screened AVM patients, only 226 (13%) patients were randomized. Of the 1,514 non-randomized patients, 1,014 patients were excluded due to a verified hemorrhage history or previous treatment. Of 500 patients who met the trial criteria, 323 patients refused to participate in it, and 177 patients were treated in clinics that did not participate in the trial. In the period from April 2007 to June 2010, only 4 AVM patients were included in the trial at the University of San Francisco (California) with a flow of more than 50 unruptured AVMs per year [10, 14]. Because there was a chance that patients would refuse to participate in the trial, the randomization principle was violated. This approach may also be a cause for a small sample size because the number of those who refused to participate in the trial was 50% more than that of the randomized ones.

— The number of patients in the intervention group (114) and especially in subgroups with different treatment techniques was too small. For example, the microsurgical technique was used in 5 patients, embolization in 30 patients, radiosurgery in 31 patients, microsurgery with embolization in 12 patients, embolization and radiosurgery in 15 patients, and microsurgery with radiosurgery in 1 patient. The advantage of a particular treatment technique cannot be demonstrated with this numerical composition of the groups.

— The choice of a treatment technique in the intervention group raised many questions. For example, 80% of AVMs in the ARUBA trial and 70% of AVMs in the SAIVMs trial were subjected to embolization or radiosurgery. Given the fact that according to meta-analysis of numerous studies on the use of different techniques in treatment of AVMs, which was published in 2011 by van J. Beijnum and co-authors [8], AVM was totally excised in 96% of cases, and full obliteration was achieved in 38% of patients in the case of radiosurgery and in 13% of patients in the case of embolization, the description of treatment techniques does not seem to correspond to the basic principles of AVM treatment [15—20]. In addition, according to the same meta-analysis, the risk of hemorrhage after microsurgical treatment is 9-fold less than that after endovascular or radiosurgical treatment. According to some authors [21], partial AVM occlusion even increases the risk of hemorrhage in the future. A high percentage of death, stroke, and disability in the intervention group of the ARUBA trial is probably due to the risks of certain treatment types associated with a high probability of incomplete AVM obliteration, which, in turn, increases the risk of hemorrhage.

— In the ARUBA trial, 90% of AVMs were grade I—III Spetzler–Martin (S–M) malformations, the so-called low-grade AVMs. These malformations are well known to be most often suitable for microsurgical treatment due to a low risk of complications. However, despite the fact that 76 (68%) patients in the interventional treatment group had low-grade AVMs, only 18 patients underwent microsurgical resection [22, 23].

— Complications after surgical interventions most often occur in the early postoperative period. Symptoms developing in the long-term period may be a manifestation of the natural course of the disease — hemorrhages from the residual part of an incompletely occluded AVM. In the ARUBA trial, the endpoint (hemorrhage or death) was reached by 10% of patients in the observation group and by 30.7% of patients in the intervention group.

In most studies of hemorrhagic stroke, the outcome has been evaluated by using the mRs at the end of the entire follow-up period. This is a quite simple way to assess the clinical condition of the patient. Potential death or disability (mRs score ≥2) was chosen as an intermediate point. Over 36 months, this outcome occurred in 6 (14%) of 43 patients in the observation group and in 17 (38.6%) of 44 patients in the intervention group. The number of deaths was similar (2 cases in the observation group and 3 cases in the intervention group). A high risk of complications (38.6%) in the intervention group significantly differs from the literature data on outcomes of treatment of small unruptured AVMs located outside functionally significant areas. Also, the trial did not analyze the causes of poor outcomes of interventional treatment (intervention techniques or AVM features).

— Initially, the ARUBA trial design included a 5-year follow-up. However, after reaching a mean follow-up of 33.3 months (interim analysis), the trial was stopped. In this regard, it should be noted that death or disability in the intervention group occurs usually directly after treatment, unlike the observation group where negative consequences of the disease can accumulate for many years. For example, in a study by H. Zaidi and co-authors [24], an analysis of a series of more than 1,000 AVMs with a mean follow-up period of more than 10 years revealed that the benefits of surgery may manifest over the years. This is associated with a cumulative risk of hemorrhage whose mean annual risk amounts to 2%, as well as with a gradual regression of focal postsurgical symptoms. According to the authors of [24], the curves of a potential risk and benefit of surgery will not intersect before 10 years, and the benefits of surgery will become apparent only after 15 years of follow-up. Given a relatively young age at which most AVMs are diagnosed, potential cumulative disability and death due to hemorrhage from unruptured AVMs may reach 100% throughout the patient’s life.

It should also be noted that radiosurgery accounted for a large percentage of operations in the intervention group of the ARUBA trial; the effectiveness of this technique is difficult to assess upon a follow-up examination earlier than 3 years, given the obliteration window.

Both in SAIVMs and in ARUBA, all treatment techniques were combined in one intervention group, with
non-microsurgical techniques prevailing among them. The degree of AVM obliteration was 63—71% [25].

Of 104 initially planned medical centers, only 39 ones participated in the trial; in this case, in 14 centers, 1 to 2 patients were included in the study, although about 60 patients with AVMs may have been treated in each of the centers during the trial. Therefore, 22 (56%) centers provided ≤5% of the total number of patients included in the trial. The main criterion for choosing the center was its experience of treating at least 10 AVM patients per year, which raises a question because outcomes of surgical treatment of AVMs directly correlate with the experience of their treatment.

Most patients were recruited from European centers (79 patients from France and 51 patients from Germany), and a smaller fraction was from North America (about 40 patients). In these centers, there are different traditions in the AVM treatment strategy. For example, the concept of endovascular and radiosurgical treatments dominates in European clinics, while the microsurgical approach is actively used in the USA [26].

In December 2016, a conference on AVM treatment problems was held in Milan, which was attended by 24 members of the European Association of Neurosurgeons, European Society of Interventional Therapy, and European Society for Radiosurgery, including representatives of the microsurgical and radiological departments of the Burdenko Neurosurgical Institute [27].

The following key issues on the treatment of AVMs were discussed and harmonized:

1. Cerebral AVMs are a complex disease associated with potentially severe natural history.
2. The ARUBA findings cannot be used in the treatment of unruptured AVMs.
3. Given the available combined treatment modalities, the choice of a treatment approach should be made with participation of all relevant experts involved in the treatment of this pathology.
4. Data on the potential risk of hemorrhage and the restrictions of everyday activities in patients with unruptured AVMs are sufficient indications for surgical treatment of unruptured low-grade AVMs (grade I and II S—M).
5. On the basis of a collective decision in each specific case, there may be indications for treating high risk (higher grade S—M) AVMs, based on a case-to-case decision of the experienced team.
6. If treatment is indicated, the primary strategy should be approved by the multidisciplinary team.

After considering the advantages and disadvantages of a randomized study, the participants proposed a prospective European multidisciplinary registry for treatment of AVMs.

Other studies carried out in accordance with the ARUBA criteria

The ARUBA trial results prompted many neurosurgeons to conduct their own research to evaluate the results of AVM treatment using various techniques. A number of papers were published, in which groups of patients were selected according to the ARUBA trial criteria in order to more correctly compare the results. These criteria included MRI-verified unruptured AVMs; an age over 18 years; no previous treatment. Below, we present the results of these trials.

In 2016, J. Wong and co-authors [28] published a study that included 155 patients who underwent microsurgical treatment. The mean follow-up period was 36 months. Total AVM excision was confirmed by cerebral angiography (CAG) in 98.1% of cases. There was reported an early postoperative deficit and permanent disability (mRs score ≥3), which amounted to 12.3% and 4.5% for the whole group, respectively, and 9.3% and 3.4% for grade I and II (S—M scale) AVMs, respectively.

M. Javadpour and co-authors [29] conducted a prospective study of the treatment outcomes in 34 patients in a microsurgery group where patients with grade I and II (C—M scale) AVMs accounted for 70.5%. All patients underwent total AVM resection, which was confirmed in each case by CAG data. There were no hemorrhagic and ischemic strokes and deaths in the follow-up period. Neurological symptoms developed immediately after surgery were persistent and remained unchanged 6 months after surgery in 14.7% (mRs score ≥1) and 6% (mRs score ≥2) of patients.

The most common complication in patients was persistent visual impairment.

A study by J. Schramm and co-authors (2017) [30] is one of the recent large surgical trials. This prospective study included 288 AVM patients (144 patients with unruptured AVMs) operated on by a single neurosurgeon within 29 years. One hundred and four patients met the ARUBA criteria. In this subgroup of 63 patients with grade I and II (S—M) AVMs, 9 (14.3%) patients had persistent disability (mRs score ≥2). Small AVMs (less than 3 cm in diameter) accounted for most (53.5%) of the 288 AVMs. On the basis of analysis of this subgroup, the authors concluded that microsurgical resection of these AVMs provided better outcomes (persistent disability was 7.8%, with significant disability amounting to 3.2%) compared to those of multimodal or conservative treatment.

For retrospective analysis, J. Nerva and co-authors [31] selected groups of patients after radiosurgery and microsurgery, 49 and 51% of patients, respectively. In the microsurgery group preoperative AVM embolization was performed in 84% of cases. In the surgery group, a persistent neurological deficit was observed in 5% of cases with grade I and II (S—M) AVMs and in 50% of patients with grade III—V AVMs. Assessment of the follow-up data revealed that there were no outcomes scored...
2 (mRs) in the group with grade I and II (S–M) AVMs, and 33% of patients in the group with grade III–V (S–M) AVMs were disabled (mRs score ≥2). Thus, the authors concluded that surgery in patients with grade I and II (S–M) AVMs who met the ARUBA trial criteria helped achieve excellent treatment results.

W. Rutledge and co-workers [32] conducted a similar retrospective analysis. The intervention group (61 patients) combined microsurgery, radiosurgery, as well as embolization, with the last being used as an independent treatment only in 1 case. Hemorrhage or death occurred in 5 (11.6%) of 43 patients after microsurgery and in 4 (26.7%) of 15 patients after radiosurgery, which was less than these indicators in the intervention group of the ARUBA trial. To compare the results, the authors recruited an observation group of 13 patients with similar parameters. Primarily, there was no significant difference between the intervention group and the observation group in functional outcomes. The poor functional outcome or death (mRs score ≥3) occurred rarely: in 2 (4.8%) of 41 and in 1 (7.7%) of 13 patients in the surgery and observation groups, respectively.

Other trials not complying with the ARUBA criteria

In 2015, M. Potts and co-authors [14] reported their experience in treatment of 112 unruptured AVMs in order to clarify the safety and efficacy of microsurgery for low-grade AVMs. The authors marked a more favorable outcome in patients with unruptured AVMs (good functional outcomes (mRs score of 0 or 1) in 91% of cases) compared to patients with ruptured AVMs (61%). The authors also analyzed all studies on microsurgery of low-grade AVMs since 1986, which included a total of 1,235 patients. They presented the analysis results as Table. The mean postoperative disability and mortality amounted to 2.2% and 0.3%, respectively.

On the basis of the analysis, the authors concluded that microsurgery should be selected as the “gold standard” in treatment of most low-grade AVMs, with exception of deep AVMs or malformations located in functionally significant areas for which radiosurgery is the method of choice.

M. Elhammady and R. Heros [33] analyzed an even narrower group of asymptomatic AVMs. The group included 31 patients after radiosurgical treatment. Grade I–III (S–M) AVMs of relatively small size accounted for 94% of the cases. The rate of obliteration after 5 years after treatment was 78%, and the annual rate of hemorrhage was 1.7%. In conclusion, the authors note that, despite a high efficiency of radiosurgical treatment, this technique in the case of grade I–III (S–M) AVMs is more relevant in elderly and somatically severe patients with small malformations and is just an alternative to microsurgical resection that is preferred when applicable, especially in young and somatically healthy patients.

D. Bervini and co-workers [34] reported a rather large series of 368 patients with unruptured AVMs who underwent microsurgical resection. The mean follow-up period was 270 days. Total resection confirmed by CAG data was achieved in 97.7% of cases. In patients with unruptured Spetzler-Ponce class A AVMs (corresponding to grade I and II S–M AVMs), a new persistent neurological deficit (mRs score ≥2 and mRs score ≥3) was observed in 14 and 2.8% of cases, respectively. After surgical treatment of patients with Spetzler-Ponce class C AVMs (corresponding to grade IV and V S–M AVMs), the deficit was present in 38.6% and 15.9% of patients. Thus, given the rate of a new neurological deficit (mRs score ≥3) in patients with Spetzler-Ponce class A and B AVMs, the outcomes of surgical treatment are better than those of conservative treatment.

In a reported series of 220 patients with low-grade AVMs followed-up after microsurgical resection, M. Morgan and co-authors [23] noted that the mean postoperative disability and mortality were 0.9% and 0.5%, respectively. There were no postoperative hemorrhages.

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Number of patients</th>
<th>Disability,%</th>
<th>Mortality,%</th>
<th>Cure,%</th>
<th>Hemorrhage,%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spetzler &amp; Martin, 1986</td>
<td>44</td>
<td>2.3</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Heros et al., 1990</td>
<td>47</td>
<td>2.2</td>
<td>2.2</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Sundt et al., 1991</td>
<td>84</td>
<td>2.2</td>
<td>0</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Saisti et al., 1993</td>
<td>67</td>
<td>1.5</td>
<td>0</td>
<td>94</td>
<td>0</td>
</tr>
<tr>
<td>Hamilton &amp; Spetzler, 1994</td>
<td>40</td>
<td>0.0</td>
<td>0</td>
<td>100</td>
<td>NA</td>
</tr>
<tr>
<td>Shaller &amp; Schramm, 1997</td>
<td>50</td>
<td>34.2</td>
<td>0</td>
<td>NA</td>
<td>2</td>
</tr>
<tr>
<td>Schaller et al., 1998</td>
<td>81</td>
<td>0.0</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Pikus et al., 1998</td>
<td>26</td>
<td>3.8</td>
<td>0</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Hartmann et al., 2000</td>
<td>48</td>
<td>6.6</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Morgan et al., 2004</td>
<td>220</td>
<td>0.9</td>
<td>0.5</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Davidson &amp; Morgan, 2010</td>
<td>296</td>
<td>0.7</td>
<td>0</td>
<td>97</td>
<td>NA</td>
</tr>
<tr>
<td>Lawton, 2014</td>
<td>232</td>
<td>2.4</td>
<td>0.5</td>
<td>98</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>1,235</td>
<td>2.2 (median)</td>
<td>0.3 (median)</td>
<td>98.5 (median)</td>
<td>0.3 (median)</td>
</tr>
</tbody>
</table>
In the mentioned large meta-analysis of treatment of all cerebral AVMs, including ruptured and unruptured ones, in particular high grade S—M AVMs, total resection was achieved in 96% of cases, and complete obliteration was achieved in 38% of cases upon stereotactic radiosurgery and in 13% of cases upon embolization. The rate of severe complications was 7.4% of cases after microsurgery, 6.6% after endovascular occlusion, and 5.1% after radiosurgery [8]. It should be noted that the presented rate of complications is much lower than that in the ARUBA trial. The results of this meta-analysis are consistent with the results and current trends in the treatment of AVMs.

Therefore, according to most of the studies, microsurgical resection is the method of choice for low-grade AVMs.

**Planned randomized studies on surgical treatment of AVMs**

Given the ARUBA trial results, the design of a large randomized BARBADOS trial is now planned and developed [35] to finally confirm preference of microsurgical treatment over other treatment/observation. The trial will include only those centers where, according to a preliminary assessment, the rate of postoperative disability in the case of unruptured low-grade AVMs is no more than 10%.

**REFERENCES**


**Conclusion**

Despite the fact that ARUBA and SAIVMs are prospective, multicenter, and randomized trials, their results are at odds with the numerous and quite good results of microsurgical AVM treatment reported in other papers. Given this fact as well as many errors in the design of these trials, the choice of a treatment approach for unruptured AVMs still remains controversial and does not have standardized criteria for the indications for surgery.

The unification of approaches to the treatment is complicated by heterogeneity of the disease, variety of treatment techniques, small number of observations in certain clinics, and differences in the experience of neurosurgeons.

The current global trend in the neurosurgical community to plan new multicenter, prospective, and randomized studies with a modernized design is most rational for overcoming these difficulties. These studies will provide the most reliable basis for defining clinical recommendations.

**Authors declare no conflict of interest.**
This article, which is actually a literature review, is devoted to one of the topical problems of vascular neurosurgery — management of unruptured arteriovenous malformations (AVMs). The main discussion covered in the literature refers to the choice of treatment for these AVMs.

In particular, much attention is paid to the comparative characteristics of the microsurgical technique and minimally invasive techniques such as endovascular interventions and radiosurgery. Combined techniques are also widely discussed. The presented work contains a thorough analysis of the literature data from 36 references. The article corresponds to the journal scope and is of undoubted practical interest because it summarizes the experience gained by many authors and may facilitate making a more adequate and reasonable decision when choosing a certain treatment modality. The study design meets the modern standards; the list of references may be considered complete. There are no major comments, no plagiarism, and no conflict of interests.

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