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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.
Navigation systems are being used in neurosurgery for more than 20 years [1]. The first available frameless neuronavigation system ISG Magic Wand was based on electromagnetic technology [1, 2]. Later on, neuronavigation systems were based on both electromagnetic and optical tracking techniques [3—5].

Most neuronavigation systems developed in 1990—2000ss were based on technically simpler optical tracking technology. The initial version of this technology was associated with the use of infrared LEDs, whose light was captured by receiving camera. Positioning of LEDs near to the patient’s head on a special holder (localizer) provided a coordinate system that integrated the individual patient’s anatomy with neuroimaging data. LEDs mounted on surgical instruments allowed a surgeon to track their movements. Bulky block of LEDs and connecting electrical cables restricted manipulation of tools, which led to the development of passive optical tracking technology. In this case, spatial position of the localizer and surgical tools was traced using special polymer spheres with an infrared reflective coating located in the field of view of the camera combined with infrared radiation source. The spheres can be located on the tool (most often, biopsy needle) or special universal adapter.

Electromagnetic field generator (both direct and alternating current) is the main element of the electromagnetic navigation system. The generator is located in the immediate vicinity of the patient’s head, and electromagnetic field produced by the generator is the basis for the coordinate system. Miniature sensor can be directly inte-
grated into the tool or fixed thereon using a special clamp. The system determines the coordinates of the tool by measuring electromagnetic field density at each point. Sensors on the tools produced by various navigation system manufacturers differ in their location and size. Sensor positioning at the proximal and distal ends of the tool enable bending the tool, when necessary, while preserving navigation accuracy. Geometrical characteristics of the tools with the only sensor located at the distal end of the tool should remain unchanged during the operation. DC generators necessitate the use of quite large sensors and the resulting field is more vulnerable to various factors (metal, electromagnetic interference). Electromagnetic field produced using AC is more resistant to external interference [6, 7]. Electromagnetic navigation system may also be implemented as a separate module within the optical navigation system structure. However, the latter option complicates the system and reduces its mobility.

The latest trends in the development of electromagnetic navigation systems include their mobility and portability, the possibility to integrate them into the existing ecosystem of an operating room, and minimization of sensor size. At the same time, our analysis of the literature showed that some methodological and practical aspects of the use of electromagnetic navigation systems should be specified. Therefore, practical application of electromagnetic navigation with various neuroimaging modalities should be assessed and the impact of various instruments on navigation accuracy should be evaluated in order to make the conclusion about the possibility of combining the method with neurophysiological monitoring and assess its practical benefits. The features of patient’s draping and positioning, location of electromagnetic field generator, and selection of localizer (patient’s localizer is a small device, which is the reference point in the navigation coordinate system) should be specified. The localizer can be directly fixed to the patient’s scalp with adhesive base (noninvasive variant) or transdermally to the skull bone using a special screw (invasive option).

Materials and methods

Electromagnetic navigation system was used for 102 operations in 98 patients (42 males and 56 females, including 18 children; median age, 34.8 years (min, 2.2 years; max, 69 years) in the period from December 2012 to December 2016. In 36 patients, the system was used for endoscopic interventions. In 19 patients, electromagnetic navigation was used in combination with neurophysiological monitoring. Computed tomography (CT) data were used as the calculated values in 67 operations. Magnetic resonance imaging (MRI) data were used in 34 operations, including 13 studies on 3T tomograph, and 21 studies on 1.5T-tomograph. CT and MRI studies carried out at our institute were used for navigation in 63 cases and the data of studies carried out at other institutions and reported in patient’s medical histories were used in 38 cases. All studies were performed in the axial projection. In most cases, the thickness of MRI slices was 1.2 mm, and the thickness of CT slices was 0.625 mm. In 5 cases, MRI data with a step size of 5 mm were used for navigation, which was a necessary measure, since high quality data could not be obtained in a short time for technical reasons.

Frameless electromagnetic navigation system Fiagon (Fiagon GmbH) was used in our study during brain surgery (both open and endoscopic). It consists of a compact portable unit with preinstalled software and an electromagnetic field generator, which can be built in a universal operating table head support or placed separately (Fig. 1).

Electromagnetic field generated around the patient’s head by a generator forms the so-called “working volume”, where tool movements can be monitored with allowance for the direction and spatial orientation of their axes. Unlike optical navigation systems, which necessitate localizer positioning on a special holder next to the fixed patient’s head located in the field of view of infrared camera, electromagnetic navigation system enables positioning of a miniature localizer directly on the patient’s head, and therefore the position of the patient’s head can be freely changed during surgery, if necessary. When using the optical navigation system and stationary fixation of the patient’s head in the Mayfield clamp, accidental displacement of the patient’s head leads to disturbed spatial relationships with the localizer, which makes navigation impossible. Positioning of electromagnetic system localizer directly on the patient’s head completely eliminates this problem, which improves the safety of the operation. As mentioned above, both non-invasive and invasive localizer fixation to the patient’s head can be used (Fig. 2).

We used both original tools, including navigated rigid and flexible pointers and tips for vacuum cleaners, and conventional neurosurgical instruments (ventricular catheters, endoscopes, forceps for bipolar coagulation, and tips for aspirators), which were navigated universal adapters placed therein, in our neurosurgical practice (Fig. 3).

Results

In our series of observations, frameless electromagnetic navigation system was used in 66 transcranial operations. Distribution of operations according to pathology type is shown in Table 1. Most operations in this group were associated with primary and secondary brain tumors. Navigation error averaged 1.9±0.5 mm.

Electrophysiological monitoring was used along with navigation systems in these operations and during epileptogenic foci resection. Pre-planning and computer modeling of the area of interest provided detailed assessment
of the individual anatomy, and the use of bipolar electrode for intraoperative navigation enabled mapping of cerebral cortex areas (Fig. 4).

In 5 cases, the data of preoperative functional MRI (fMRI) and tractography were used for navigation. It should be noted that modern image processing systems enable including fMRI results, as well as the structure of the conduction tracts, directly to the DICOM format. The use of navigation system, integrating data related to specific features of the functional neuroanatomy, enables cross comparison of these methods during intraoperative neurophysiological control.

At the same time, we observed interference and significant high-frequency noise distorting electrophysiological data in all 7 operations with simultaneous application of direct cortical stimulation.

Taking into account the effect of brain displacement increasing during the operation, especially when the process is located deep in the brain substance, the role of the navigation system is somewhat leveled and the surgeon have to rely on additional intraoperative navigation methods, such as intraoperative ultrasound and fluorescence diagnostics [1, 8—10]. The use of neuronavigation in treatment of various pathological processes (e.g., removal of various foreign bodies) of the skull base is of great importance for surgeons [11—14].

At the same time, it should be noted that the smaller linear dimensions of the navigation tools in the electromagnetic navigation system, compact size of adapters for neurosurgical tools (aspirator tips, forceps for bipolar coagulation), and no need in continuous maintaining the line of sight between the tools and camera provide the surgeon performing “awake craniotomy” with more freedom within the operating field and enable navigation with almost no delays, using complex drape and changing the position of patient’s head and operating table angulation in wide range, when necessary.

Our observations have shown that positioning and fixation of the localizer directly on the patient’s head does not require much effort and reduces the positioning error rate due to the ease of fixation process and completely eliminates the problem of accidental displacement of the patient’s head with respect to localizer.

Therefore, the localizer should be placed directly on the patient’s head in all cases and fixation option should be selected depending on the clinical situation. In our opinion, fixation with a bone screw is the most reliable option and its invasiveness is not higher than that due to locking spike of the Mayfield clamp.

In addition, some operations with the use of electromagnetic navigation, especially in pediatric patients, does not require rigid fixation of the patient’s head (rigid fixation disables the use of optical systems in these operations).

In particular, electromagnetic navigation is the best choice for shunting operations. Navigation of ventricular catheters can be carried out both using a special pointer for catheter navigation and with a universal adapter for navigation of neurosurgical tools (Fig. 5).

Furthermore, the guide port of the endoscope can be navigated during the ventricular endoscopy, using installed adapter.

Errors and difficulties in application of intraoperative electromagnetic navigation system during transcranial operations

There were no cases of technical system failure leading to cessation of operations in our series of observations. In 5 cases, significant navigation error (more than 3 mm) was associated with the use of neuroimaging data with an increment of more than 3 mm, resulting in “stepped” artifacts in the model and reducing registration accuracy. Registration is understood as the process of combining the virtual model of the patient’s head with corresponding reference anatomical points on the patient’s head. After complete registration, navigational tool movement along the patient’s head results in visualization of intracranial structures corresponding to its position in orthogonal projections on the screen. In another 3 cases, combination of patient’s anatomical data with neuroimaging data was complicated due to the presence of artifacts from the head locks, which are commonly used in CT studies. In these cases, registration error was 4 mm. Registration quality also affected the total error. Excessive recording rate and inconsequential touching points on the patient’s head surface lead to errors in alignment of patient’s individual anatomy and the virtual model by the system and require repeated registration (4 patients). In 6 cases, the use of non-invasive localizer fixation resulted in an unrecoverable navigation error (>5 mm). This was due to its poor fixation to the skin or subsequent displacement by surgeon’s or assistant’s hand. In one case, an unrecoverable navigation error was associated with localizer fixation on the Mayfield clamp and accidental displacement of the patient’s head due to insufficiently secure fixation. In most transcranial operations, the patient’s head is draped in such a way that repeated registration of the patient is impossible even with the use of the electromagnetic system.

We observed no significant interference between the standard metal surgical instruments (clamps, forceps, aspirators) located near the patient’s head and the navigation system in all our cases. The use of conventional light-alloy Mayfield clamp for head fixation, the arc for a skin flap fixation, and retraction systems had no impact on the navigation system functioning. Similar results were also obtained in the article by Hayhurst et al. [5]. In 2 cases, where massive wound retractor located in close vicinity of the patient’s localizer were used, we noted the interference and navigation error over 10 mm due to significant distortion of the electromagnetic field. Change or repositioning of the retractor eliminated the interference and restored navigation accuracy.
Our observations have shown that intraoperative use of electromagnetic field generator simultaneously with such neuromonitoring options as electrocorticography with application electrodes and direct cortical stimulation resulted in interference in all 7 cases. No interference was observed when using transcranial motor evoked potentials, somatosensory potentials, and visual evoked potentials. Temporary deactivation of electromagnetic field generator completely eliminates the aforementioned problem.

Thirty-six transnasal endoscopic procedures were carried out using electromagnetic frameless navigation system (Table 2). Navigation error averaged 2.5±0.8 mm.

Most patients had various skull base tumors (mostly pituitary tumors), and various inflammatory processes in the basal sinuses. We used both invasive and non-invasive options of localizer fixation on the patient’s head during endoscopic operations. In our opinion, localizer fixation to the bone in the optimal option in the case of transphenoidal endoscopic operations. Its small size compared to the headband (noninvasive localizer fixation option) does not hinder patient’s registration, and do not disable placement of anesthetic depth monitor on the patient’s head.

**Errors and difficulties in application of intraoperative electromagnetic navigation system in endoscopic operations**

The aforementioned errors associated with the use of navigation systems in transcranial open operations also arise in endoscopic operations. It should be kept in mind that although non-invasive localizer fixation to the skin is sufficiently secure, its displacement with the skin is still possible. The skin should be first defatted with alcohol at the intended localizer site, since otherwise the fixation may be insufficiently secure. We observed 3 cases of localizer displacement (it was displaced by surgeon’s or assistant’s hand in two cases and due to inadequate skin preparation at the site of fixation in one case).

We believe that invasive localizer fixation is the most appropriate option during endoscopic operations, since it is the most secure one. Correct draping of patient’s head, which enables repeated registration of the patient, when necessary, or intraoperative navigation precision control is an important factor in the case of transnasal endoscopic operations. Treatment of the medial area of patient’s face and frontal skin and their draping should be carried out so that to provide access to anatomical landmarks, such as the outer and inner corners of the eyes, philtrum, glabella, and frontal skin. More compact arrangement of instruments and surgical team during endoscopic interventions increased the likelihood of the impact of various massive tolls and objects on the navigation accuracy. We found that running high-speed drill or side table located in the vicinity of the patient’s localizer resulted in electromagnetic field distortion and loss of navigation precision. Elimination of this interference resulted in automatic recovery of navigation accuracy. At the same time, simultaneous navigation using pointer and running drill in the nasal cavity did not resulted in errors, apparently, due to sufficient distance between the tool and localizer.

In our view, localizer fixation using a headband hinders surgeon’s work, since it limits the recording area in the frontal region. In our case, the dimensions of the
Fig. 2. Variants of patient’s localizers.

a — non-invasive mounting of a localizer using a headband; b — non-invasive mounting of a localizer to the skin with an adhesive pad; c — invasive localizer fixation to the bone with a screw.

Fig. 3. Navigation tools.

a — a universal pointer for patient registration; b — a universal adapter for neurosurgical tools; c — rigid navigation pointer; d — flexible navigation pointer; e — navigated aspirator tip.
headband disabled simultaneous application of noninvasive anesthetic depth monitor, which could adversely affect the anesthetic management of the operation.

**Discussion**

Comparative accuracy of frameless optical and electromagnetic navigation systems for a long time remained a subject of debate. An analysis carried out by J. Rosenow et al. [15] and A. Sieskiewicz et al. [16], who studied optical and electromagnetic navigation systems, found no fundamental differences between these systems in terms of accuracy. In this paper, we did not compare two types of navigation systems, since we believe that the published evidence of their equivalence in terms of accuracy is sufficient. Analysis of our series of observations also confirmed the statement of U. Spetzger et al. [17] that the human factor has a major impact on system accuracy.

We found no significant difference between CT and MRI data used as calculated values in terms of navigation accuracy. We also found no significant difference when using the results of 1.5T- and 3T-scans for navigation, although S. Poggi et al. [18] suggests that there is a negative impact of MRI image distortion on the navigation accuracy.

---

**Table 1. Distribution of transcranial open operations according to neurosurgical pathology type**

<table>
<thead>
<tr>
<th>Pathology type</th>
<th>Number of patients (operations)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain tumor</td>
<td>24 (24)</td>
</tr>
<tr>
<td>CSF shunting operations</td>
<td>8 (8)</td>
</tr>
<tr>
<td>Drainage of liquid space-occupying masses (cysts, abscesses, hematomas)</td>
<td>9 (9)</td>
</tr>
<tr>
<td>Decompression of the orbits in the case of thyroid ophthalmopathy</td>
<td>5 (8)</td>
</tr>
<tr>
<td>Resection of epileptogenic foci</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Vascular pathology (EC-IC bypass, aneurysms)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Reconstruction of posttraumatic orbital defects</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Paranasal sinus pathology (inflammatory processes, cerebrospinal fluid leak, foreign bodies)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Total</td>
<td>63 (66)</td>
</tr>
</tbody>
</table>

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**Fig. 4. Application of neuronavigation during surgery for an intracerebral tumor.**

a — a 56-years-old patient. Ds: glioblastoma of the left temporal lobe. There were no preoperative speech disorders; b — the results of computer simulation of the individual anatomy of the cortical vessels; c — direct cortical stimulation with bipolar electrode equipped with navigation adapter. Electromagnetic field generator was switched off during stimulation. When stimulation in not carried out, the electrode may be used as a navigation pointer; d — the results of temporal cortex mapping. The numerals indicate zones associated with speech disorders (1 — paraphasia, 2, 4 — speech inhibition, 3 — aphasia); e — alignment of the preoperative planning, navigation, and neurophysiological mapping data; f — the results of the control CT in the early postoperative period. Radical tumor resection. Neurological status: no speech disorders.
The use of CT data to build a virtual model of the patient’s head improves its linear resolution due to the smaller scan step compared to that of MRI and significantly improves the segmentation result. Automated or semi-automated overlapping of CT and MRI data sets, when CT data are used for registration and MRI data are used for navigation itself, is an optimal option. However, this is not always possible and also increases radiation exposure of the patient and economic costs.

Integration of fMRI data in the neuronavigation system enables selecting the optimum size of craniotomy based on the location of functionally active zones. Tractography data, when combined with the results of neurophysiological monitoring, provide more accurate assessment of the location of the subcortical pathways with respect to the lesion, even despite the brain displacement, reducing the risk of persistent neurological deficit in the postoperative period [19, 20]. This statement is also confirmed by the results reported by S. Ohue et al [21].

In our opinion, compliance with imaging protocol, accurate registration, and correct positioning and fixation of localizers are the main technical factors affecting the accuracy of navigation.

Portability of electromagnetic navigation system and sufficient ease of installation and operation enables its successful use during urgent neurosurgical interventions, such as thrombolysis and drainage of intracerebral hematomas.

Our experience shows that the use of a stand-alone electromagnetic field generator instead of that built in the operating table head support provides greater flexibility in patient positioning and reduces the likelihood of localizer displacement out of the electromagnetic field or to its margin, which leads to serious distortions and loss of navigation precision. In general, the use of electromagnetic navigation during transcranial and transnasal endoscopic surgery, especially in reoperations, can improve surgeon’s orientation in the area of interest and reduce the risks associated with the erroneous interpretation of endoscopic information. However, it should be remembered that neuronavigation data may not be absolute even provided the relative preservation of anatomical landmarks.

Combination with neurophysiological monitoring enables application of electromagnetic navigation during operations in functional areas. No interference was observed when recording scalp EEG using needle electrodes. However, it should be taken into account, that there is a high-frequency noise due to running electromagnetic field generator, which occur during direct cortical stimulation and electrocorticogram recording.

Neuromonitor filters partially eliminate interference, but it is advisable to disconnect the electromagnetic field...
generator in order to obtain intact data. However, it should be noted that the need for simultaneous application of direct cortical stimulation and navigated pointer does not seem be a high-demand option from a practical point of view.

We observed no navigation data errors associated with reconnection of the generator.

**Conclusion**

The analysis of our series leads to conclusions that electromagnetic navigation is in general safe and effective technique that can be used in the surgical treatment of patients with various pathological processes in the brain. In our series, navigation error averaged 1.9±0.5 mm for transcranial operations and 2.5±0.8 mm for endoscopic operations, which is comparable with data obtained by other authors [5, 6, 16, 22], who explored the possibilities of electromagnetic navigation.

The use of electromagnetic navigation is advisable for a wide range of transcranial and endoscopic neurosurgical operations. Indications for electromagnetic navigation are similar to those for optical navigation systems. Electromagnetic navigation is most convenient during operations that do not require fixation of patient’s head, in particular, shunting operations, drainage of various space-occupying lesions (cysts, hematomas, abscesses), when optimizing the size of craniotomy and selecting craniotomy options. In the case of reoperations, abnormal anatomical relationships and landmarks necessitate the use of neuronavigation systems in almost mandatory manner. It is not always advisable to use neuronavigation when removing large hemispheric or deep brain tumors, since increasing brain displacement significantly enhances navigation error during the operation. At the same time, the relative constancy of anatomical landmarks and

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**Table 2. Distribution of transnasal endoscopic operations according to neurosurgical pathology type**

<table>
<thead>
<tr>
<th>Pathology type</th>
<th>Number of patients (operations)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skull base tumors</td>
<td>19 (19)</td>
</tr>
<tr>
<td>Inflammatory changes of paranasal sinuses</td>
<td>13 (13)</td>
</tr>
<tr>
<td>Basal cerebrospinal fluid leak</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Foreign bodies</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Total</td>
<td>36 (36)</td>
</tr>
</tbody>
</table>

---

**Fig. 6. The results of neuronavigation in a patient with a skull base tumor.**

Patient B, 66 years old. Ds: disseminated recurrent clival chordoma invading C2 vertebra. Preoperative MRI images show, that pathological process involves not only the clivus, but also the posterior surface of the second cervical vertebral body. Tumor fragment located in this area caused severe compression of the upper cervical spinal cord (a, b). The use of electromagnetic navigation system enabled total resection of the primary tumor node. Flexibility of the tool tip also enabled safe resection of the tumor fragment located on the posterior surface of C2 body, while maintaining navigation accuracy. There was no evidence of recurrence 4 years after the operation and radiotherapy (c).
minimal brain dislocation in the case of basal tumors, e.g., meningiomas, enable using neuronavigation to accurately determine location of large vessels bordering the tumor. The use of electromagnetic navigation considerably facilitates the surgeon’s work in the case of pathological processes involving the cranioventral junction, e.g., disseminated skull base chordomas (Fig. 6).

The system is compact and easy to setup and use, and therefore it can be easily integrated into the structure of various operating rooms and does not require any special training. The use of CT or MRI scan data obtained on tomographs produced by different manufacturers for navigation have no significant impact on system performance. The availability of CT or MRI images whose parameters correspond or are close to patient scanning protocol in terms of scan plane orientation, scan area width, and slice thickness makes additional preoperative imaging studies unnecessary.

From a practical point of view, the use of invasive patient localizer is advisable during both direct and endoscopic procedures. In our opinion, the use of headband or pad does not provide secure localizer fixation and gives rise to errors.

The use of stand-alone electromagnetic field generator allows surgeon to easily change its position depending on patient’s positioning on the operating table.

In all cases, the use of straight navigated pointers is sufficient for navigation. In our opinion, the possibility to bend pointer without loss of navigation accuracy is seem to be quite important, but its practical applicability is limited to selected cases (e.g., bent tip of the pointer allowed us to use navigation when removing a fragment of clival chordoma located behind the edge of C1 vertebral body). The use of straight navigation pointers along with a universal adapter for neurosurgical tool navigation seems to be more appropriate for routine use.

Application of electromagnetic navigation does not restrict the use of the entire spectrum of required intraoperative neurophysiological studies at corresponding surgical stages. Stage-by-stage application of neuronavigation should be observed in order to obtain adequate research results.

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Authors declare no conflict of interest.
Commentary

This study analyzes the use of electromagnetic neuronavigation in treatment of 102 patients with different brain diseases.

In the introduction, the authors compare the results obtained using various navigation systems, from stereotaxic to modern optical and electromagnetic neuronavigation. The study includes a comprehensive analysis of the used navigation device and describes reference points and possible causes of guidance errors. The results of application of this system were compared to those of the systems previously used in neurosurgery; navigation accuracy, advantages, and disadvantages of the known methods are shown. Investigation of the main nuances of the existing electromagnetic neuronavigation methods, as well as brain shift effect and registration difficulties associated with the use of flexible instruments (e.g., flexible endoscope) during surgery seems to be of greatest importance.

The authors comprehensively evaluate the navigation method under study referring to the manufacturers represented in the Russian Federation. Taking into account that neuronavigation is necessarily and widely used in the surgery for intracranial neoplasms, this study is useful for practical neurosurgery. Time-proved and novel modern methods were thoroughly analyzed for the first time in the Russian Federation. At the end of the article, the authors present the modern views on the development of robotics as the future direction in neurosurgery aimed at minimizing surgical trauma when approaching brain structures and leveling the adverse side effects associated with surgeon’s manual work.

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Extended Endoscopic Endonasal Posterior (Transclival) Approach to Tumors of the Clival Region and Ventral Posterior Cranial Fossa. Part 2. Topographic and Anatomical Aspects and Surgical Technique

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Purpose — to present the main topographic and anatomical features of the clivus and adjacent structures for improving and optimizing the extended endoscopic transnasal posterior (transclival) approach in removal of clival and ventral posterior cranial fossa lesions.

Material and methods. We performed a topographic and anatomical study of 25 cadaver heads, the vascular bed of which was filled with colored silicone using the original technique for visualizing the bed features and individual variability.

Results. We present the main anatomical landmarks necessary for performing the extended endoscopic endonasal posterior approach. Superior, medial, and inferior transclival approaches provide access to the anterior surface of the upper, middle, and lower neurovascular complexes of the posterior cranial fossa.

Conclusion. The endoscopic transclival approach can be used to reach ventral posterior cranial fossa lesions. The endoscopic transnasal transclival approach is an alternative to transcranial approaches to clival lesions.

Keywords: endoscopic transclival approach, clivus, cranial nerves, posterior cranial fossa, skull base anatomy.

Abbreviations::

FM — foramen magnum
SCA — superior cerebellar artery
ICA — internal carotid artery
PICA — posterior inferior cerebellar artery
HC — hypoglossal canal
AICA — anterior inferior cerebellar artery
DM — dura mater
EETA — endoscopic endonasal transsphenoidal access

Surgical interventions in the clival region are associated with a number of limiting factors: a depth of the operating wound with a complex anatomical environment involving the main blood vessels and cranial nerves as well as infiltrative growth of most tumors in this region.

Various transcranial and transfacial approaches to lesions of the clival and craniovertebral junction region have been developed: subfrontal transbasal, subtentorial anterior transpetrosal (Kawase’s technique), retrosigmoid, and far-lateral approaches that provide rather limited access to a particular region and have several significant disadvantages. The disadvantages include the need for extensive resection of the skull base structures, traction of the brain and displacement of the brainstem structures and cranial nerves (which are necessary to reach the deep midline neurovascular structures), and a constricted view of the midline posterior cranial fossa [1–3].

In recent years, endoscopic endonasal surgery has been actively developed, which has already supplanted some transcranial and transfacial approaches used in treatment of clival tumors. The endoscopic transnasal transclival approach to the posterior cranial fossa structures overcomes many of the indicated disadvantages. In particular, it provides a direct view of the midline skull base structures, without brain traction, as well as a panoramic view of the ventral surface of the brainstem after partial or total resection of the clivus [4].

When viewed through the nasal cavity, the outer surface of the clivus appears convex and inclined downwards. The inferior surface of the sphenoid bone body lies anterior to the basilar portion of the occipital bone. The vomer base is represented by two wings that articulate with the inferior surface of the sphenoid bone. Superiorly, the vomer expands as two wings that respectively articulate with the inferior surface of the sphenoid bone. Laterally, each of the vomer’s wings extends to the so-called vaginal process that tightly articulates with the medial plate of the pterygoid process of the sphenoid bone.

A narrow vomerovaginal canal occurs between the vomer’s wing and the vaginal process (Fig. 1). On the superior surface of the pterygoid process of the palate, near the vomerovaginal canal, there is the palatovaginal canal (Fig. 1) that opens anteriorly through the medial part of the posterior wall of the pterygopalatine fossa and transmits the pharyngeal branch of the pterygopalatine gan-
region and the small pharyngeal branch of the maxillary artery. The vomerovaginal canal is located medial to the pterygopalatine canal and is directed towards the anterior end of the latter (Fig. 1) [5].

When exposing the upper clivus, a direct vision endoscope (0°) is moved into the nasal cavity, along the superior nasal meatus, towards the sphenoid sinus opening. The right middle nasal concha is reflected laterally or removed, and the inferior nasal concha can also be reflected aside. The posterior part of the nasal septum is separated from the sphenoidal crest and resected approximately 1 cm from the posterior margin of the nasal septum to enable a view when manipulating instruments through both nostrils. Dissection of the anterior wall of the sphenoid sinus at the sphenoidal concha and sphenoidal crest level provides a triangular corridor to the sphenoid sinus, which is laterally confined by the superior nasal concha and posterior ethmoidal air cells. Resection of the superior nasal concha and posterior ethmoidal air cells (posterior ethmoidectomy) extends the surgical corridor to the sphenoid sinus. The pterygoid (Vidian) canal is identified by drilling the sphenoid sinus floor in the mediolateral direction. The canal usually appears as a bone groove in the sphenoid sinus floor region (Figs. 1, 2). Totally, there are three canals in the sphenoid sinus floor region, which extend anteroposteriorly, from the medial to lateral margin: vomer, palatine, and pterygoid canals [1]. The vomerovaginal canal that resembles a small bone groove is located most medially (Figs. 1, 2).

When drilling the sphenoid sinus floor from the medial to lateral portion, the palatovaginal canal, also called the palatosphenoidal canal, is usually exposed first; it may be mistaken for the pterygoid canal because both canals contain arterial branches of the sphenopalatine artery and nerve branches of the greater petrosal nerve. These bone canals open into the pterygoid fossa. The palatovaginal canal transmits the pharyngeal nerve from the pterygopalatine ganglion and the pharyngeal artery from the third portion of the maxillary artery, which are much smaller than the Vidian nerve and artery in the Vidian canal [1, 2]. The posterior end of the pterygoid canal that transmits the homonymous artery and nerve opens to the superior part of the anterolateral edge of the foramen lacerum (Fig. 2). In the foramen, the deep petrosal nerve from the sympathetic plexus of the ICA merges with the greater petrosal nerve to form the pterygoid canal nerve. When viewed anteriorly, along the hard palate axis, the lateral part of the bony skull base is largely covered by the upper jaw body. The basilar part of the occipital bone can be visualized through the inferior nasal cavity and through the posterior nasal aperture (choana) through which the nasal cavity communicates with the nasopharynx [6].

The posterior end of the pterygoid canal opens onto the inferolateral surface of the anterior genu (foramen lacerum segment) of the ICA (Fig. 2). This anatomical relationship makes the pterygoid canal an important landmark for identification of the foramen lacerum segment of the ICA during the extended transnasal approach [7]. In a study by T. Funaki et al. [2], the dural porus of the abducens nerve occurred at a distance of 4.9 mm (range, 4 to 6 mm), on average, above the distal portion of the pterygoid canal.

The petroclival fissure that is located along the lateral margin of the clivus separates the occipital bone and the petrous part of the temporal bone. This fissure is deeper on the outer surface of the skull base than on the inner one and is filled with cartilage. The fissure extends from the foramen lacerum to the jugular foramen. The foramen lacerum is located at the junction of the sphenoid, temporal, and occipital bones. The foramen is confined anteriorly by the junction of the body, greater wing, and adjacent roots of the pterygoid processes of the sphenoid bone, posteriorly and laterally by the petrous apex, and medially by the clival part of the occipital bone. The Cl segment of the ICA occupies the medial part of the foramen lacerum [8, 9]. The posterior end of the pterygoid (Vidian) canal opens into the superior part of the anterolateral margin of the foramen lacerum. In the foramen lacerum, the deep petrosal nerve from the sympathetic plexus of the ICA merges with the greater petrosal nerve to form the Vidian nerve [2].

An extended approach required in some pathological processes in the clival region is based on an accurate
knowledge of the topographic and anatomical relationships between structures throughout the entire nasal corridor to the clivus (Fig. 3) [10].

The endoscopic transclival approach, like other endoscopic approaches to the skull base, has its drawbacks: complexity of hemostasis, complications associated with the development of postoperative nasal cerebrospinal fluid leak, and a two-dimensional (planar) image typical of modern endoscopes. It is necessary to remember that extensive resection of the clivus and DM in the clival region increases the risk of postoperative cerebrospinal fluid leak, which can reach 33% (Fig. 3b) [1, 11].

Approach to the upper, middle, and lower clivus

Dissection of the clivus, when the right and left halves of its upper, middle, and lower parts are sequentially trephined, exposes the relationships between the extra- and intracranial structures. The mean vertical size is 17.3, 13.7, and 15.2 mm for the upper, middle, and lower clivus, respectively. The projection of the border between the upper and middle clivus onto the brainstem corresponds to the middle of the pons, and the border between the middle and lower clivus corresponds to the pontomedullary sulcus. Dissection of the upper, middle, and lower clivus exposes the anterior surface of the superior half of the pons, inferior half of the pons, and the medulla oblongata, respectively [2, 12].

According to our studies, additional resection of the dorsal sella increases the approach area by 1.34 cm², on average, and also expands the angle of surgical approach by 6—8°.

Trepanation of the upper clivus

The bony septum of the sphenoid sinus is removed; then, the bone structures under the sella turcica are drilled in the mediolateral direction to expose the clival dura as well as in parallel to the ICA direction to prevent its injury. The upper clivus articulates with the petrous apex at a distance of approximately 10 mm lateral to the midline, behind the ICA [2]. Fibrous cartilage fills the fissure along the junction between the petrous apex and the clivus. Care must be taken to avoid damaging the abducens nerve when drilling the most lateral part of the upper clivus because it crosses the superior margin of the petroclival junction. The DM of the upper clivus can easily be separated into two layers: periosteal (external) and meningeal (internal). The basilar venous plexus as well as the superior and inferior petrosal sinuses are located between the two dural layers. Dissection of the basilar venous plexus that is located on the posterior surface of the upper clivus and connects the posterior ends of the paired cavernous sinuses can be accompanied by pronounced and persistent bleeding. The venous plexus becomes less pronounced towards the FM. The posterior end of each cavernous sinus together with the superior and inferior petrosal and basal sinuses forms a characteristic venous confluence. The abducens nerve perforates the meningeal layer of DM and runs through the venous confluence to pass below the petrosphenoidal ligament (Gruber’s ligament). Then, the nerve passes around the lateral portion of the ICA and reaches the medial surface of the optic nerve (V2) in the lateral wall of the cavernous sinus. Preservation of the Gruber’s ligament upon drilling the clivus can provide anatomical integrity of the abducens nerve. Dissection of the DM of the upper clivus is associated with a potential risk of injury to the abducens nerve, especially to its intradural segment, because this segment is difficult to identify, and venous bleeding complicates its identification. The mean distance between the dural pori of the abducens nerves is 20.9 mm (range, 18—25 mm) [2]. J. Barges-Coll et al. [13] reported that the horizontal distance between the abducens nerves was 10 mm along the pontomedullary sulcus and 18.5 mm in the venous confluence region. The intradural segment of the abducens nerve is often accompanied by the dorsal meningeal artery that usually ascends from the meningo-hypophyseal branch of the ICA to the dorsum sellae level. In 6% of cases, the dorsal meningeal arteries branch from the intracavernous ICA below the meningo-hypophyseal trunk origin. The artery, distal to its origin, runs posteriorly through the cavernous sinus and, together with the abducens nerve, reaches the DM of the dorsum sellae and clival region where it passes medially along the abducens nerve and below the Gruber’s ligament. The use of a 45° endoscope for lateral examination helps visualize the intradural segment of the abducens nerve, dorsal meningeal artery, and Gruber’s ligament [13].

Intradural structures

Dissection of the DM of the upper clivus below the sella turcica exposes the superior half of the anterior pontine surface and prepontine cistern. The uppermost part of this region is the place where the pons joins the medulla oblongata, and the mesencephalic leaf of the interpeduncular cistern membrane (also known as the Liliequist membrane in the English language literature) is located (Figs. 4, 9) [2]. Exposure of the pontocerebellar cistern on the lateral side of the anterior pontine membrane is limited by the ICA and the petrous apex. The superior part of the basilar artery and its pontine perforating branches are visualized throughout the entire artery (Fig. 5). The anterior pontomesencephalic segment of the SCA, which passes around the brainstem near the pontomesencephalic junction, can be found with a 45° endoscope in the area of the upper border of this approach (Figs. 5, 6). This approach enables visualization of the third cranial nerve only. The trigeminal nerve that is located at the upper clivus level and runs to the pontocerebellar cistern is located in lateral parts of this approach (Fig. 6). Extending the exposure by drilling the lingual process of the sphenoid bone and the petrous apex with or without transposition of the ICA provides a frontal view of the trigeminal nerve and the trigeminal cave (Meckel’s cavity) (Fig. 6). The oculomotor nerve emerges from the anterior surface of the midbrain and is located above the SCA (Figs. 5, 8—10) [2].
**Extension of the approach to the upper clivus**

Extension of the approach to the upper clivus is accompanied by elevation of the pituitary gland, resection of the dorsum sellae, and exposure of the interpeduncular cistern. The main purpose of extending the approach upwards is to increase the angle of surgical action in the vertical plane by 6—8°, on average. The wound depth from the plane of the nasal cavity entrance to the anterior parts of the sella turcica floor is known to range 77 to 92 mm (mean, 82 mm). The angle of surgical action along the wound in the vertical plane is 18—22° (mean, 20°). The angle of surgical action in the horizontal plane (by width) amounts to 19—29° (mean, 23°) [14].

Our study revealed that the angle of surgical action to the clivus (<ABC in Fig. 8) amounts to 20—23°; after trepanation of the dorsum sellae, the angle of surgical action to the clivus is expanded by 6—8° (<A1BA in Fig. 8) and amounts to 28—30° (<A1BC in Fig. 8).

Elevation of the pituitary gland together with the intact sellar dura through the standard approach to the upper clivus is often difficult because the periosteal layer of the sellar dura is intimately adherent to the DM covering the ICA and sellar diaphragm (Figs. 4, 9). This DM layer forms the pituitary fossa roof that intimately blends with the upper dural ring adhered to the ICA [2]. Separation of the pituitary capsule from the medial wall of the cavernous sinus is helpful for elevation of the pituitary gland.
and exposure of the dorsum sellae (Figs. 4, 9). The periosteal and meningeal layers of DM are especially pronounced in the region of the sella turcica floor and lower surface of the pituitary gland. The periosteal layer is adherent to the sphenoid bone, and the meningeal layer encapsulates the pituitary gland. The two-layer structure formed of DM layers lines the sella turcica floor and is especially pronounced in the intercavernous sinuses that are located between the two layers. The medial wall of the cavernous sinus, which separates the lateral surface of the pituitary gland from the ICA, is constituted by a single thin meningeal dura layer. The pituitary gland capsule is a very thin translucent membrane that is tightly adherent to the pituitary gland, adjacent to the medial wall of the cavernous sinus, and can be separated from it by a neat dissection (Figs. 4, 10) [15].

The pituitary gland is separated from the DM structures by dissection of the DM between the pituitary gland capsule and the medial wall of the cavernous sinus. This enables transposition of the pituitary gland upwards for further resection of the dorsum sellae (Fig. 10). Here, it is necessary to be very careful to avoid excessive transposition and detachment of the inferior hypophyseal artery that originates from the meningohypophyseal trunk, lateral to the dorsum sellae, and runs medially, supplying the posterior lobe of the pituitary gland (Fig. 10) [15]. This approach exposes the interpeduncular cistern and leaflets of the Liliequist membrane in the region where the supratentorial and infratentorial parts of the subarachnoid space join. The oculomotor nerve is located in the lateral wall of the interpeduncular cistern and forms filaments to which layers of the Liliequist membrane are attached (Figs. 5, 9, 11, 12a). The trunk of the SCA and posterior cerebral artery can be exposed in all specimens using this approach (Figs. 5, 12a). Dissection of the dien cephalic layer of the Liliequist membrane, which protrudes over the interpeduncular cistern, exposes segments of the posterior communicating artery and ICA in the chiasmatic cistern and carotid cistern region (Fig. 11) [15].

A 70° endoscope may be required in the region of the upper border of the extended approach to the upper clivus. Extension of the access area during the transclival approach with resection of the dorsum sellae is shown in Figure 11.

**Approach to the middle clivus**

The main landmarks in the middle clival region are the upper borders of the inferior paraclival segments of the ICA and, inferiorly, the pharyngeal tubercle. The anterior surface of the middle clivus corresponds to the area where the vomer is attached to the sphenoid sinus floor and upper part of the occipital bone. Dissection of the nasopharynx is performed similarly to that during the approach to the lower clivus. The lateral borders of the surgical corridor to the middle clivus include the upper part of the pterygoid process superiorly and the prominence of the auditory tube posteriorly. The mean distance between the medial edges of the pterygoid processes is 24.9 mm [2, 10]. Exposure of the foramen lacerum and petroclival fissure at the lateral border of the middle clivus is impossible without resection of the pterygoid process root. Resection of the posteromedial wall of the maxillary sinus and the orbital process of the palatine bone exposes the pterygopalatine fossa, Vidian canal, and round foramen. Exposure of the anterior surface of the pterygoid process requires lateral retraction of the pterygoid fossa contents, including the Vidian nerve, in-
Fig. 6. Endoscopic image of structures of the upper clival region in combination with a lateral extended approach.

a: 1 — chiasm, 2 — left anterior cerebral artery, 3 — left optic nerve, 4 — left ICA, 5 — basilar artery, 6 — right ICA, 7 — right optic nerve; b: 1 — mammillary bodies, 2 — left posterior cerebral artery, 3 — left oculomotor nerve, 4 — DM covering the left ICA, 5 — left superior cerebellar artery, 6 — pons, 7 — basilar artery, 8 — left ICA; c — lateral displacement of the ICA in the left cavernous sinus cavity: 1 — left oculomotor nerve, 2 — dissector, 3 — left ICA.

Fig. 7. Endoscopic image of neurovascular structures of the upper clival region on the left.

a: 1 — ventral surface of the cerebellar hemisphere, 2 — artery accompanying the trigeminal nerve, 3 — trigeminal nerve, 4 — acoustico-facial group of nerves, 5 — cerebellar tonsil, 6 — AICA, 7 — pons, 8 — superior cerebellar artery, 9 — branches of the superior cerebellar artery; b: 1 — trigeminal nerve, 2 — ventral surface of the cerebellar hemisphere, 3 — posterior surface of the petrous pyramid, 4 — dural porus of the acoustico-facial group of nerves, 5 — facial nerve, 6 — vestibulocochlear nerve, 7 — glossopharyngeal nerve, 8 — cerebellar tonsil, 9 — pons.
frontal nerve, large and small palatine nerves, pterygoid ganglion, and terminal branches of the maxillary artery. The pterygoid process is drilled backwards, until the ICA is exposed. Posteriorly, the Vidian canal faces the anterior genu of the ICA (foramen lacerum segment of the ICA). The initial part of the Vidian nerve is covered by fibrous cartilage at the anterolateral edge of the upper part of the foramen lacerum where the deep petrosal and greater superficial petrosal nerves merge to form the Vidian nerve [16].

Trepanation of the middle clivus

The vomer is removed; then, the bone structures of the middle clivus are drilled using a small diameter cutter (3 to 4 mm) with diamond coating until the DM is exposed. The trapezoid shape of the middle clivus is bounded by the foramen lacerum laterally, ICA superiorly, and petroclival fissure inferiorly. Dissection of the DM during the approach to the middle clivus is laterally limited by the inferior petrosal sinuses that course along the intracranial side of the petroclival fissures. The mean transverse dimension between the upper and lower parts of the inferior petrosal sinuses is 21.9 and 38.6 mm, respectively [2]. Drilling of the lower part of the petrous apex extends the approach laterally to the petrosal segments of the ICA [2].

Intradural structures

Dissection of the DM in the middle clival region exposes the lower half of the anterior surface of the pons and preoptic cistern as well as the medial part of the cerebellopontine cistern. The anterior pontine membrane that separates the preoptic and cerebellopontine cisterns becomes less noticeable when courses downwards. The approach to the middle clivus exposes the entire part of the cisternal portions of the abducens nerves (Fig. 12). Connections of the facial and vestibulocochlear nerves with the pons are also visible, but most of the cisternal nerve segments are hidden behind the petrous apex (Figs. 7, 12). It is quite difficult to visualize the entire part of their cisternal segments, even with angled endoscopes. The exit zone of the facial nerve root can occur in the lateral region of the middle clivus, near the boundary between the middle and lower clivus (Figs. 7, 12). It can be visualized more clearly using a 45° endoscope directed upwards from the lower clivus level because the root exit zone is situated in the area between the olive and the
pons, at the lateral margin of the pontomedullary sulcus. Drilling of the inferior surface of the petrous apex (inferior petrosectomy) and opening of the anterior wall of the internal auditory canal expose the entire cisternal segment and a part of the meatal segment of the facial and vestibulocochlear nerves. The lower part of the basilar artery and the initial part of the AICA are usually visualized during an approach to the middle clivus. In all 25 cases of our study, the AICA originated from the basilar artery at the middle clivus level. If the artery origin site is the basilar artery bending that extends laterally to the cerebellopontine angle, inferior petrosectomy may be required to expose the anterior pontine segment of the AICA. Petrosectomy can also help expose the premeatal and postmeatal segments of the AICA. Although the site of PICA origin is usually located at the lower clivus level, the cranial loop of the curved PICA can also extend to the middle clival region (Figs. 12, 14) [2, 17, 18].

Our experience suggests that the use of a high-speed drill with a variable spatial configuration (drill flexion angle of up to 15°) is very helpful in trepanation of the middle and lower clivus.

**Approach to the lower clivus**

The lower clivus is located behind the posterior wall of the nasopharynx that communicates with the nasal cavity through the choana (posterior nasal aperture). The choanae are paired openings that are formed by the sphenoid bone body superiorly, perpendicular plates of the palatine bone and medial pterygoid plates laterally, horizontal plates of the palatine bone posteriorly, and vomer medially (along the midline) [19]. The auditory (Eustachian) tubes open on the lateral wall of the nasopharynx; their apertures are located along the posterior edge of the medial pterygoid plate. Behind the auditory tube aperture, there is a pronounced mucosal elevation, the so-called cushion of the auditory tube (torus tubarius), formed by the cartilaginous part of the Eustachian tube (Fig. 3c). The Eustachian tube and tubal elevation are the lateral boundaries of the lower approach to the clivus. The mean transverse dimension between the auditory tube openings is 24.1 mm, and the mean distance between their elevations is 14.7 mm [2, 20]. The pharyngeal recess (Rosenmüller fossa) is located laterally in the posterolateral corner of the nasopharynx, behind the auditory tube elevation. The parapharyngeal segments of the ICA run deeply at the lateral edges of the Rosenmüller

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**Fig. 11.** Endoscopic image of structures of the retrosellar region after resection of the dorsum sellae.
1 — basilar artery, 2 — right posterior cerebral artery, 3 — left posterior cerebral artery, 4 — left posterior communicating artery, 5 — left oculomotor nerve, 6 — mamillary bodies, 7 — midbrain, 8 — DM of the clival region.

**Fig. 12.** Endoscopic image of neurovascular structures in the middle clivus projection.
a — after dura dissection. 1 — left posterior cerebral artery, 2 — left oculomotor nerve, 3 — left SCA, 4 — pontine branches of a basilaris (upper line corresponds to the left AICA), 5 — DM, 6 — pons, 7 — left abducens nerve, 8 — basilar artery, 9 — right posterior cerebral artery; b — upper parts of the left cerebellopontine angle. 1 — left trigeminal nerve, 2, 10 — cerebellar tonsil, 3 — cerebellopontine cistern, 4 — left facial nerve, 5 — opening of the internal auditory canal, 6 — left vestibulocochlear nerve, 7 — glossopharyngeal nerve, 8 — caudal group of nerves, 9 — left PICA, 11 — pons.
fossa. To access the lower clivus, a linear incision of the mucosa is used, which is performed on the posterior wall of the nasopharynx, just above the pharyngeal tubercle. The attachment site of the longus capitis muscle to the clivus is usually projected onto the mucosa as a V-shaped elevation that corresponds to the pharyngeal tubercle projection. The muscular structures on the posterior wall of the nasopharynx are divided into three layers. The pharyngobasilar fascia is the most superficial layer of tissue that is located above the nasopharyngeal mucosa and covers the longus capitis muscle. It is firmly attached to the lower surfaces of the occipital and temporal bones. Further, it gradually becomes thinner and merges with the superior constrictor of the pharynx at the soft palate level. The superior constrictor of the pharynx is connected to the raphe of pharynx that is attached to the pharyngeal tubercle. The upper edge of the superior pharyngeal constrictor is located at the C1 level and is not always identified during an approach to the lower clival region. At its upper edge, the pharyngobasilar fascia grows into fibrous cartilage at the border between the sphenoid and occipital bones and the foramen lacerum region. The second layer is represented by the longus capitis muscle. The pharyngeal segment of the ICA is located lateral to the muscle. Along the lateral margin of attachment of the longus capitis muscle, the petroclival fissure is filled with fibrous cartilage. The third, deepest, layer of the posterior nasopharynx consists of the rectus capitis muscle and long neck muscle. The anterior rectus capitis muscle is a short thin muscle that covers the anterior part of the atlanto-occipital junction. The muscle is usually attached in the supracondylar groove region, above the occipital condyle, but its attachment site can be located in the jugular tubercle region, in which case it may be mistaken for the medial edge of the occipital condyle. The hypoglossal nerve and branches of the ascending pharyngeal artery course along the lateral margin of the anterior rectus capitis muscle [21].

Trepanation of the lower clivus

Retraction and resection of the anterior rectus capitis muscle expose the occipital condyles and hypoglossal canal. The occipital condyle and hypoglossal canal are the lateral boundaries of the approach to the lower clivus when a 0° endoscope is used. When 30 and 45° endoscopes guided over the cartilaginous part of the Eustachian tube are used, drilling of the pterygoid process enables visualization of the outer part of the jugular foramen. Drilling of this part and exposure of the jugular foramen in the mediolateral direction are technically challenging and should be performed very carefully because the auditory tube cartilage is tightly adherent to the cartilage in the lower part of the foramen lacerum [22].

The clivus portion located below the level of the anterior margin of the pharyngeal tubercle and the occipital condyle extending downwards and laterally upwards is drilled out. Trepanation of the clivus is limited laterally by the hypoglossal canals that are located postero-medially to their extracranial apertures. More extensive dissection of the clivus can be achieved in the region located above the hypoglossal canal where dissection of the clivus is laterally restricted by the petroclival fissure and jugular foramen. According to our data, the mean width of the endoscopic surgical corridor was 38.6 mm above the HC region and 26.6 mm at its level. The jugular tubercle is located on the intracranial surface of the skull base, in the triangular area among the petroclival fissure, jugular foramen, and HC. This region consists of a solid compact substance constituting the thickest part of the lower clivus [2]. Trepanation of bone structures in this region requires great care to avoid damage to the HC and cisternal portions of the IXth, Xth, and XIth cranial nerves that are closely associated with the DM covering the jugular tubercle. The apical ligament of the odontoid process extends from the dens apex to the anterior edge of the FM and is located between the anterior atlanto-occipital membrane and the cruciform ligament extending superiorly. The upper vertical band of the cruciform ligament and tectorial membrane are attached to the superior surface of the clivus. The alar ligament consists of two tough cords that start on each side of the dens apex, are obliquely directed, and extend superiorly and laterally, attaching to the medial surface of the occipital condyle. In turn, the apical odontoid ligaments have a minimal function in maintaining stability between the head and neck, while dissection of the alar ligament can cause instability simultaneously in two joints: atlanto-occipital and atlantoaxial. Drilling of the cellular structure of the occipital condyle bone with preservation of the articular surfaces and cortical layer of the bone on its medial surface may prevent the development of instability. The well-developed dural venous network located around the HC connects with the marginal sinus around the FM and hypoglossal venous plexus within the HC. The dural sinuses may be dangerous in terms of venous bleeding during dissection of the DM of the lower clivus [5].

Intradural structures

Dissection of the DM in the lower clival region exposes almost the entire anterior surface of the medulla oblongata. The pontomedullary sulcus is projected onto the transition point between the middle and lower clivus, and the anterior edge of the FM coincides with the level of the hypoglossal nerve root exit from the medulla oblongata [2]. The first cervical nerve is located just below the FM (Fig. 13). Dissection of the DM between the FM and the atlas exposes the upper cervical spine segments and C1 nerves, although sometimes this requires dissection of the apical and upper vertical bands of the cruciform ligament. The approach to the lower clivus provides primarily access to the premedullary cistern that is bounded by the pontomedullary membrane superiorly and medially and by the cerebellomedullary cistern, which originates from the posterior edge of the olive (anterior to the glosopharyngeal, vagus, and accessory nerves), laterally (Fig. 13) [14]. The approach to the lower clivus extends only to a small anterior portion of the cerebellomedullary
cistern. The glossopharyngeal, vagus, accessory, and hypoglossal cranial nerves, which are exposed during resection of the lower clivus, originate from the medulla oblongata and are located close to the PICA (Fig. 13). The border between the middle and lower clivus is located above the level of the cisternal part of the glossopharyngeal nerve [21]. The cisternal part of the glossopharyngeal and vagus nerves can be exposed by drilling the jugular tubercle that corresponds to the bone region above the HC (Figs. 7b, 12b). The accessory nerve roots originating from the medulla oblongata are often hidden behind the hypoglossal nerve roots, hypoglossal, and vertebral artery (when viewed anteriorly). Drilling of the HC expands the corridor and facilitates exposing the accessory nerve roots, but can lead to bleeding from the venous plexus of the HC and the meningeal branch of the ascending pharyngeal artery as well as to damage to the hypoglossal nerve. Trepanation of the lower clivus provides visualization throughout the intradural parts of the vertebral arteries. In most cases, the initial portion of the vertebral artery is located anterior to the hypoglossal nerve roots and then ascends to the junction with the contralateral vertebral artery in the pontomedullary sulcus region. Trepanation of the lower clivus also enables visualization of the anterior medullary and lateral medullary segments of the PICA (Figs. 13a, 14). In our study, the PICA was entirely visualized in 24 out of 25 cases. In one case, the PICA originated from the vertebral artery at the level of the border between the middle and lower clivus (Fig. 13). The PICA may not be visualized if it branches from the extradural part of the vertebral artery [22, 23]. The anterior spinal arteries and their trunks were detected in all 25 specimens.

A variant of additional extension of the endoscopic transclival approach to lower third clivus tumors (with resection of the occipital condyle)

After removal of the condyle, the vertebral artery can be visualized at the site of its entry to the DM of the posterior cranial fossa, which enables direct monitoring of the course of blood vessels (Fig. 14). In this approach, the cranial nerves of the caudal group, in particular the hypoglossal nerve that runs anterior to the occipital condyle, can be affected. Particular care should be taken when manipulating with the vertebral artery in the C2 lower part region, where the artery runs most medially (Fig. 14) [24, 25].

Alar ligament preservation

Several authors [25, 26] have found that dissection of the alar ligament increases the range of atlanto-occipital and atlantoaxial angular motion. Therefore, most of the passive atlanto-occipital and atlantoaxial stability is provided by the alar ligaments. To expose the anterolateral part of the foramen magnum, the spongy bone of the condyle should be maximally drilled out, thereby partially sparing the cortical layer of the osseous part of the articular surface (i.e., performing supra-articular resection of the condyle). In this case, the attachment site of the alar ligament is not affected. The alar ligament attachment site is the lower border of the posteromedial resection of the condyle. If only the alar ligament is dissected, the craniocevical stability is not impaired.

If it is necessary to extend the corridor downwards, including resection of the C1 anterior arch and odontoid process, and resect both alar ligaments, then the development of craniocevical instability should be expected, which will further require stabilization surgery.
Discussion

To reduce the invasiveness of transcranial surgery, several craniotomy techniques have been proposed, in particular several variants of the retrosigmoid approach to tumors located in the upper, middle, and lower neurovascular complexes of the cerebellopontine angle [27]. The EETA enables effective approaches to lesions, with the skull base being maximally preserved. The use of an endoscope facilitates manipulations associated with resection of the longus capitis tendons, trepanation of bone structures of the clivus, and control of bleeding from the various venous plexuses adjacent to the clivus. However, extensive trepanation of the clivus and a large dural defect increase the risk of postoperative cerebrospinal fluid leak. Various techniques are used to reconstruct the skull base and reduce the risk of cerebrospinal fluid leak, which include the use of a balloon catheter, a nasoseptal flap, and dura reconstruction with micro-sutures [28, 29]. The risk of postoperative cerebrospinal fluid leak associated with these modern techniques amounts to 0—9.5% [30, 31].

Understanding the relationships between the extent of clivus involvement in the pathological process and the intradural neurovascular complexes is extremely important. For example, more than 50% of chordomas are characterized by intradural spread, and previously a significant part of chordomas were removed via transcranial approaches [32]. Currently, intradural neoplasms in the clival region, such as chordomas, epidermoid cysts, neurinoma cysts, meningiomas, and brainstem cavernous malformations, can be operated using the endoscopic transclival approach [2]. The transclival approach can also be used for clipping of posterior cranial fossa aneurysms located on the midline if the aneurysm can not be clipped using transcranial approaches or embolized using an endovascular technique. Aneurysms originating from the SCA, AICA, and PICA can be operated using the superior, middle, and inferior transclival approaches, respectively [2].

Therefore, the EETA may be considered as an independent and main approach to skull base lesions. The advantage of EETA is a good direct view of the midline structures. In addition, the advantages of EETA in comparison with transcranial approaches to the skull base include no need for traction of the brain structures and lateroposition of the vertebral artery. The approach enables visualization of an extended extra-intradural space from the crista galli to the craniovertebral junction (Fig. 3a).

Because the endonasal corridor is not associated with damage to the integrity of the oropharynx and soft palate structures, this significantly reduces the risk of bacterial contamination and infectious complications. In addition, patients have a low postoperative risk of swallowing and speech impairment; immediately after surgery, they are capable of oral alimentation without risk of dysphagia.

However, application of the transnasal approach may be associated with the risk of damage to lateral portions of the cranial nerves (oculomotor, abducens, glossopharyngeal, vagus).

The EETA is contraindicated in the case of critical topography of the neurovascular structures located medially or ventrally to the tumor. A relative contraindication is a significant lateral displacement of the tumor at the foramen magnum level, posterior to the occipital condyle, because there is a risk of injury to the caudal group of nerves and craniovertebral instability [14, 25].

Authors declare no conflict of interest.
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Innovative techniques of minimally invasive endonasal endoscopic surgery for tumors of the clival region and ventral posterior cranial fossa are highly desired in clinical practice. In this regard, the topicality of research on endonasal endoscopic neurosurgery is beyond doubt.

The present article is a logical continuation of Part 1 of the authors’ publication devoted to the topographic anatomical features of the clivus and adjacent structures for the purpose of clinical application of the extended endoscopic endonasal posterior (transclival) approach to tumors of the clival region and ventral posterior cranial fossa.

The authors present the main topographic and anatomical features of the clivus and surrounding structures for the purpose of improving and optimizing the extended endoscopic endonasal posterior (transclival) approach in removal of lesions of the skull base and ventral posterior cranial fossa.

The authors conducted an advanced topographic anatomical study on 25 cadaveric heads, the vascular bed of which was filled with colored silicone according to the authors’ procedure in order to visualize its features and individual variability. The main anatomical landmarks necessary for performing the extended endoscopic endonasal posterior (transclival) approach are described in detail. The obtained results have confirmed the fact that the superior, middle, and inferior transclival approaches provide access to the ventral surface of the upper, middle, and lower neurovascular complexes of the posterior cranial fossa.

This work is a continuation of the authors’ topographic anatomical studies aimed to develop endoscopic endonasal approaches to the vascular and cerebral structures in the posterior cranial fossa region. The topicality of this issue is clearly and convincingly presented in the Introduction. The authors have had a good knowledge of the current literature on this issue and critically analyzed it. The article describes in detail the topographic anatomy and sequence of the proposed surgical and technical approach and its potential complications. The article is supplemented with high-quality illustrations.

The study is original and carefully performed. The objective data obtained by the authors can be successfully used in clinical practice for development and improvement of the transclival approach.

Yu.A. Shcherbuk (St. Petersburg, Russia)

Commentary

The paper presents quantitative criteria for evaluating the extended endoscopic endonasal posterior (transclival) approach, which determine its rationality and minimal invasiveness of the approach.

In connection with the study, it seems interesting to know the author’s opinion on the influence of various forms of the cerebral cranium as well as typical and individual structural features of the sphenoid sinus, Blumenbach clivus, and ventral posterior cranial fossa in brachy-, dolicho-, and mesocranic skulls on the qualitative and quantitative parameters of the extended endoscopic endonasal posterior (transclival) approach used for removal of tumors of the clival region and ventral posterior cranial fossa. Probably, this will be the object of further research.

The present article demonstrates a high scientific and methodological level of the conducted research and a high practical significance of its results. The authors convincingly proved that the extended endoscopic endonasal posterior (transclival) approach may be used in surgical treatment of clival region lesions for accessing pathological formations of the ventral posterior cranial fossa and is an alternative to transcranial approaches.

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V.N. Nikolenko (Moscow, Russia)
Use of a Mini-Approach for Performing EC-IC Bypass in Occlusive Lesions of the Brachiocephalic Arteries

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Purpose — to evaluate the advantages and disadvantages of a mini-approach for performing EC-IC bypass.

Material and methods. The mini-approach was used in 35 patients (32 males and 3 females) with symptomatic occlusive lesions of the brachiocephalic arteries (BCAs) who were treated at the Department of Vascular Neurosurgery of the Federal Center of Neurosurgery in Novosibirsk in the period between January and December 2014. The mini-approach was performed through a skin incision of up to 5.5 cm in the donor artery projection. The approach was planned based on comparison of the MSCT-angiography data.

Results. In all cases, the mini-approach enabled performing EC-IC bypass in the optimal location, with the minimal involvement of the donor artery and the minimal size of craniotomy. Complications (shunt thrombosis) in the early postoperative period occurred in 3 (8.5%) cases. There were no cases of marginal wound necrosis. The mean bed-day was 7 days.

Discussion. We analyzed the literature regarding using the mini-approach in combination with various mapping variants based on neuroimaging data.

Conclusion. The approach has a high potential for wide application in clinical practice. The disadvantage is the narrowness and depth of the surgical wound, which complicates manipulations when performing EC-IC bypass and requires special skills.

Keywords: EC-IC bypass, mini-approach, brachiocephalic arteries.

Abbreviations:
BCAs—brachiocephalic arteries
MRI—magnetic resonance imaging
MSCT-angiography—multislice computed tomography angiography
STA—superficial temporal artery
MCA—middle cerebral artery
EC-IC bypass—extracranial-intracranial bypass

The extracranial-intracranial bypass (EC-IC bypass) is a surgical technique to improve cerebral perfusion caused by occlusion of the brachiocephalic arteries (BCAs) with hemodynamic insufficiency [1, 2].

Currently, neurosurgical interventions through a mini-approach became possible with the advancement of neuroimaging and new computed technologies [3—5].

Material and methods

A mini-approach was used in 35 patients (32 men and 3 women) with symptomatic occlusive lesions of BCAs who were treated at the Department of Vascular Neurosurgery of the Federal Center of Neurosurgery in Novosibirsk from January to December 2014. The approach was made from the right side in 19 cases and from the left side — in 16. The age of patients ranged from 36 to 69 years, the mean age — 56.4 years.

A mini-approach was planned based on comparison of data from multislice computed tomography angiography (MSCT-angiography) using visualization software. A point on the donor artery locating at the minimum distance to the recipient artery with an optimal size and location was identified during 3D-image simulation using the 3D-cursor mode based on angio-architectonics of branches of the superficial temporal artery (STA) and anatomical landmarks (Fig. 1). A mini-approach was mapped on the head relative to this point.

A mini-approach was performed through a skin incision of up to 5.5 cm in the donor artery projection. The size of craniotomy was up to 3.5 cm. A linear skin incision with a length from 3.5 to 5.5 cm was used to approach the parietal branch of the STA as a donor artery in 33 (94.2%) cases (Fig. 2a). In 2 (5.8%) cases, an arc incision with a length from 7 to 12 cm was made along hairy part of the head, when the frontal branch of the STA was used as a donor artery (Fig. 2). The temporal muscle was dissected by a linear incision and pulled to sides. Craniotomy was performed using a high-speed drill; the size of craniotomy ranged from 1.52 to 3.03 cm (Fig. 3). The dura mater was opened in a cruciform manner. A recipient M4 segment of the middle cerebral artery (MCA) was used in 32 (91.4%) cases and a recipient M3 segment of MCA was used in 3 (8.5%) cases. In all cases, the recipient artery was located within the approach. After creating microanastomosis, the dura mater was sutured, leaving a

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small defect around the donor artery. The bone defect was closed with autologous bone containing a hole for shunt in 30 (85.7%) cases and the bone flap was fixed with titanium plates. Autologous bone was not implanted in 5 (14.2%) patients. The average length of surgery was 3 hours 27 minutes.

**Results**

Clinically significant complication in the early postoperative period was noted in 1 (2.8%) patient. In 3 (8.5%) cases, shunt thrombosis was developed. These complications were noted at the beginning of using the technique. Of these, 2 (5.7%) cases of thrombosis were detected on control MSCT-angiography the next day after surgery and were not accompanied by neurological symptoms. In 1 (2.8%) case secondary to thrombosis on the second postoperative day, lacunar ischemic stroke was developed in the territory of the right MCA, which was manifested as monoparesis of the left hand. There

*Fig. 1. Patient, 51 years old. Preoperative planning based on data of MSCT-angiography of the brain.*

a — 3D-image; b — axial view; c — sagittal view; d — coronal view.

*Fig. 2. Patient, 51 years old. Intraoperative image.*

a — identification of the parietal branch of the STA in the projection of soft tissue incision; b — end-to-side anastomosis was created with loop sutures; c — the length of postoperative suture.
was no marginal wound necrosis in any patient. An average length of hospital stay was 7 days.

**Discussion**

Methods of creating EC-IC bypass through a mini-approach with neuronavigation instruments and without have been reported [6]. Y. Kaku et al. [5] used 3D MSCT-angiography with preoperative computed planning to identify the most appropriate donor and recipient vessels. The technique reduces tissue injury, operative time, and blood loss; it provides excellent cosmetic results and can be useful for patients with systemic diseases and cardiac dysfunction. This approach requires excellent skills in creating microvascular anastomosis in the narrow and relatively deep operative field a narrow and deep field, which is the only drawback of this technique indicated by the authors [5].

A mini-approach with 3D MR-angiography was used by G. Fischer et al. [1]. In addition to the mentioned advantages of the technique, the authors noticed absence of navigation error with a mini-approach. The approach mitigates the risk of meningeal hemorrhages, significantly reduces scar formation, and enables selection of optimal donor and recipient vessels preoperatively involving a shorter length of a donor vessel and optimal functioning of the anastomosis. MRI provides soft tissue imaging without radiation. without the use of damaging radiation and facilitates imaging of soft tissue components. without visualization of bone landmarks. The authors indicate the following limitations: additional time on preoperative planning, possible injury to a donor or recipient vessel during performing an approach, limited potential to use a different donor or recipient, and surgeons have to possess an extensive experience performing this technique.

According to I. Nakagawa et al. [6], subtraction angiography (SA), 3D modeling and preoperative planning facilitate more high-precision imaging of an appropriate donor and recipient vessel compared to CT and MR imaging. A skin incision, a length of the selected donor, an incision of the temporal muscle and a size of craniotomy, postoperative pain syndrome, and the risks of perioperative complications are minimized. The authors [6, 7] note one drawback of SA — a risk of symptomatic cerebral ischemia and multiple examinations can result in a large cumulative radiation dose that may harm patients.

**Conclusion**

A mini-approach is a minimally invasive technique of EC-IC bypass performing, has less operative trauma, intraoperative blood loss, a good cosmetic effect and risk of infection. Preoperative planning using 3D- and MSCT-angiography data significantly shortens operative time, since neuronavigation equipment are not required, and provides a high-precision identification of the appropriate recipient vessel. This approach has a high potential of wide application in clinical practice.

The narrowness and depth of an operative field complicates EC-IC bypass performing and requires special skills.

**Authors declare no conflict of interest.**
The technique of EC-IC bypass performing has undergone minimal changes since the first operation performed by Yasargil MG in 1967 and the changes have been associated with the advent of new technologies and techniques. The creation of EC-IC bypass through the described mini-approaches involves intraoperative neurosurgical navigation enabling the identification of an recipient artery preoperatively and prepare with a high precision. This approach has long been used for surgical revascularization of the brain in patients with chronic cerebral ischemia both in Russia and abroad, as shown in a dedicated series of publications. In contrast to the majority of papers describing single or small series of clinical cases, this paper analyzes a larger series — 35 cases. The authors propose an original method of preoperative planning, which allowed them to perform brain revascularization through a mini-approach.

The authors reasonably mention that the use of a mini-approach is the most technically complicated stage in the creation of EC-IC bypass. This is especially true in patients with severe cerebral cortex atrophy and large ischemic foci, since the opening of the arachnoid mater in these patients causes abundant outflow of CSF and displacement of brain structures, including a recipient artery, under bone structures.

This greatly complicates performing EC-IC bypass and control over its functioning, resulting in a higher incidence of postoperative anastomotic thrombosis (in the analyzed paper, shunt thrombosis was observed in 8.5% of cases only in the early postoperative period) and reduces the hemodynamic value of a shunt. Therefore, we would advise to use mini-approaches during EC-IC bypass surgery primarily when there are indications, for example, in brain revascularization under regional anesthesia. In other cases, mini-approaches do not yield significant benefits over classic EC-IC bypass and only raise the technical complexity of a surgery in an unjustified way.

Meanwhile, we consider the proposed method of preoperative planning of brain revascularization to be absolutely justified, especially for selective revascularization of brain areas with the highest perfusion impairment.

In general, this paper draws attention to an actual problem of surgical brain revascularization in the treatment of chronic cerebral ischemia.

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A Supraorbital Trans-Eyebrow Approach in Surgery Of Chiasmatic-Sellar and Anterior Cranial Fossa Tumors

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Objective — to analyze 31 resections of chiasmatic-sellar region (CSR) and anterior cranial fossa (ACF) tumors using the supraorbital trans-eyebrow approach (STA).

Material and methods. We analyzed medical histories of 31 patients who underwent tumor resection using STA in the period between October 2013 and April 2017. We analyzed the age and gender of patients, size and location of the tumor, presence of a neurological deficit, vision and olfactory functions before and after surgery, surgery duration, amount of intraoperative blood loss, rate of frontal sinus trephination and nasal liquorrhea, hemorrhagic and ischemic complications after surgery, Simpson grade of tumor resection, patient’s condition before and after surgery (Glasgow Outcome Scale and Karnofsky Scale), and degree of patient satisfaction with the cosmetic result of surgery.

A total of 26 meningiomas (20 sphenoid plate, tubercle, and diaphragm tumors, 3 lesser sphenoid wing meningiomas, 2 orbital roof tumors, and 1 anterior clinoid process meningioma), 3 frontal lobe gliomas, and 2 pituitary adenomas were resected.

Results. In all 31 operations, the approach was adequate and enabled tumor resection without lethal outcomes. The mean surgery duration was 174.6±64.4 min. The mean blood loss was 190±96.6 mL (50—380 mL).

After surgery, none of the patients developed motor deficits and new epileptic seizures. Neurological deficit aggravation in the form of impaired vision and mental disorders occurred in 8 (25.8%) patients. Vision impaired in 4 (12.9%) patients, improved in 6 (19.3%) patients, and remained unchanged in 21 (67.7%) patients. An endocrinological deficit in the form of partial hypopituitarism developed in 3 (9.6%) patients; in 4 (12.9%) patients, there were mental disorders that regressed by the end of the first month of therapy.

There were no intracerebral and subarachnoid hemorrhages. In 2 (6.4%) patients, small epidural hematomas were diagnosed, which did not require surgical treatment. There were only good outcomes (a GOS score of 4 or 5). After surgery, the median Karnofsky index in the STA group was 90±7.

Conclusion. The STA is adequate for removal of CSR and ACF tumors under proper selection of patients. It provides an adequate view of anatomical structures and enables successful tumor resection through a less traumatic access.

Keywords: supraorbital trans-eyebrow approach, chiasmatic-sellar tumors, anterior cranial fossa tumors.

Mini-approaches with a size of a keyhole are becoming popular in neurosurgery of the last three decades due to wide implementation of modern neurodiagnostics methods: X-ray computed tomography (CT) and magnetic resonance imaging (MRI), microscopes, micro-instruments and neuronavigation [1—12]. Advocates and opponents of supraorbital trans-eyebrow keyhole approach discuss the advisability of its use, benefits and drawbacks [13—17].

Supraorbital trans-eyebrow approach (STA) is minimally traumatic and gives a good view of the anatomical structures in the chiasm-sellar region (CSR) and anterior cranial fossa (ACF) and allows adequate surgical manipulation in these areas. It is an analogue of the standard supraorbital approach, differing by a smaller size of a trephine opening and less injury to soft tissues [18—22].

The purpose of this study is to analyze treatment outcomes of 31 patients with CSR and ACF tumors using supraorbital trans-eyebrow approach and define its benefits and limitations.

Material and methods

This study is a retrospective analysis of medical records and video-recordings of operations on 31 patients (26 women and 5 men) with ACF and CSR tumors operated on using STA in the period from October 30, 2013 to April 06, 2017 at the Department of Neurosurgery of the Interregional Clinical and Diagnostic Center (Kazan).

Preoperatively, all patients underwent contrast-enhanced MRI and angiography (magnetic resonance angiography, multislice computed tomography or cerebral angiography). The choice of approach was decided by a consultation between several neurosurgeons and a neurologist only after careful analysis of examination results.

In the first 24 hours after surgery, all patients underwent brain CT; preoperative and postoperative neurologic and ophthalmologic states were compared.

We assessed the age and gender of patients, size and location of the tumor, presence of neurological deficit, vision and olfactory functions before and after surgery, length of surgery, volume of intraoperative blood loss,
rate of frontal sinus trephination and nasal liquorhea, hemorrhagic and ischemic complications after surgery, Simpson grade of tumor resection, patient’s condition before and after surgery (Glasgow Outcome Scale and Karnofsky Scale), degree of patient’s satisfaction with the cosmetic effect of an operation (a VAS score of 0—10). Three months postoperatively, all patients underwent MRI of the brain. Most patients were re-examined by a neurosurgeon, some patients underwent a telephone survey. The follow-up period was 16.2±13.5 months (2 to 38 months).

A total of 26 meningiomas were resected (20 sphenoid plate, tube and diaphragm tumors, 3 lesser sphenoid wing tumors, 2 orbital roof tumors, and 1 anterior clinoid process), 3 frontal lobe gliomas and 2 pituitary adenomas (Table 1).

1. Patients with meningiomas (n=26): the mean age of patients was 57.1±8.4 years (41 to 75 years). The average meningioma size was 24.5±7.9 mm and ranged from 8 to 40 mm.

Prior to surgery, 6 (23.1%) patients had no neurologic deficit, 20 (76.9%) patients had neurologic deficit, most of them (16 (61.5%) patients) in form of chiasmatic syndrome. One (3.8%) lacked olfaction, 3 (11.5%) had right-sided hemiparesis up to 4.5 scores unrelated to the tumor.

Twenty one (80.7%) patients complained of vision impairment, 15 (57.7%) patients complained of headache and 1 (3.8%) patient — epileptic seizures. In 1 (3.8%) patient, tumor did not cause symptoms (Table 2).

Karnofsky index of 70 scores was observed in 3 patients, 80 scores — in 11, and 90 scores — in 12. The median preoperative Karnofsky index was 80±7 scores.

Twenty four patients were operated on through unilateral supraorbital trans-eyebrow approach and 2 patients with sphenoid tube and diaphragm meningiomas were operated on with bilateral supraorbital trans-eyebrow approach. The decision to use bilateral approach was made at the stage of planning the operation because that both internal carotid arteries and optic nerves passed through the tumor stroma on MRI scans. A bilateral approach provided different viewing angles and trajectories to approach the tumor, which reduced the risk of injury to the carotid arteries and optic nerves and increased the extent of surgical resection.

Patients with gliomas (n=3): 2 women (46 and 47 years old) and 1 man (70 years old) had gliomas (Grade I—II) in basal parts of the frontal lobe. The maximum sizes of tumors were 54, 47 and 78 mm, respectively. Two patients had epileptic seizures. Karnofsky index was 90 scores in 2 patients and 100 scores — in 1 patient. There was no neurologic deficit.

Patients with pituitary adenomas (n=2): 1 female (46 years old) and 1 male (57 years old) had endosuprasellar hormone-inactive pituitary adenomas with a size of up to 20 mm. In both cases chiasmatic syndrome was revealed, Karnofsky index was 90 and 80 scores.

Surgical procedure

General endotracheal anesthesia was used for operations. All patients received third-generation cephalosporins as antibacterial prophylaxis 1 h before surgery and patients with pituitary adenoma and sphenoid tube and diaphragm meningioma underwent prophylaxis therapy of acute adrenal insufficiency due to the potential risk of injury to the hypothalamic region and the pituitary stalk (administration of 75 mg hydrocortisone 9 h before surgery and 100 mg — 1 h before surgery).

The patient was positioned supine; the patient’s head was secured in a Mayfield holder. The head should be elevated above the chest level by 15°. The head was rotated 10—15° towards the healthy side for orbital roof tumors and lesser sphenoid wing and by 30—45° for chiasm-sellar tumors (Fig. 1).

Skin incision with a length of 4—5 cm was made along the line of the brow laterally to the supraorbital notch. A burr hole was put laterally to the temporal line in the area of the sphenofrontal suture. Using a craniotome, two cuts were made from this burr hole: one straight medially and the second arc-shaped. The trephine opening is approximately 3.5x2.5 cm. The dura mater is opened in an arc fashion with a base on the upper orbital rim (Fig. 2).

Further manipulations were performed using a microscope. The frontal lobe was mobilized. CSF cisterns of the internal carotid artery and optic chiasm were opened; CSF cisterns of Sylvian fissure were opened if necessary. Afterwards, a tumor was resected.

After tumor removal, the dura mater was re-approximated in a watertight fashion. When the frontal sinus was opened, the frontal sinus mucosa was excised, the sinus was packed with a muscle or adipose tissue fragment using biological glue, and at the end of the operation the defect was covered with periosteum. Bone flap was fixed to the skull bones. Soft tissues were sutured in layers. Intradermal cosmetic suture was made (Fig. 3).

After surgery, all patients were transferred to the intensive care unit to monitor the condition.

Results

In all 31 operations, the approach was adequate and allowed tumor resection without lethal outcomes (Fig. 4).

The average length of surgery was 174.6±64.4 min (range, 100 to 375 min). The mean blood loss was 190±96.6 ml (50—380 mL). Blood loss at the stage of approach was 10±6.2 ml (5—20 mL).

The resection extent of meningiomas is presented in Table 3. Gliomas were macroscopically completely removed. One pituitary adenoma was removed totally, the second pituitary adenoma — subtotally.

Frontal sinus trephination was performed in 5 (16.1%) operations. There were no cases of postoperative nasal liquorhea.
Aggravation of neurologic deficit was observed in 8 (25.8%) patients in form of visual impairment and mental disorders. None of the patients had motor deficits and new epileptic seizures after the surgery.

According to ophthalmologic examination, after surgery vision deteriorated in 4 (13%) patients, vision improved in 6 (19.3%) and remained unchanged in 21 (67.7%) (Table 4).

Mental disorders developed in 4 (12.9%) cases in the early postoperative period, which regressed by the end of the first month of therapy. All patients were operated on the dominant left hemisphere. The first case was a female patient after resection of tuberculum sellae meningioma who had a verified small ischemic focus in the territory of Heubner’s artery on postoperative CT. The second case was a female patient with orbital roof meningioma who developed postoperative edema of the frontal lobe on the side of manipulation. The third case was resection of glioma from the basal parts of the frontal lobe and the fourth — after subtotal resection of pituitary adenoma.

Three (9.6%) patients after surgery developed endocrinological deficit in the form of partial hypopituitarism (adrenocorticotropic hormone deficiency) and transient diabetes insipidus that required medical correction. In the first case it was a female patient with pituitary adenoma, in the other two cases — patients with sphenoid diaphragm and tubercle meningioma. Endocrinological deficit regressed within 7—10 days. In 1 (3.2%) case, transient neuropathy of the oculomotor nerve developed, which fully regressed within 3 months.

Postoperatively, 2 (6.4%) patients were diagnosed with small epidural hematomas that did not require surgical treatment. Intracerebral and subarachnoid hemorrhages were not observed.

Postoperative wound healed by primary intention without infectious complications and wound liquorhea in 31 (100%) patients (examples in Fig. 5). Subcutaneous CSF accumulation was observed in 2 (6.4%) patients after surgery treated with conservative therapy.

Glasgow outcome scale showed only good outcomes (4 and 5): 8 (25.8%) patients were discharged from the hospital with 4 scores and 23 (74.2%) patients with 5 scores. By the time of discharge, Karnofsky index was 60 scores in 1 (3.2%) patient, 70 scores — 4 (12.9%) patients, 80 scores — 9 (29.1%), and 90 scores — 17 (54.8%) patients. In 3 (11.1%) patients the condition on Karnofsky scale deteriorated (occurrence of endocrinological deficiency, oculomotor nerve neuropathy and mental disorders: disorientation in space and time, retrograde amnesia, confabulation). In 1 (3.7%) patient, Karnofsky score increased (vision improved). The median Karnofsky score after surgery was 90±7 scores in the STA group (Table 5).

The average length of follow-up was 16.2±13.5 months (2 to 38 months). Twenty five (80%) patients were available for follow-up. Two patients died: one female patient 14 months after surgery because of kidney and liver failure and the second female patient — 31 months after surgery because of heart failure.

Tumor recurrence occurred in 1 (3.2%) patient with sphenoid tubercle meningioma. The patient underwent radiosurgery treatment within the tumor area.

Three (9.6%) patients noted complete lack of olfaction after surgery (2 patients with tubercle and diaphragm meningioma and 1 — with pituitary adenoma); 1 (3.2%) patient with sphenoid diaphragm and tubercle meningioma developed unilateral anosmia (Table 6).

One (4%) patient developed eyebrow palsy, 3 (12%) patients — hypoaesthesia in the supraorbital region. Nine (36%) patients noted the appearance of a small fossa in the area of the lateral orbital rim (defect from putting of burr hole), which did not cause discomfort and as they say it was not noticeable to others.

All patients were surveyed using the VAS scale to estimate satisfaction with cosmetic effect of surgery: 6 scores were reported by 1 (4%) patient, 7 scores — 1 (4%), 8 scores — by 3 (32%), 9 scores — by 3 (32%), and 10 scores — by 17 (68%) patients. The average VAS score was 9.36. The median VAS score was 10±1.

Discussion

Surgery on ACF base and CSR has always been described as a complicated area in neurosurgery. The close
Fig. 1. Positioning of a patient and planning of a supraorbital trans-eyebrow approach.

Fig. 2. Stages of supraorbital trans-eyebrow approach.
a — view of a trephine opening prior to dissection of aponeurosis; b — size of bone flap sawn during supraorbital trans-eyebrow craniotomy; c — view of a trephine opening after opening of the dura mater.

Fig. 3. Stages of surgical wound suturing in supraorbital trans-eyebrow approach.
a — bone flap fixation with a Craniofix system; b — view of a trephine opening after suturing aponeurosis; c — view of a postoperative wound after its suture with intradermal suture.
association between pathologic processes in ACF with large great vessels and cranial nerves required a good visualization of this area through broad frontal-temporal approaches [23—27]. In recent decades, a multitude of approaches to ACF have been developed, with pterional, subfrontal and supraorbital being the most popular [28—30]. At the end of the XX — beginning of the XXI century, papers focused on supraorbital trans-eyebrow approach were published. Popularizers of this approach were neurosurgeons A. Perneczky and R. Reisch [8, 9]. Supraorbital trans-eyebrow approach belongs to keyhole-approaches. A keyhole surgery is aimed at performing an operation through a small trephine opening. A view of the skull base structures with such a technique is not inferior to classic approaches, as proven in several studies [32]. An important condition is the correct choice of the approach location to open well the anatomy of the area of interest and form a convenient surgical corridor [33, 34].

STA has the anterolateral location that provides adequate and short trajectory to CSR and ACF lesions [32]. An advantage is that STA does not require temporal lobe traction and opening of Sylvian fissure, thus minimizing development of neurologic complications and epileptic seizures. The world literature reports a rate of 8—12% for epileptic seizures after transcranial surgery. In our study, none of patients had epileptic seizures after surgery. STA demonstrates another important advantage — low blood loss, which does not exceed 15 ml.

With good skills in performing the STA technique, it may well become a routine approach to small (less than 5 cm) sphenoid plate, tubercle and diaphragm meningiomas providing good control over tumor resection at all stages of the operation. Orbital roof meningiomas due to their location closely to the supra-orbital region are a direct indication for STA. Olfactory meningiomas are also suitable candidates for resection through STA, but in some cases, the small size of a trephine opening may hinder complete removal of tumors in a region of eematrix deep in the olfactory fossa [35]. STA can also be an alternative to transnasal approaches in pituitary adenoma surgery with supra- and parasellar growth, particularly in neurosurgical clinics where transnasal surgery is not mastered. Frontal lobe gliomas are more variable in shape, size, and histological structure than meningiomas and pituitary adenomas. But in some cases, when glioma is located in the basal parts of the frontal lobe and extends to subcortical ganglia, STA can be more beneficial in terms of trajectory and is less traumatic than classic approaches.

However, STA is not a universal approach to CSR and ACF. Due to small craniotomy, despite good viewing

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*Fig. 4. MRI of a patient with tubercle and sphenoid plate meningioma.*

a, b, c — preoperative scans; d, e, f — postoperative scans.
In this approach, it limits the space for manipulation and can be inconvenient in some situations. Therefore, this approach can be problematic to remove large tumors (more than 5 cm), tumors extending to the middle cranial fossa, invading into the ethmoid bone, with calcified areas on CT and MRI, and with profound edema of the frontal lobe. However, a thorough preoperative analysis of the situation and the microsurgical stage of the operation, planning the location of approach, the use of special microinstruments, and early trephination of basal cisterns for early brain relaxation and, in some cases, the use of endoscope can provide successful outcome. In addition, the surgeon must have sufficient experience in removing such tumors through classic approaches before beginning to master a keyhole-surgery.

Preoperatively, each patient is recommended to perform radiography or computed tomography of the skull to acquire data on the size and configuration of the frontal sinuses for projection of their margins on the forehead skin [36]. Neuronavigation is useful. A contraindication to STA is a large frontal sinus that extends to the area of planned approach. Sometimes, in spite of additional procedures, the sinus is opened, which can cause nasal liquorrhea and infectious complications. Frontal sinus trephination requires its proper watertight closure. First, the frontal sinus mucosa is excised and the sinus is then packed with muscle or adipose tissue fragment using biological glue; the defect is covered with a periosteal or fascia flap. In our study, there were no complications associated with frontal sinus trephination. It is recommended to follow-up all patients after surgery for the presence of nasal liquorrhea and possible endocrine disorders [37].

Since most patients complain of vision impairment before surgery, maintaining or even improving vision is one of the main tasks of the operation. The world literature noted that in 59.19% (25—80%) of cases vision improves, in 29.5% — remains unchanged and in 13% — deteriorates. Expansion of visual fields is typically regarded as improvement [38]. According to our intraoperative observations, vision deteriorated in patients with severe compression of the optic nerves by the tumor, severe adhesion of the tumor to optic nerves and optic nerve atrophy.

The choice of a side for the approach depends on many factors. In case of tumor laterality, ipsilateral side is preferred. If the tumor is located mainly in the area of...
one optic nerve, but medially to it, the contralateral side is more convenient in some cases allowing tumor resection from under the nerve without much injury. If the patient has no vision on one side, then this side is advisable for the approach to preserve the healthy nerve. In 2 operations, we deliberately used bilateral approach to have control over the tumor on both sides and minimize injury to the optic nerves and carotid arteries tightly covered by the tumor. In this case, the use of a bilateral STA allowed us to avoid a large traumatic approach and achieve good control during tumor removal.

Anosmia was recorded in 3 (11%) patients after surgery. A. Perneczky and R. Reish in a series of cases [8, 9] reported that unilateral anosmia developed in 6% of patients and bilateral one with impaired sense of taste — in 2%. S. Czirjak in a series of cases [1] observed anosmia in 10% of patients. Anosmia can often occur even with a small traction of the frontal lobe. To minimize injury to the olfactory nerves, retractors should be placed as laterally as possible relative to the midline. Currently, neurosurgeons are slightly concerned on this complication, although lack of olfaction reduces the quality of life of both the patient and relatives.

STA provides a good cosmetic result. Despite that the approach is performed on the visible part of the face, which confuses many neurosurgeons, in most cases, no trace of the operation remains on the face of the patient in 3 months [34].

Since each patient requires an individual approach, STA is typically adequate to access the following tumors: anterior clinoid process, tuberculum sellae and orbital roof meningiomas; gliomas of the basal parts of the frontal lobe; pituitary adenomas and craniopharyngiomas.

Along with general complications that occur in any neurosurgical operation, there are a number of complications typical only for STA: 1) numbness of the forehead skin in case of injury to the supra-orbital nerve; 2) paralysis of the muscle that raises the eyebrow (the frontal abdomen of the epicranius muscle) in case of injury to the frontal branch of the facial nerve; 3) nasal liquorhea during frontal sinus trephination and improper watertight closure; 4) poor cosmetic effect resulting from individual characteristics of skin, bad suturing, burns caused by long intense illumination from a microscope and persistent pseudomeningocele.

**Conclusion**

STA is an adequate approach for resection of CSR and ACF tumors. It provides the necessary view of the anatomical structures and successful tumor resection. This is a valuable method for patients with CSR and ACF tumors who meet the inclusion criteria.

**Authors declare no conflict of interest.**

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**Table 5. Treatment outcomes for patients on the Glasgow outcome scale and Karnofsky scale**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>STA, abs. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOS, scores</td>
<td>8 (25.8)</td>
</tr>
<tr>
<td>4</td>
<td>23 (74.2)</td>
</tr>
<tr>
<td>5</td>
<td>1 (3.2)</td>
</tr>
<tr>
<td>70</td>
<td>4 (12.9)</td>
</tr>
<tr>
<td>80</td>
<td>(29.1)</td>
</tr>
<tr>
<td>90</td>
<td>17 (54.8)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>On Karnofsky scale, scores</th>
<th>STA, abs. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>1 (3.2)</td>
</tr>
<tr>
<td>70</td>
<td>4 (12.9)</td>
</tr>
<tr>
<td>80</td>
<td>(29.1)</td>
</tr>
<tr>
<td>90</td>
<td>17 (54.8)</td>
</tr>
</tbody>
</table>

**Table 6. The rate of olfaction impairment**

<table>
<thead>
<tr>
<th>State of olfaction function</th>
<th>STA, abs. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anosmia</td>
<td>4 (16)</td>
</tr>
<tr>
<td>Hyposmia</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Normosmia</td>
<td>20 (80)</td>
</tr>
<tr>
<td>Total of patients</td>
<td>25 (100)</td>
</tr>
</tbody>
</table>
This paper focuses on craniotomy, which has become “fashionable” in recent years. The accumulated experience of surgical treatment of ACF and CSR tumors in 31 patients allowed the authors to share their own experience and draw certain conclusions on this approach.

However, some of the statements are disputable. In particular, the choice of approach cannot be a goal in itself and should be based on patient safety, therefore it cannot be accepted that bilateral STA may be preferable to unilateral pterional approach for resection of tuberculum sellae meningiomas.

The authors do not justify the advisability of choosing STA for resection of relatively small pituitary adenomas (diameter of 20 mm). The authors argue that “STA can be used as an adequate alternative for transnasal approach”, which is disputable. The possibilities of the discussed approach are limited for removal of intra- and parasellar components of pituitary adenomas.

The work is interesting, the authors pay great attention to the nuances of planning surgical approach, its advantages and drawbacks. The paper is illustrated by pre- and postoperative images showing the extent of surgical removal. Photographs of patients’ faces demonstrate good postoperative cosmetic effect.

M.A. Stepanyan (Moscow, Russia)
Analysis of the Results of Total Cervical Disc Arthroplasty Using a M6-C Prosthesis: a Multicenter Study

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Cervical spondylosis and intervertebral disc (IVD) degeneration are the most common cause for compression of the spinal cord and/or its roots. Total IVD arthroplasty, as a modern alternative to surgical treatment of IVD degeneration, is gaining popularity in many neurosurgical clinics around the world.

Aim — the study aim was to conduct a multicenter analysis of cervical spine arthroplasty with an IVD prosthesis M6-C (Spinal Kinetics, USA).

Material and methods. The study included 112 patients (77 males and 35 females). All patients underwent single-level discectomy with implantation of the artificial IVD prosthesis M6-C. The follow-up period was up to 36 months. Dynamic assessment of the prosthesis was based on clinical parameters (pain intensity in the cervical spine and upper extremities (visual analog scale — VAS); quality of life (Neck Disability Index — NDI); and subjective satisfaction with the results of surgical treatment (Macnab scale) and instrumental data (range of motion in the operated spinal motion segment, degree of heterotopic ossification (McAfee-Suchomel classification), and time course of degenerative changes in the adjacent segments).

Results. The mean level of pain in the cervical spine (VAS) was 6.7±1.5 cm before surgery and 1.2±0.8 cm after surgery, and the mean level of pain in the upper extremities reduced from 6.9±1.7 to 1.3±1.1 cm (t-test, \(p<0.001\)). The mean quality of life index (NDI) amounted to 41.1±5.7% before and 11.1±4.4% after surgery (t-test, \(p<0.001\)). The mean range of motion in the operated segment at baseline was 6.4±2.5° and increased to 8.8±2.6° at 36 months after surgery. During the entire follow-up period, initial and moderate signs of heterotopic ossification were detected in 17 (15.1%) and 12 (10.7%) patients, respectively. Degeneration of the adjacent segments occurred in 2.8% of cases. Postoperative complications developed in 4.4% of cases.

Conclusion. Total arthroplasty of degenerated cervical IVDs with the prosthesis M6-C may significantly reduce the severity of pain, improve the quality of life in patients, preserve the normal range of motion in the operated spinal motion segment, and reduce the time of temporary disability.

Keywords: cervical spine, intervertebral disc degeneration, spondylosis, dynamic fixation, total arthroplasty, intervertebral disc prosthesis M6-C.

Abbreviations: IVD — intervertebral disc VAS — visual analogue scale of pain NDI — Neck Disability Index — quality of life as assessed by the index of movement restrictions in the cervical spine HO — heterotopic ossification DW MRI — diffusion-weighted magnetic resonance imaging MSCT — multi-slice computed tomography

Spondylosis and degenerative disease of the cervical intervertebral discs (IVDs) are the most common cause for compression of the spinal cord and/or its roots [1]. To date, surgery (anterior cervical discectomy and interbody stabilization) is usually indicated in the case of conservative therapy failure in patients with signs of cervical radiculopathy or myelopathy [2]. This operation is characterized by high level of patients’ satisfaction with the treatment and effective spinal fusion in 95% of cases [3, 4]. However, rigid cervical fixation leads to restriction of movement in the operated spinal motion segment, which is an inducing factor for the development of degenerative disease in adjacent IVDs and, as a consequence, reoperation [4].

Total IVD arthroplasty, as a modern alternative to surgical treatment of IVD degeneration, is gaining popularity in many neurosurgical clinics around the world [5, 6]. IVD arthroplasty is aimed at full restoration and preservation of the physiological range of motion in the spinal motion segment, which prevents degeneration of adjacent IVDs, neutralizes pain and neurologic symptoms [7].

To date, several artificial IVDs have been developed. Of these, Discovery (Depuy Spine), ProDis (Spine Solutions), Mobi-C (LDR), Rotaio (Medizintechnik GmbH), Bryan (Medscape), M6 (Spinal Kinetics, Switzerland) are the most popular ones.

The studies on the application of IVD prostheses demonstrated high efficacy in terms of clinical and radio-
graphic outcomes in patients with IVD degeneration as compared to spinal fusion. The development of various structures of the functional IVD prostheses is aimed at optimizing postoperative outcomes. However, interpretation of the results of their application is ambiguous.

The study is aimed at a multicenter analysis of the use of IVD prosthesis M6 (Spinal Kinetics) for the cervical spine arthroplasty.

Material and methods

The study was carried out at the Neurosurgery Center of the Railway Clinical Hospital, Irkutsk-Passenger Station (Irkutsk), Neurosurgical Department of the Regional Clinical Hospital (Krasnoyarsk), and Neurosurgical Department of the 1477th Naval Clinical Hospital (Vladivostok). The study was approved by the ethics committee of the Irkutsk State Medical University. Each involved patient gave written informed consent. Indications and contraindications for IVD arthroplasty with M6-C prosthesis were used as inclusion and exclusion criteria.

Criteria for inclusion in the study: single-level cervical IVD degeneration from C4 to C7 vertebral body (Pfirman grade I—II [8]), minimal degenerative changes in the facet joints (Fujiwara grade I—II [9]), persistent pain resistant to conservative treatment (4—6 weeks), preserved interbody space height (more than 50% of the overlying one), and no evidence of segmental instability in the spinal motion segment and posterior osteophytes.

Contraindications to inclusion in the study: osteoporosis, segmental instability, spondylolysis with compensatory changes the facet joints and restriction of movement, congenital stenosis of the spinal canal, previous surgical procedures on the spinal motion segment.

The study group was examined to assess clinical and radiographic parameters before surgery, at discharge, and during control examinations recommended 6, 12, 24, and 36 months after surgery.

Surgical technique. Operation field was treated with antiseptic solution in triplicate followed by Cloward’s method (4 slices), General Electric (USA) and the severity of degeneration of adjacent segments (MRI-grams, 1.5 T scanner, Siemens Magnetom Essenza (Germany). Technical characteristics of the surgery, such as duration of the operation, blood loss, hospital stay and activation time were also assessed as additional results of the study.

Statistical analysis was performed using Microsoft Excel 2010 software. Descriptive statistics are represented as M±SD, where M is mean value and SD is standard deviation. Categorical variables are represented in percentage terms. Statistical validity of preoperative values, as well as the values in the early and late postoperative period (p-value) was determined using Student’s t-test or, in the case of nonparametric values, using Mann-Whitney test. The differences were considered significant at p<0.05.

Results

The study included 112 patients (77 males, 35 females) aged 23 to 45 years (mean age 33.6±6.4 years). The average height of the patients was 175.3±7.9 cm, body weight — 69.4±9.7 kg. In 68 (60.7%) cases, surgery was carried out at the level of C5—C6, in 42 cases (37.5%) — C6—C7, and in 2 cases (1.8%) — C4—C5. Mean operation time was 94±14.07 min, average blood loss — 48.9±7.4 ml. Hospital stay time averaged 8.2±1.5 days.

Assessment of pain intensity using VAS showed positive dynamics in the form of significant decrease in the severity of postoperative pain on the average from 6.7±1.5 to 2.1±1.3 cm and from 6.9±1.7 to 2.2±1.5 cm, respectively, for pain in the cervical spine and upper extremities 6 months after surgery (t-test; p<0.001), while maintaining its minimum value throughout the follow-up period. Thirty six months after total arthroplasty, VAS pain severity score was 1.2±0.8 cm in the cervical spine and 1.3±1.1 cm in the upper extremities (Fig. 3).

Analysis of the quality of life index in terms of Neck Disability Index (NDI) showed significant positive dynamics of patients’ functional status after total arthroplasty as compared to preoperative period: on the average, from 41.1±5.7 to 17.9±6.6% 6 months after the operation (t-test; p<0.001). Subsequent follow-up showed no statistically significant changes in the quality of life in 36 months, 11.1±4.4% (Fig. 4).

Analysis of patients’ satisfaction with the results of surgery according to the subjective Macnab scale over
time showed mostly good and excellent outcomes (90%) (Fig. 5), which proves the functional viability of the operated spine and social adaptation of the majority of patients.

All patients underwent functional spondylography of the cervical spine at the time specified by the study protocol to assess radiological outcomes of the total arthroplasty. The range of motion in the operated spinal motion segment was maintained within physiological limits: the range of motion in the operated segment averaged 6.4±2.5° before surgery, 8.6±2.3° 6 months after the operation, and 8.8±2.6° in 36 months (Fig. 6). No signs of structure instability were observed.

According to our data over the entire follow-up period, mild and moderate signs of heterotopic ossification (McAfee-Suchomel grade I—II) were observed in 17 (15.1%) and in 12 (10.7%) cases, respectively.

MRI in the late postoperative period verified degeneration of adjacent spinal motion segments (Pflrmann grade II—III) in 2.8% of cases.

Data analyzing verified 5 (4.5%) complications: 2 cases of dysphagia and 1 case of dysphonia, which were associated with traction of the trachea and esophagus, as well as innervation of the nn. laryngei during surgical approach. In 2 patients, subfascial hematomas were detected. In all cases, the complications spontaneously resolved in the early postoperative period. There were no adverse effects associated with insertion of stabilizing structures itself.

Discussion

For many years, anterior cervical fusion demonstrated high efficacy in the treatment of patients with IVD degeneration [10]. However, numerous studies of surgical outcomes with rigid stabilization indicate the absence of physiological biomechanical stress distribution on adjacent spinal motion segments. Some patients who underwent spinal fusion surgery for IVD degeneration, required reoperations on adjacent segments (12—25% of cases) [11, 12].

Active development of modern spinal neurosurgery led to discovery of the novel concept of dynamic fixation of the operated segments. Total IVD arthroplasty technique is one of these innovations, and it is currently considered to be a highly surgical treatment for patients with IVD degeneration. Insertion of the dynamic structures preserves physiological range of motion in the operated segment [13].

Full recovery of IVD function and biomechanics of the affected spinal motion segment is the main task of IVD prosthesis [13]. Modern IVD prostheses include artificial nucleus pulposus, which consists of hydrogel or polyurethane and enables axial compression, as well as artificial annulus, which consists of fibrous material and provides controlled amplitude of segment mobility [14].

There are no unambiguous indications for total IVD arthroplasty in current neurosurgical practice. However, most of the authors [15, 18, 20, 21] adhere to the following indications: single-level or multi-level IVD degeneration in the form of the “soft-tissue” hernia with maintained disk height; signs of radiculopathy and/or my-
elopathy, minimal changes in the facet joints, and inefficient conservative treatment for 6 weeks. In some studies, traumatic IVD hernia were also considered as indication to the total IVD arthroplasty [16, 17]. At the same time, according to D. Jadik et al. [18], insertion of artificial prostheses is contraindicated in the case traumatic IVD hernia.

Total IVD arthroplasty procedure is characterized by various clinical efficacy in patients with IVD degeneration. For example, the series of P. Mummaneni et al. [19], who used Prestige ST IVD prosthesis (Medtronic), demonstrated decrease in VAS pain severity score from 8.3 to 2.7 cm and improvement in the quality of life as assessed by NDI from 57 to 39 points in the early postoperative period. In the study by L. Chen et al. [20], who used Discover prosthesis (Depuy Spine), VAS pain score decreased from 7.8 to 2.3 cm and the quality of life as assessed by NDI improved from 47.8 to 28.6 points. R. Davis et al. [21], who used the Mobi-C prosthesis (LDR), observed decrease in VAS pain score from 6.4 to 3.5 cm in the early postoperative period. The study of P. Sukhomel et al. [22] verified clinical efficacy of ProDisc IVD prosthesis (Spine Solutions) by decrease in VAS pain score from 6.4 to 2.7 cm and improvement of NDI quality of life index from 35 to 26 points. According to our data, the severity of pain as assessed by VAS decreased from 6.7 to 1.2 cm in the cervical spine and from 6.9 to 1.3 cm in the upper extremities, and the quality of life as assessed by NDI improved from 41.1 to 11.1 points.

The range of motion of the operated spinal motion segment is the most important radiological and biomechanical characteristic of the effectiveness of the total IVD arthroplasty. In our clinical series, the range of motion of the operated segment increased by an average of 8.7°, which is consistent with data from other clinical series. J. Obernauer et al. [23], who used Rotaio prosthesis (Medizintechnik GmbH) for arthroplasty, noted increase in the range of motions in the segment by 8.6°. L. Chen et al. [20], who used Discover IVD prosthesis (Depuy Spine), detected increase in the range of motion in the operated vertebral motion segment by an average of 7.9°. In the study by R. Davis et al. [21], increase in the range of motion in the segment after prosthetic repair of the IVD using Mobi-C implant (LDR) averaged 8.3°.

Heterotopic ossification (HO), a histogenesis disorder characterized by bone formation in soft tissues that normally do not have osteogenic properties, is the most urgent problem of the use of IVD arthroplasty. The rea-
**Fig. 4.** Evaluation of clinical outcomes in the study group patients: the dynamics of the functional state of patients as assessed by NDI.

**Fig. 5.** The subjective patients' satisfaction with the surgery according to the Macnab scale.

**Fig. 6.** Change in the range of motion (M±SD) in the operated segment.
sons and histopathogenesis of heterotopic ossification are not fully understood. There are some inducing factors: metabolic disorders, impaired microvascular circulation, and impaired neurogenic control over mesenchymal cell differentiation into osteoblasts [24]. The role of genetic factors in heterotopic ossification was also proved [25]. HO includes several stages, from the stage of damaged tissues lysis and migration of connective tissue cells into the lesion to the stage of maturation and stability of the newly formed tissue. Morphological picture of HO is represented by cancellous bone, where intertrabecular spaces are filled with adipose tissue and isolated blood vessels [26].

According to the professional literature, heterotopic ossification is a common complication of IVD prosthetic replacement. For example, in clinical series of R. Bertagnoli et al. [27] consisting of 27 patients who underwent total IVD arthroplasty with ProDisc prosthesis (Spine Solutions), no signs of HO were observed within 1 year after surgery. After a 2-year follow-up period, grade I—II heterotopic ossification foci were detected in 9.4% of cases. In the study by R. Sola et al. [28], who used Bryan prosthesis (Medscape), HO was detected in 60% of cases after a 5-year follow-up period. Sukhomel P. et al. [22], who used the ProDisc prosthesis (Spine Solutions), detected signs of grade I—II HO in 38% of patients and grade III HO in 15.4% of patients. In our study, grade III heterotopic ossification foci were detected in 10.7% of patients, there were no grade III and IV foci.

Degeneration of adjacent spinal motion segments after total IVD arthroplasty in the late postoperative period was significantly more rare compared to the surgery for interbody stabilization. However, according to some authors, the percentage of involvement of adjacent segments varies in wide range (Table). According to P. Mummaneni et al. [19], total arthroplasty is followed by degeneration of adjacent segments in 4.9% of patients. R. Sola et al. [28] reported the development of degenerative diseases of adjacent segments in 17% of cases. In our observations, degeneration of adjacent vertebral segments was observed in 2.8% of patients. The diagnosis of IVD degeneration is based on the interpretation of MRI data in standard modes. It should be noted that the state of the IVD cannot be assessed using T1 and T2-weighted MRI images at the early stages of degeneration [29]. Improvement of MRI techniques enables quantification of the severity of IVD degeneration. Diffuse-weighted magnetic resonance imaging (DW MRI) evaluates the state of IVD tissue by monitoring of the movement of free water molecules at the cellular level and estimates the level of its degeneration at the early stages. We have developed and implemented into clinical practice the method to evaluate the level of IVD degeneration using the DW MRI procedure and measured diffusion coefficient [30]. DW MRI is undoubtedly a promising method for diagnosis of IVD degeneration. Currently, the studies focusing on the investigation of the relationship between

### Comparative characteristics of the studies on the total IVD arthroplasty

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of patients</th>
<th>Operation duration, min</th>
<th>Used IVD prosthesis</th>
<th>Decrease in the VAS pain score in the cervical spine, grade, %</th>
<th>Decrease in the VAS pain score in the upper extremity, grade, %</th>
<th>Improvement of the quality of life, NDI, %</th>
<th>Decrease in the range of motion in the operated segment, °</th>
<th>Percentage (grade) of HO</th>
<th>Degenerative disease of the adjacent segments, %</th>
<th>Complications, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>D. Jadik et al. [18]</td>
<td>55</td>
<td>18</td>
<td>Prestige ST</td>
<td>8.8 to 2.4</td>
<td>7.7 to 2.7</td>
<td>5.2 to 1.7</td>
<td>6.6 to 1.7</td>
<td>—</td>
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<tr>
<td>P. Mummaneni et al. [19]</td>
<td>318</td>
<td>15</td>
<td>Discover</td>
<td>8.6 to 2.4</td>
<td>7.7 to 2.7</td>
<td>5.2 to 1.7</td>
<td>6.6 to 1.7</td>
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<tr>
<td>L. Chen et al. [20]</td>
<td>108</td>
<td>30</td>
<td>Prod-C</td>
<td>8.9 to 3.5</td>
<td>7.7 to 2.7</td>
<td>5.3 to 1.7</td>
<td>6.3 to 2.7</td>
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<tr>
<td>R. Davis et al. [21]</td>
<td>225</td>
<td>30</td>
<td>Mobi-C</td>
<td>8.8 to 2.4</td>
<td>7.7 to 2.7</td>
<td>5.2 to 1.7</td>
<td>6.6 to 1.7</td>
<td>—</td>
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<tr>
<td>P. Sukhomel et al. [22]</td>
<td>318</td>
<td>30</td>
<td>Vobi-C</td>
<td>8.6 to 2.4</td>
<td>7.7 to 2.7</td>
<td>5.2 to 1.7</td>
<td>6.6 to 1.7</td>
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<td>S. Babishad et al. [23]</td>
<td>54</td>
<td>12</td>
<td>SA</td>
<td>8.8 to 2.4</td>
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<td>6.6 to 1.7</td>
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<td>R. Bertagnoli et al. [27]</td>
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<td>12</td>
<td>Prod-C</td>
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<td>7.7 to 2.7</td>
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<td>6.6 to 1.7</td>
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<tr>
<td>J. Obernauer et al. [23]</td>
<td>318</td>
<td>12</td>
<td>Bryan</td>
<td>8.6 to 2.4</td>
<td>7.7 to 2.7</td>
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<td>50</td>
<td>Bryan</td>
<td>8.6 to 2.4</td>
<td>7.7 to 2.7</td>
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<td>6.6 to 1.7</td>
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<tr>
<td>R. Sola et al. [28]</td>
<td>225</td>
<td>48</td>
<td>Vobi-C</td>
<td>6.4 to 2.7</td>
<td>5.3 to 2.4</td>
<td>5.2 to 1.7</td>
<td>6.6 to 1.7</td>
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<tr>
<td>P. Sukhomel [22]</td>
<td>54</td>
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<td>Bryan</td>
<td>8.6 to 2.7</td>
<td>7.7 to 2.7</td>
<td>5.2 to 2.4</td>
<td>6.6 to 1.7</td>
<td>—</td>
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</tr>
<tr>
<td>Our data</td>
<td>112</td>
<td>36</td>
<td>Vobi-C</td>
<td>6.4 to 2.7</td>
<td>7.7 to 2.7</td>
<td>5.2 to 1.7</td>
<td>6.6 to 1.7</td>
<td>—</td>
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DW MRI method, morphological and immunohistochesmral markers of IVD degeneration are being carried out [31—34].

Given that total IVD arthroplasty is a novel technique, we must admit that currently available information on the clinical and radiological efficacy of artificial IVD prostheses is not sufficient. Moreover, the problem of formation of heterotopic ossification foci after total prosthetic replacement of the IVD still remains unsolved. At the same time, almost all prostheses are completely replaced by bone tissue with formation of spinal fusion in the operated segment 5 years after total IVD arthroplasty. Therefore, the implanted prosthesis becomes an “expensive” cage. Given these facts, multicenter studies involving a larger number of respondents should be continued, including the detailed study of long-term clinical and radiological outcomes, the development of the methods to prevent HO after prosthetic replacement of the IVD, and specification of the indications for the use of dynamic fixators.

Conclusion

Application of the total IVD arthroplasty technique in patients with IVD degeneration with M6-C prosthesis can significantly reduce the severity of pain, improve patients’ quality of life, preserve physiological range of motion in the operated spinal motion segment, and reduce the time of patients’ temporary disability.

Funding source. The original study was conducted as a part of the scientific program supported by the Russian Science Foundation grant (project No 15-15-30037).

Authors declare no conflict of interest.
The article focuses on the surgical treatment of degenerative diseases of the cervical spine. The authors reported the results of surgical treatment of patients with single-level degeneration of the cervical intervertebral discs using arthroplasty. This technology is quite widely used by spinal neurosurgeons all over the world. However, there are only scarce reports representing large groups of patients within one study in the Russian literature. This method should be considered as one of the surgical treatment options, having specific indications and contraindications. It must be admitted that it can be considered as an alternative to the conventional stabilizing operations in some cases. The authors clearly formulated all the criteria for inclusion of patients in the study, followed the developed algorithm, and therefore obtained clearly interpretable results. The results show significant decrease in the severity of pain in the postoperative period (on the average, from 6.7±1.5 to 2.1±1.3 cm and from 6.9±1.7 to 2.2±1.5 cm on the VAS scale for the pain in the cervical spine and upper extremities, respectively, 6 months after surgery). Analysis of the quality of life based on the Neck Disability Index (NDI) showed significant positive dynamics of the functional status of patients after total arthroplasty compared to preoperative period: on the average, from 41.1±5.7 to 17.9±6.6%. From this it follows that the duration of hospital stay was 8.2±1.5 days. The range of motion in the operated segment remained within physiological limits, indicating that the surgical objectives of the operations were achieved. There were no signs of instability of the structure. Importantly, the patients were followed for no more than 36 months. It is promising to analyze long-term outcomes of patients in order to accumulate new data and to obtain reliable information. In view of the above, the article can be recommended for publication in the journal.

A.G. Nazarenko (Moscow, Russia)
Percutaneous Endoscopic Discectomy in the Treatment of Patients with Degenerative Diseases of the Lumbosacral Spine

N.A. KONOVALOV, D.S. ASYUTIN, V.A. KOROLISHIN, I.U. CHERKIEV, B.A. ZAKIROV

Burdenko Neurosurgical Institute, Moscow, Russia

Modern surgery uses a variety of treatments for spine pathology. Endoscopic techniques have become particularly popular across the world over the past decade.

In this article, we summarize our experience and analyze the immediate and long-term results of surgical treatment of lumbar disc herniation using a percutaneous fully endoscopic technique for removing the herniated intervertebral disc, which is new for Russian medical practice.

**Objective** — to evaluate the efficacy of percutaneous endoscopic discectomy in the treatment of herniated lumbar discs in patients with radicular pain syndrome.

**Material and methods.** We conducted a cohort retrospective study that included 69 patients who underwent herniated disc removal using the percutaneous endoscopic technique. Surgery was performed through two approaches: the intralaminar approach was used in 44 patients, and the transfornaminal approach was used in 25 patients. To assess the efficacy of surgery, we used a visual analogue scale (VAS) of pain: the intensity of local pain (VAS1) and the intensity of radicular pain (VAS2). Changes in the quality of life and ability to work were assessed by using the Oswestry scale; patient satisfaction with treatment was assessed by using the MacNab scale.

**Results.** The mean follow-up period after surgery was 24 months. An analysis of changes in the pain syndrome (VAS 1 and VAS2) before surgery and in the early postoperative period demonstrated a significant regression of pain regardless of the approach type ($r=0.125$). Patients’ survey (MacNab scale) in the long-term postoperative period revealed no unsatisfactory results; excellent, good, and satisfactory results were observed in 21 (30%), 32 (46%), and 16 (24%) patients, respectively.

**Conclusion.** Percutaneous endoscopic discectomy is an effective surgical treatment for degenerative diseases of the lumbosacral spine, providing excellent and good treatment outcomes in most operated patients.

**Keywords:** intervertebral disc herniation, minimally invasive surgery, percutaneous endoscopic discectomy.

It has been shown that the use of endoscopic technique in treatment of patients with a herniated intervertebral disc significantly reduces the risk of iatrogenic complications, as well as surgical trauma of soft tissues, which is achieved through a smaller skin incision (0.5—0.8 cm) and muscle traction, as well as due to better view of the surgical field, less bleeding, and simple and faster surgical approach compared to classical methods of discectomy [1, 2].

Minimally invasive surgical methods in degenerative diseases of the spine are gradually being introduced into the medical practice of the Russian Federation [3]. However, the number of Russian articles on this subject is still limited [4—9].

In the current work, we present our experience of using percutaneous endoscopic discectomy in the treatment of patients diagnosed with a "hernia of the intervertebral disc at the level of the lumbar spine” in the Burdenko Neurosurgical Institute.

**Materials and Methods**

A total of 69 patients (37 men, 32 women) with intervertebral disc herniation at the lumbar level underwent surgical treatment using percutaneous endoscopic discectomy (PED) in the period from March 2013 to February 2016. The mean age of the patients was 45 years (from 25 to 99 years). The distribution of patients by gender and age is presented in Table 1.

Pain syndrome was the predominant clinical manifestation of the disease. Local and radicular pain syndrome was observed in 67 (97%) patients, isolated local discogenic pain syndrome in 1 (1%) patient, radicular pain in 9 (13%) patients. Hypesthesis in the innervation zone of the compressed root was detected in 37 (54%) patients, hyperpathy in 2 (3%). Decrease in Achilles reflex on the side of pain was noted in 15 (22%) patients, paresis of foot muscles in 12 (17%), pelvic disorders in 1 (1%).

The intensity of the pain syndrome was assessed by a visual analogue scale (VAS). The intensity of local pain syndrome is designated as VAS1, the intensity of radicular pain syndrome as VAS2 (Table 2). Changes in the quality of life and ability to work were assessed by using the Oswestry scale (ODI); patient satisfaction with treatment was assessed by using the MacNab scale.

All patients underwent magnetic resonance imaging (MRI) of the lumbosacral spine no earlier than 3 months before the intervention. The distribution of patients based on the level of lesion of the intervertebral disc is presented in Table 3.

All surgical interventions were performed using a set of instruments and endoscopes Spine Tip for PED at the endoscopic rack manufactured by Karl Storz, intrain-
tive cone-beam O-arm computed tomograph and Medtronic navigation system.

Taking into account the features of the toolkit, the planning of the surgical approach was performed based on the level of the herniated intervertebral disc localization. Patients with a hernia at the level of the intervertebral foramen or with a slight migration of the free fragment (Grade 0—I according to the classification proposed by G. Choi [10]) were selected for transforaminal access.

Interlaminar PED was performed on 44 patients with a herniated intervertebral disc at L5—S1, of which in 5 cases the approach was made using intraoperative computed tomography (CT) and navigation.

Transforaminal PED was used in 25 cases, in 5 patients the approach was made using CT navigation.

On average, the follow-up period after the surgery was 24 months (from 14 to 47 months); the mode was 16 months.

The dynamics of clinical symptoms, duration of the surgery, duration of hospitalization, and need for pain medication at different stages of hospitalization have been analyzed. The quality of life and ability to work were assessed by using the Oswestry scale; patient satisfaction with treatment was assessed by using the MacNab scale.

The intensity of the pain syndrome was assessed before and after the surgical treatment (at discharge), as well as 6 months after the surgery using VAS scale, which the patients filled out themselves.

Results

One of the important criteria for assessing the effectiveness of the method used was the dynamics of analgesics intake. Prior to the surgery, 86% of patients received various analgesics, most often meloxicam and diclofenac. The effect of the therapy was short and insignificant.

Postoperative pain syndrome required the prescription of non-steroidal anti-inflammatory analgesics (ketoprofen) in 43 (62%) patients. The number of intramuscular injections of a standard dose (a solution of 100 mg of ketoprofen in 2 ml of water for injection) ranged from 1 to 4, averaging at 2 injections.

The severity of the pain syndrome according to VAS1 and VAS2 before and after the surgical treatment is presented in Fig. 1. From the above graph it is clear that there is a significant regression of the pain syndrome in the postoperative period, and this effect does not depend on surgical approach ($r=0.12$).

In the early postoperative period the patients evaluated the outcomes of the surgical treatment on the MacNab scale as following: excellent — 19 (27%) patients, good — 32 (46%), satisfactory — 16 (24%), unsatisfactory — 2 (3%). In the long-term postoperative period, there were no unsatisfactory outcomes, excellent outcomes were reported by 21 (30%), good ones by 32 (46%), and satisfactory by 16 (24%) patients.

The dynamics of the patients’ assessment of their condition is presented at Fig. 2.

For intralaminar PED technique, the average duration of the surgery was 73.4 min (range: 30 to 130 min), for transforaminal PED technique the duration of the surgery was 67 min (range: 40 to 105 min). It was not possible to estimate the blood loss due to the peculiarities of the surgical technique (the need for constant irrigation with saline solution), but it was obvious that it was minimal. The duration of the surgery with the use of intraoperative navigation was 70±1.3 min, the number of X-ray images was 3.0±1.2.

Complications

Two (3%) patients experienced deepening of the existing paresis of the foot after the surgery. This complication is most likely due to the high strength of the current used to stop bleeding from the epidural veins after the removal of the fragment. One patient experienced incomplete removal of the hernia fragment, which required revision in the early postoperative period. Revision and

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Table 1: Distribution of the patients by gender and age

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Abs.</th>
<th>%</th>
</tr>
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<tr>
<td>Gender</td>
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<tr>
<td>Male</td>
<td>37</td>
<td>54</td>
</tr>
<tr>
<td>Female</td>
<td>32</td>
<td>46</td>
</tr>
<tr>
<td>Age, years</td>
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<td></td>
</tr>
<tr>
<td>18—59</td>
<td>60</td>
<td>87</td>
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<tr>
<td>above 60</td>
<td>9</td>
<td>13</td>
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</table>

Table 2: The intensity of the pain syndrome before surgery, VAS

<table>
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<tr>
<th>Type of pain</th>
<th>VAS score ($n=69$)</th>
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<tr>
<td></td>
<td>Average</td>
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<tr>
<td>Spine (VAS1)</td>
<td>8±0.6</td>
</tr>
<tr>
<td>Leg (VAS2)</td>
<td>6.1±1</td>
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</table>

Table 3: Distribution of the patients by the level of the vertebral-motor segment and the midline

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Abs.</th>
<th>%</th>
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<tr>
<td>Level of lesion</td>
<td></td>
<td></td>
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<tr>
<td>L2—L3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>L3—L4</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>L4—L5</td>
<td>21</td>
<td>31</td>
</tr>
<tr>
<td>L5—S1</td>
<td>46</td>
<td>67</td>
</tr>
<tr>
<td>Total</td>
<td>69</td>
<td>100</td>
</tr>
<tr>
<td>Variant of the disc herniation localization</td>
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<td></td>
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<tr>
<td>median</td>
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<td>3</td>
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<tr>
<td>median—paramedian</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>paramedian</td>
<td>57</td>
<td>82</td>
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<tr>
<td>lateral</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>69</td>
<td>100</td>
</tr>
</tbody>
</table>

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Fig. 1. The dynamics of the severity of the pain syndrome on VAS1 and VAS2 scales.

Fig. 2. The dynamics of assessment on MacNab scale.
removal of the fragment were carried out by endoscopic method. Three patients had a rupture of the dura mater during the epiduroscopy after the elimination of compression and removal of the herniated disc. It should be noted that in the postoperative period no liquor cyst or liquororhea was observed in any of the patients with intraoperative damage to the dura mater. One patient had an epidural hematoma in the early postoperative period, which caused compression of the spine and associated pain. The use of epidural blockade led to regression of pain syndrome.

The statistical analysis did not identify the effect of complications on the duration of hospitalization and disability of patients, as well as on the quality of life assessed by rank correlations and multivariate analysis of the Cox proportional risks regression model ($p \leq 0.05$).

Fig. 3. The type of installed and fixed reference frame on the patient’s skin.

Fig. 4. Navigationally-controlled percutaneous endoscopic discectomy by interlaminar approach.

a — defining the location of the instrument using a navigation pointer and the trajectory of the cannulated endoscopic port; b — dilatation of soft tissues and installation of the cannula under the navigation control; c — insertion of the endoscope into the cannulated port; d — the projection of the instrument on the workstation of the navigation system: blue cylinder indicates the direction and position of the tool to be navigated; e — the projection of the instrument on the workstation of the navigation system: the continuation of the yellow cylinder shows the trajectory.
Within the next 12 months after the surgery, second herniation of the intervertebral disc occurred in 2 (3%) patients.

The technique of performing PED using a navigation system

The challenge in modern minimally invasive surgery with a navigation system is the need for rigid fixation of the reference frame. All authors describing a method of conducting intraoperative CT with subsequent navigation, note the need to anchor the reference frame to the posterior crest of the ilium. In the case of endoscopic intervention for herniated intervertebral disc of the lumbar spine, the trauma from the installed reference frame is usually more pronounced and causes stronger pain syndrome than the wound from endoscopic intervention.

In our series, there were no invasive installation of the reference frame. The reference frame was fixed to a sterile surgical field along the midline in the lumbar region of the spine or in the gluteal region on the ipsilateral side of the access (Fig. 3). After integration of the obtained CT images and at the beginning of the manipulations, the reference frame was tightly fixed with a sterile polyethylene film until the light-reflecting balls were strengthened in order to prevent the increase in the margin of error due to the displacement of the frame. A sterile polyethylene field manufactured by "Opsite" was used. After fixing the reference frame, a CT scan was performed followed by subsequent integration of the examination into a S7 workstation, after the integration of one of the tools used for approach, the access path was calculated (Fig. 4).

Clinical example of intraoperative navigation in PED

Patient K., 56 years old, is engaged in moderate physical labor, works for an energy company. Complains of pain in the lumbar spine and in the left leg along the back of the thigh and ankle. These complaints were ongoing for 3 months. He was treated conservatively in a polyclinic by a neurologist with no apparent effect. Clinical presentation: cranial nerves - no pathology; tendon, periosteal reflexes on the arms and legs are symmetrical, there are no pareses or sensory abnormalities, the symptoms of tension on the left from 30°. MRI of the lumbosacral spine showed the presence of a paramedian disc herniation at L5—S1 on the left (Fig. 5a). On the 2nd day of hospitalization, the patient underwent a surgery: interlaminar PED with intraoperative navigation control. The duration of the operation was 65 minutes, the blood loss was minimal, there were no abnormalities, ca. 2 ml of the altered intervertebral disc tissue was removed. Complete regress of radicular pain syndrome was noted in the postoperative period. Complaints of moderate pain in the surgery area were managed by 4 intramuscular injections of ketoprofen. The patient was discharged on the 1st day after the surgery. In the postoperative period, there was no relapse of pain syndrome; there was no recurrence of the herniated disc on the control MRI (see Fig. 5b). The postoperative scar is less than 0.5 cm long (see Fig. 5c).

Conclusions

Percutaneous endoscopic discectomy is an effective surgical treatment for degenerative diseases of the lumbosacral spine, providing excellent and good treatment outcomes in most operated patients. Our experience of the use of intraoperative navigation in percutaneous endoscopic discectomy of the lumbar spine demonstrates the following: reduction of radiation load on the patient and the staff; accurate positioning of the endoscope due to the use of multi-plane visualization; ability to monitor the position of the instrument in real time. The method of percutaneous endoscopic discectomy is low-traumatic and lead to early discontinuation of analgesics, which demonstrates its advantages.

Authors declare no conflict of interest.
REFERENCES


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Commentary

The article is devoted to one of the most acute problems of modern neurosurgery: treatment of herniated intervertebral discs of the lumbosacral spine. Thanks to technical progress, a plethora of methods is currently available for treating this pathology, and the selection of the optimal method has become extremely important.

The authors present their personal experience in the use of percutaneous endoscopic discectomy and conduct a detailed analysis of the effectiveness of this method. Sufficient attention is devoted not only to clinical indicators, but also to organizational and technical characteristics (duration of surgery, x-ray load, etc.).

We do however question the discussion of the effectiveness of pain relief with non-steroidal analgesics. In our opinion, this indicator is undoubtedly of interest for research, but it is partially subjective and requires additional objectification. Since patients have different thresholds of pain sensitivity, it may be worthwhile to average the pain indicators using scales prior to administration of pain medications.

Particular attention should be paid to very detailed description of the surgical technique with navigation. We are presented with a method of fixing the navigation frame to the body of the patient without additional incisions (which are usually necessary), and the efficiency and X-ray load are estimated for the use of navigation and without it. From a practical point of view, this method of fixation is very interesting and allows one to use navigation in standard surgeries on the spine without increasing the surgical injury. However, it may be necessary to further investigate the navigational error with this type of fixation of the navigation frame.

From scientific value point of view, the material will be useful in a comparative analysis of existing methods of surgical treatment of herniated intervertebral discs of the lumbosacral spine.

*S.O. Arestov (Moscow, Russia)*
Use of the IntelliVent-ASV Mode for Maintaining the Target EtCO$_2$ Range in Patients with Severe TBI

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1Burdenko Neurosurgical Institute, Moscow, Russia; 2Emergency Hospital of Minsk, Minsk, Belarus; 3CHUV-University Hospital of Lausanne, Lausanne, Switzerland; 4Hamilton Medical, Bonaduz, Switzerland

Purpose — the study purpose was to evaluate the efficacy of the IntelliVent-ASV mode in maintaining the target range of PaCO$_2$ in patients with severe TBI.

Material and methods. The study included 12 severe TBI patients with the wakefulness level scored 4—9 (GCS). This was a crossover design study. Two ventilation modes were consecutively used: IntelliVent-ASV and P-CMV, for 12 h each. When using the P-CMV mode, the ventilation parameters were set to maintain PaCO$_2$ in a range of 35—38 mm Hg. The IntelliVent-ASV mode involved the Brain Injury ventilation algorithm. The target range of EtCO$_2$ was set in accordance with the delta PaCO$_2$-EtCO$_2$ to maintain PaCO$_2$ in a range of 35—38. At the beginning of each ventilation period and every 3 hours, the arterial blood gas composition was analyzed. When PaCO$_2$ occurred out of the 35—38 range, appropriate adjustments were made to the ventilation parameters. In the P-CMV mode, the Pinsp and RR parameters were adjusted to achieve the target PaCO$_2$ range. In IntelliVent mode, a shift of the target EtCO$_2$ range was adjusted in accordance with a changed PaCO$_2$-EtCO$_2$ difference. In all patients, ICP, blood pressure, and EtCO$_2$ were monitored; the arterial blood gas composition was analyzed every 3 h; the frequency of manual settings of ventilation parameters was recorded.

Results. The EtCO$_2$ and PaCO$_2$ parameters were found not to be significantly different in the P-CMV and IntelliVent modes, but the spread in these parameters was significantly lower in the IntelliVent ventilation mode. The PaCO$_2$ parameter occurred out of the target range significantly less often in the IntelliVent mode than in the P-CMV mode. The mean frequency of manual respirator settings needed to maintain the target EtCO$_2$ range was significantly lower in the IntelliVent-ASV mode than in the P-CMV mode.

Conclusion. The IntelliVent-ASV mode provides more efficient maintenance of PaCO$_2$ in the target range compared to traditional artificial ventilation using fewer manual settings of the ventilation parameters.

Keywords: artificial ventilation, traumatic brain injury, IntelliVent-ASV.

Abbreviations:
AV — artificial ventilation
ARDS — acute respiratory distress syndrome
PEEP — positive end-expiratory pressure
COPD — chronic obstructive pulmonary disease
TBI — traumatic brain injury
EtCO$_2$ — end-tidal carbon dioxide pressure at the end of exhaled breath
FiO$_2$ — fraction of inspired oxygen
MV — respiratory minute volume, minute ventilation volume
PaCO$_2$ — arterial partial pressure of CO$_2$
Pinsp — inspiratory pressure created by the ventilator
Ppeak — peak inspiratory pressure
Pplato — plato inspiratory pressure
P-CMV — pressure-controlled continuous mandatory ventilation
SpO$_2$ — pulse oximetry, a non-invasive method to measure oxyhemoglobin saturation in arterial blood
TV — tidal volume, the volume of air that is inhaled or exhaled in a single breath
RR — respiratory rate

Ventilatory support is a key component in the management of critical care patients with severe traumatic brain injury (TBI). Approaches to artificial ventilation (AV) in patients with brain injury have their own specifics. Maintaining partial pressure of CO$_2$ in arterial blood (PaCO$_2$) within narrow therapeutic range is critically important. PaCO$_2$ is one of the main regulators of cerebral vascular tone. Hypercapnia and hypocapnia should be avoided in patients with severe TBI. Hypercapnia causes dilation of cerebral arteries and disrupts autoregulation of cerebral circulation to increase intracranial pressure. In contrast, hypocapnia causes vasoconstriction and worsens cerebral ischemia [1, 7]. The physician regulates the PaCO$_2$ level during AV by adjusting minute ventilation volume according to arterial blood gas composition and capnography data.

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In recent years, new intelligent modes of AV based on the concept of patient feedback have been actively implemented in clinical practice. The Hamilton Medical’s IntelliVent mode is particularly promising for respiratory support to patients with severe TBI. The IntelliVent-ASV mode implements algorithms to adjust minute ventilation volume, level of positive end-expiratory pressure (PEEP) and oxygen fraction based on EtCO₂ and SpO₂ monitoring using pulse oximetry and capnometry sensors integrated into the ventilator. The algorithms for maintaining target EtCO₂ and SpO₂ ranges are set according to the clinical condition. The IntelliVent-ASV mode has four algorithms: normal lungs, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS) and brain injury. The Brain Injury algorithm of IntelliVent maintains a narrow range of EtCO₂ by adjusting minute ventilation volume and the target SpO₂ level is achieved by adjusting the fraction of oxygen. The PEEP level in the Brain Injury algorithm is adjusted manually to prevent an increase in intrathoracic pressure and violation of venous drainage of the brain. At EtCO₂ value outside the set range, IntelliVent-ASV automatically increases (in case of hypercapnia) or decreases (in case of hypocapnia) minute ventilation volume.

The IntelliVent-ASV mode was effective in providing optimal respiration to post-cardiac surgery patients [1] and patients with acute respiratory failure caused by COPD and ARDS [2—4]. Moreover, several papers have shown the efficacy of the IntelliVent-ASV mode during weaning from AV [5, 6]. Currently, there are no papers focused on using the IntelliVent-ASV mode in patients with acute brain injury.

The aim of the study was to evaluate the efficacy of the IntelliVent-ASV mode in maintaining the target range of PaCO₂ in patients with severe TBI.

Material and methods

This study included 12 patients (8 males and 4 females, the mean age was 37.6±9.6 years) with severe isolated TBI. The inclusion criteria: <72 hours after TBI, the wakefulness level scored 4—9 (Glasgow Coma Scale). Exclusion criteria: age below 18 years, severe lung injury with the EtCO₂ and PaCO₂ difference of >10 mm Hg, hemodynamic instability requiring norepinephrine infusion at a rate of >0.5 mg/kg/min.

All patients included in the study were treated using the Hamilton G5 ventilator and sedated with propofol to the level of spontaneous breathing depression. Neur muscular blockers were used when necessary.

This study was a crossover design study. Two AV modes were consecutively used: IntelliVent-ASV and P-CMV with 12 h each. The sequence of modes was determined by randomization.

In the P-CMV mode, the ventilation parameters were set to maintain the PaCO₂ within a range of 35—38 mm Hg.

The IntelliVent-ASV mode involved the Brain Injury ventilation algorithm. The target range of EtCO₂ was set in accordance with the delta PaCO₂—EtCO₂ to maintain PaCO₂ in a range of 35—38 mm Hg. The target range of PaCO₂ was set to be within a range of 35—38 mm Hg.
SpO₂ was shifted as much as possible to the right to 97—100% (Fig. 1).

The gas composition of arterial blood was analyzed at the beginning of each AV period and in each 3 h subsequently. When PaCO₂ occurred beyond the limits of 35—38 mm Hg, appropriate adjustments to ventilation parameters were made. In the P-CMV mode, the Pinsp and respiratory rate (RR) parameters were adjusted to achieve the PaCO₂ target range. In the IntelliVent mode, the shift of the EtCO₂ target range was adjusted in accordance with the changed PaCO₂—EtCO₂ difference.

All the patients underwent monitoring of intracranial pressure using a Codman parenchymal sensor and an invasive blood pressure monitoring. In addition, bedside monitoring involved ECG, EtCO₂ and SpO₂ monitoring.

Criteria for terminating the study: development of severe intracranial hypertension resistant to deepening sedation and the use of hyperosmolar solutions; deterioration of pulmonary function with an increase in the
PaCO₂—EtCO₂ difference >10 mm Hg; aggravation of the patient condition requiring transportation for diagnostic or therapeutic measures. Patients who met these criteria were excluded from the study.

Respiratory monitoring data from the ventilator was collected using the Study Recorder software. In addition, the EtCO₂, FiO₂, PEEP, MV, TV, Pplat, Ppeak, Pinsp, SpO₂ parameters were manually recorded every hour. Statistical data analysis was performed using Statistica 7.0 software package.

The study was approved by the local Ethics Committee of the Burdenko Neurosurgical Institute (protocol No. 5, 2013).

Results and discussion

The study found that the EtCO₂ and PaCO₂ values did not differ significantly when using the P-CMV and IntelliVent modes. The PaCO₂ level was 36 (35—37) mm Hg in the IntelliVent mode and 36 (34—38) mm Hg in the P-CMV mode (p=0.35). The EtCO₂ level was 33 (32—37) mm Hg and 34.5 (31—39) mm Hg in the IntelliVent and P-CMV ventilation modes, respectively (p=0.39). There was no significant differences between PaCO₂ and EtCO₂ during AV in the IntelliVent-ASV and P-CMV modes but the spread of these parameters was significantly less when using the IntelliVent ventilation mode (Figs. 2, 3).

The gas composition of arterial blood in each AV mode was analyzed 4 times over 12 h. Thus, 48 points for the analysis of blood gas composition in each ventilation mode were received for 12 patients. We selected three ranges of PaCO₂: target (33—38 mm Hg), hypocapnia (<33 mm Hg) and hypercapnia (>38 mm Hg). Fig. 4 shows the distribution of PaCO₂ in three ranges for each AV mode. It is seen that the PaCO₂ value occurs beyond the target range significantly less often with the IntelliVent mode than with P-CMV.

The mean frequency of manual ventilator settings to maintain the target EtCO₂ range was significantly lower in the IntelliVent-ASV mode than when using the P-CMV mode. During the 12-h period of AV in the IntelliVent-ASV mode, the mean frequency of manual adjustments was 0.66±0.89 and in the P-CMV mode — 2.9±1.7 (p=0.04) (Fig. 5).

Our research demonstrated that the IntelliVent-ASV mode provides a narrower target range of PaCO₂ in patients with TBI while reducing the need for manual set-

![Fig. 4. Change in PaCO₂ in different AV modes.](image)

![Fig. 5. The effect of AV mode on the frequency of manual adjustment of ventilation parameters.](image)
tings of ventilation parameters and this therefore reduces workload on medical personnel.

Our data are consistent with the data of other authors who studied the efficacy of the IntelliVent-ASV mode in patients without brain injury.

F. Lellouche et al. [1] compared the IntelliVent-ASV mode with conventional AV in post-cardiac surgery patients. To assess the safety of AV, the authors identified 3 zones of ventilation: optimal (TV=6—10 mL/kg, Pplat<30 mbar, EtCO₂=30—45 mm Hg, SpO₂=94—98%), acceptable (TV=10—12, Pplat=30—35 mbar, EtCO₂=25—30 or 45—50 mm Hg, SpO₂=85—93%) and not acceptable (TV >12 mL/kg, Pplat >35 mbar, EtCO₂ >50 mm Hg, SpO₂<85%). The frequency of AV episodes with the duration of >30 seconds in the zone of “not acceptable” ventilation, as well as the duration of AV in each of the predefined zones were compared. In addition, the frequency of manual settings of PEEP, FiO₂ and minute ventilation volume was estimated. The study demonstrated that the number of AV episodes in the “not acceptable” zone of ventilation was significantly lower with the IntelliVent mode than in conventional AV. The duration of ventilation in the “optimal” zone was significantly longer and the duration of ventilation was significantly shorter in the “acceptable” and “not acceptable” zones in the IntelliVent-ASV mode compared to conventional AV. 100% of patients who received AV in standard mode required manual correction of ventilation parameters meanwhile manual adjustment of ventilation parameters was only required in 13% of patients when using the IntelliVent-ASV mode [1].

Our data because of the small number of cases do not allow a reliable statistical analysis. Meanwhile, the identified trends suggest that the automatic adjustment of minute volume and decrease in fluctuations of PaCO₂ will be safer for patients and reduce the risks of secondary ischemic brain injury caused by hypocapnia or hypercapnia episodes [7]. Further studies will clarify the clinical significance of the benefits provided by the IntelliVent-ASV mode regarding optimization of autoregulation of cerebral vessels and cerebral hemodynamics.

Conclusions

The IntelliVent-ASV mode is more effective in maintaining the target PaCO₂ range compared with conventional artificial ventilation. The frequency of manual adjustment of ventilation parameters during AV in the IntelliVent mode is significantly lower than in the standard ventilation mode.

Authors declare no conflict of interest.

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Currently, intelligent AV modes based on the concept of patient feedback are actively implemented in clinical practice. However, the results of their practical use are very limited in the available literature. In particular, there are no recommendations on using intelligent modes of AV with feedback loops for the treatment of patients with severe traumatic brain injury (STBI). However, the use of intelligent AV modes in critical care patients after general surgical manipulations significantly reduces the duration of ventilation and patient stay in the intensive care unit.

The need for correction of intracranial hypertension in patients with STBI does not allow simply using for them the principles of respiratory support developed for patients after general surgery. The critical task in treating patients with STBI is to maintain the target PaCO\(_2\) values.

This paper shows the possibility of maintaining carbon dioxide in arterial blood within the target range (PaCO\(_2\) 32–38 mm Hg) when using the intelligent IntelliVent-ASV mode. It is also shown that this mode of AV maintains the target PaCO\(_2\) values more effectively than traditional ventilation mode (CMV-PC).

According to the authors, another advantage of the IntelliVent-ASV mode is a lower frequency of adjusting ventilation parameters, which reduces workload on physicians and nursing staff. This factor reduces the likelihood of errors associated with staff overfatigue.

This paper is undoubtedly of practical value for all doctors and nurses managing patients with STBI.

A.V. Shchegolev (St. Petersburg, Russia)
Unilateral Posteroventral Pallidotomy in the Treatment of Drug-Induced Dyskinesia in Parkinson’s Disease

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1Research Center of Neurology, Moscow, Russia; 2Semenov Institute of Chemical Physics, Moscow, Russia

Material and methods. We analyzed surgical treatment of 14 patients with PD complicated by DID who underwent unilateral PVP at the Research Center of Neurology in the period between 2012 and 2015. The clinical type of DID was mainly represented by peak-dose choreoathetoid dyskinesia, more pronounced in the distal limbs, and predominantly unilateral. The severity of drug-induced dyskinesia was assessed on the UPDRS scale (part IV-A) before surgery and at 1 week and 6 months after surgery.

Results. One week after pallidotomy, all of the 14 patients had a regression of contralateral dyskinesia by 68.3±9.7%; 50% of patients had a regression of ipsilateral dyskinesias by 43%, on average. In 50% of cases, the dose of levodopa was reduced by 15%, on average. On examination at 6 months after surgery, regression of contralateral dyskinesia was 55.7±8.8%, and the severity of ipsilateral DID returned to the preoperative level. The use of pallidotomy significantly improved the indicators of daily activity and quality of life of patients. There were no significant postoperative complications. Three patients had mild speech disorders in the form of dysarthria, which regressed 2—3 weeks after surgery.

Conclusion. Our experience confirms that unilateral PVP is an effective and safe surgical treatment of PD complicated by DID. Microelectrode registration of neuronal activity and test stimulation improve results of surgical treatment.

Keywords: Parkinson’s disease, drug-induced dyskinesia, pallidotomy, microelectrode registration.
activity of Globus Pallidus externus (GPe) neurons was represented by both tonic and burst activity with a mean discharge frequency of 54 spikes/s and a variation coefficient of 1.2. In contrast, neuronal activity of the Globus Pallidus internus (GPi) neurons was characterized only by tonic activity with a mean discharge frequency of 95 spikes/s and a variation coefficient of 0.8. In a number of cases, rhythmic neurons were found in the GPi, the discharge frequency of which correlated with the tremor rhythm (see the Figure).

Usually, 2 to 3 parallel recording electrodes were used for MER. Also, the micromacroelectrode was used for test stimulation via the macroelectrode contact with current parameters of 0.5—2.0 mA, 160—190 Hz, and 90 ms and with evaluation of the therapeutic and side effects of stimulation. The emergence of motor, visual, mental, or speech disorders during stimulation with a current strength of at least 2 mA was regarded as an inadequate position of the electrode tip in the functionally important brain structures adjacent to the GPi (inner capsule, optic tract). In these cases, an alternative target point was chosen. If test stimulation with the special macroelectrode was not accompanied by neurological disorders, destruction at this point was achieved using radiofrequency thermal ablation (temperature, 70—80 °C; duration, 60—90 s). Surgery was performed under local anesthesia during the OFF-period, in the absence of DIDs. Usually, improvement of motor functions (normalization of muscle tone, inhibition of tremor) occurred as early as at the stage of placing the electrode tip into the target point (response to insertion), which was a predictor of a sustained postoperative effect after completing destruction.

All patients underwent a comprehensive neurological examination including assessment by using the UPDRS (part IV-A), PDQ-39 quality of life questionnaire, and Schwab-England scale before surgery and at 1 week and 6 months after surgery.

Results

One week after pallidotomy, contralateral dyskinesia regressed by 68.3±9.7% ($p=0.01$) in all 14 patients; 50% of patients had regression of ipsilateral dyskinesia by 43%, on average. All 14 patients achieved a positive effect in the form of reduced rigidity, bradykinesia, and tremor. In 50% of cases, the dose of levodopa was reduced by 15%, on average. On examination at 6 months after surgery, contralateral DIDs regressed by 55.7±8.8% ($p=0.01$), and severity of ipsilateral DIDs returned to the preoperative level (Table). There was no significant difference in the effect of PVP on various clinical types of DIDs. The use of pallidotomy significantly improved indicators of daily activity and quality of life: by 20% in the ON-period and 30% in the OFF-period (Schwab-England scale) and by 31% (PDQ-39 questionnaire).

The greatest positive effect on motor functions was observed on the contralateral to surgery side; improvements on the ipsilateral side were less significant and decreased in the next 6 months. At 6 months after surgery, the dose of levodopa was returned to the baseline value in all patients. There were no significant postoperative complications: 3 patients developed mild dysarthria speech disorders that regressed 2 to 3 weeks after surgery.

Discussion

Despite a significant increase in the number of deep brain stimulation (DBS) surgeries in the world, many authors have believed that destructive surgeries in extrapyramidal pathology are competitive, in particular, in the case of unilateral operations. This statement is valid for both invasive and non-invasive destructive surgery [5, 7, 10, 12—21].

In functional neurosurgery, destructive techniques include stereotactic radiofrequency ablation, radiosurgery (Gamma-knife), and high-intensity focused ultrasound (HIFU).

Radiofrequency ablation remains the most popular technique, but radiosurgery using a Gamma knife (GK) device is still in use [15, 19]. Despite of its noninvasiveness, the radiosurgical technique is unsafe and entails complications [22].

In recent years, HIFU has been increasingly used in functional neurosurgery [13]. According to the literature data [23], HIFU is more effective and safer than GK in many parameters, and the effect of procedure develops immediately after ultrasound treatment. However, the use of HIFU in functional neurosurgery currently has a number of limitations, in particular, the temperature required for destruction can not be achieved in some cases. For example, for this reason, W. Chang et al. [13] were not able to complete thalamotomy in 28% of patients.

The efficacy and safety of unilateral PVP using MER in the treatment of motor disorders in PD has been recognized by many authors [7, 24]. In 1999, A. Lang et al. [6] analyzed the results of 11 on evaluation of the efficacy of PVP. Application of unilateral pallidotomy led to improvement in motor functions in the OFF-period by 28% (UPDRS, part III), improvement in daily activity by 28% (UPDRS, part II), and reduction in contralateral DIDs by 77% and ipsilateral DIDs by 43%. Unilateral PVP did not lead to a decrease in the daily dose of levodopa [16]. In our study, drug-induced dyskinesia after unilateral PVP regressed by 68.3±9.7% on the contralateral side and by 50% on the ipsilateral side, on average. Half of patients achieved a decrease in the daily dose of levodopa by 15% in the early postoperative period; however, at 6 months after surgery, the dose of levodopa was returned to the preoperative values.

While regression of contralateral DIDs retains for a long time, ipsilateral DIDs recur within a year after sur-
In our series, all patients had recurrence of ipsilateral DIDs at 6 months after surgery.

The surgery effect varies during a long-term follow-up. For example, one of the studies [4] demonstrated that sustained improvement after treatment of DIDs was retained up to 12 years. Another study [25] demonstrated a decrease in the PVP efficacy: regression of DIDs amounted to 27% after a 1-year follow-up and 7% after a 4-year follow-up. Two other studies [6, 26] confirmed preservation of the achieved effect for dyskinesia and tremor on the side contralateral to pallidotomy after a 2-year follow-up. The reason for the rather contradictory results may be inaccuracy in identification of the target point, different amount of destruction, and different interpretation of subjective symptoms and scoring scales [27].

The risk of side effects of pallidotomy is less than that of thalamotomy. Older patients better tolerate pallidotomy. The risks of side effects of pallidotomy, such as speech, swallowing, and cognitive impairments, are higher in the case of bilateral surgery [4]. Careful selection of patients and neuropsychological examination minimize the risks of cognitive and behavioral complications.

The efficacy of surgical treatment directly depends not only on the correct selection of patients but also on the choice of the optimal destruction area. The size of the destruction area is not so much important as its correct localization [26, 27]. L. Laitinen, who revived interest in pallidotomy in the 1980s, believed that the target point in the posteroventral Globus Pallidus should be located more lateral, including the GPe (ventroposterolateral pallidotomy). Currently, most researchers believe that pallidotomy should involve the posteroventral Globus Pallidus. Other authors think that destruction should involve, along with the sensorimotor region of the GPi, the subpallidal white matter that is a dense bundle of the pallidofugal fibers (ansotomy). However, the experimental data obtained by a group of researchers on monkeys demonstrated inadvisability of this technique [25]. In our group, the target point corresponded to the posteroventral location of the GPi in all cases.

The efficacy of unilateral pallidotomy and that of unilateral DBS of the GPi are comparable [9]. According to R. Gross [3], the efficacy of unilateral pallidotomy is similar to that of unilateral DBS of the GPi or subthalamic nucleus (STN), but inferior to the efficacy of bilateral DBS of the STN. However, when comparing destruction and stimulation, it is necessary to allow for the cost factor of a DBS system, which is tens-fold higher than that of PVP. In addition, it is important to consider the need for periodic correction of the neurostimulation program, which limits application of the technique in patients living at a significant distance from the clinic.

**Conclusion**

Our experience in surgical treatment of PD supports the tendency of recent years to make a more balanced choice of the functional neurosurgery technique — to use not only stimulation but also, in the presence of indications and with allowance for a potential risk, the destructive technique. In this paper, we have demonstrated that unilateral posteroventral pallidotomy is an effective
and safe surgical treatment of drug-induced dyskinesias in Parkinson’s disease. Microelectrode registration of neuronal activity and test stimulation provide accurate positioning of the electrode, which improves treatment outcomes. The rational choice of surgical treatment for Parkinson’s disease, including the possibility of combining stimulating and destructive techniques of functional neurosurgery, expands the capabilities of effective care to this complex category of patients.

Authors declare no conflict of interest.

Changes in the severity of contralateral drug-induced dyskinesias (DIDs) at 1 week and 6 months after surgery

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Received: 31.01.17.
The authors presented their own experience in the use of radiofrequency posteroventral pallidotomy for treatment of drug-induced dyskinesias in 14 patients with Parkinson’s disease.

The most common and effective technique of treating complications of pharmacotherapy in Parkinson’s disease today is stimulation of the deep brain structures. Neurostimulation, in contrast to destructive surgery, enables one-stage bilateral impact on the deep brain structures. Recently, there has been renewed global interest in destructive surgery in patients with Parkinson’s disease. This was promoted by both the development of modern neuroimaging techniques and the emergence of non-invasive methods for destruction of the deep brain structures.

Unilateral destructive surgeries for Parkinson’s disease are less effective than bilateral neurostimulation. However, there is a limited category of patients with unilateral dyskinesia who are non-responsive to unilateral pallidotomy, which determines the significance of this work.

The main comment on the paper is that the authors do not specify which selection criteria they used in choosing unilateral pallidotomy. Whether this was patients’ refusal or contraindications for neurostimulation, or all patients had predominantly unilateral dyskinesias?

The authors analyze the treatment outcomes in patients at 1 week and 6 months after surgery. The result of pallidotomy after 1 week is related to both the destruction area itself and perifocal edema around the area, which usually regresses within a few months after surgery. It is the outcome at 6 months after surgery that is the true result of pallidotomy. Therefore, the use of unilateral pallidotomy by the authors provoked a decrease in the severity of dyskinesias in the contralateral limbs by 56%, on average, and no influence on dyskinesias in the homolateral limbs without a reduction in the dose of levodopa, which corresponds to the literature data.

I hope that the authors will continue their work in this direction and publish the results of the influence of unilateral pallidotomy on the severity of parkinsonian syndrome and cognitive functions, including the follow-up period.

A.A. Tomskiy (Moscow, Russia)
Simultaneous Reconstruction of the Carotid and Vertebral Arteries Using a Temporary Intraluminal Shunt (a Clinical Case and Literature Review)

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The article describes a case of one-stage surgical treatment of a patient with progressive chronic cerebral ischemia caused by combined steno-occlusive lesions of the carotid and vertebral arteries. The disease was complicated by intolerance to temporary occlusion of the carotid artery due to an incomplete circle of Willis. We performed extra-anatomic carotid-vertebral artery bypass with subsequent ipsilateral carotid endarterectomy. A temporary intraluminal shunt was used at the main stage of reconstructive surgery.

We use this clinical case to analyze the issues of surgical treatment for combined lesions of the carotid and vertebral arteries and the techniques for prevention of associated ischemic complications.

Keywords: extra-anatomical reconstruction of vertebral arteries, carotid endarterectomy, temporary intraluminal shunt.

Prevention and treatment of ischemic stroke remains the most important medical and social issue in all economically developed countries in the world. The results of large multicenter studies [1, 2] have convincingly demonstrated the important role of reconstructive surgery in patients with isolated stenoses of the brachiocephalic arteries, which enabled the development of protocols for surgical treatment of these patients. At the same time, the management of patients with multifocal lesions of the major cerebral arteries still requires clarification. This is particularly the case for combined atherosclerotic lesions of the carotid and vertebrobasilar arterial territories. According to epidemiological studies [3], the frequency of combined hemodynamically significant lesions of the carotid and vertebral arteries (VAs) amounts to 26.7%. In this case, even a paucisymptomatic course of the disease is associated with both a significantly increased risk of ischemic stroke in any of the arterial territories and more severe clinical manifestations of the stroke [4]. The reason is a more pronounced deficit of collateral circulation in this group of patients, which in turn is associated with higher risks of reconstructive surgery of the brachiocephalic arteries. In similar cases, a personalized approach to the planning of surgical treatment, the choice of non-standard options for reconstruction of the brachiocephalic arteries, intraoperative neuromonitoring, and use of brain protection techniques become of particular importance [5]. The article presents a rare variant of surgical treatment for a multifocal steno-occlusive lesion of the carotid and vertebral arteries in a patient with an incomplete circle of Willis and intolerance of temporary carotid occlusion.

Clinical case

A 75-year-old male patient K. presented (13.11.2016) with complaints of dizziness, general weakness, periodic unsteady gait, and instability of blood pressure. According to the medical history, the patient underwent surgery for coronary heart disease (mammary-coronary bypass, coronary angioplasty and stenting). In 2013, the patient underwent right carotid endarterectomy (CEA) using a temporary intraluminal shunt because of critical atherosclerotic stenosis of the right internal carotid artery (ICA). The latest worsening occurred 2 months before admission, when the patient developed first episodes of dizziness and, later, unsteady gait.

Ultrasound of the brachiocephalic arteries revealed deterioration of left ICA stenosis, up to 65%, combined with a severe hemodynamically significant lesion of the carotid and vertebral arteries (VAs) amounts to 26.7%. In this case, even a paucisymptomatic course of the disease is associated with both a significantly increased risk of ischemic stroke in any of the arterial territories and more severe clinical manifestations of the stroke [4]. The reason is a more pronounced deficit of collateral circulation in this group of patients, which in turn is associated with higher risks of reconstructive surgery of the brachiocephalic arteries. In similar cases, a personalized approach to the planning of surgical treatment, the choice of non-standard options for reconstruction of the brachiocephalic arteries, intraoperative neuromonitoring, and use of brain protection techniques become of particular importance [5]. The article presents a rare variant of surgical treatment for a multifocal steno-occlusive lesion of the carotid and vertebral arteries in a patient with an incomplete circle of Willis and intolerance of temporary carotid occlusion.

At admission, neurological symptoms were represented by minimal symptoms in the form of unsteady gait, feeling confused when performing coordination
tests, and flattening of left nasolabial fold. The severity of neurological deficit was scored 2 on the National Institutes of Health Stroke Scale (NIHSS) and also 2 on the modified Rankin scale.

Given the need to perform two reconstructive interventions — on the CCA in the bifurcation region and on the first segment of the VA — we decided to use DeBakey carotid endarterectomy and resection of an excessive length of the CCA with simultaneous carotid-vertebral transposition. The revealed signs of collateral circulation insufficiency at the circle of Willis level indicated the necessity to use a temporary intraluminal shunt during surgery.

Surgery was performed under general anesthesia. Given the necessity of carotid occlusion during reconstruction, multimodal neurophysiological monitoring, including transcranial ultrasound dopplerography (TCD) with continuous detection of the blood flow in the M1 segment of the left middle cerebral artery (MCA), and bifrontal cerebral oximetry (CO) were used for intraoperative monitoring of cerebral ischemia signs. The baseline CO value was 65±2% (Fig. 2). The baseline linear blood flow velocity in the left MCA was 60 cm/s.

The course of surgery. An approach to the neurovascular bundle of the bifurcation and to the proximal CCA was performed through a linear skin incision along the medial edge of the sternocleidomastoid muscle on the left, from the mastoid process level to the clavicular notch between the legs of the sternocleidomastoid muscles. Additionally, a medial approach to the first segment of the subclavian artery in the VA origin area was performed through the same skin incision. During the approach, large branches of the thoracic duct were coagulated and transected, and the vertebral vein was sutured and transected. Upon isolation of the subclavian artery and its branches, a gross deformity of the left VA with a pronounced excess of its length and dysplasia signs in the form of a pathological thinning of the vascular wall in the region of the ostium located along the posterior wall of the subclavian artery as well as multiple branching of the thyrocervical trunk were revealed. Given the topographic anatomical features, the optimal variant of VA reconstruction was resection of an altered proximal VA and transposition of the artery to the CCA. This variant of carotid artery reconstruction was chosen because of the presence of local stenosis in the left ICA bifurcation region in combination with the need for resection of an excessive length of the CCA and elimination of a gross deformity in the proximal third region, which interfered with performing a carotid-vertebral anastomosis. Given a critical decrease in the linear blood flow velocity in the left MCA from 60 to 0—5 cm/s and a sharp drop in the CO level to 47±2% during test occlusion of the left CCA (Fig. 2), we decided to use a temporary intraluminal arterial shunt during surgery. The overall scheme of performed reconstruction is shown in Figure 3.

After systemic heparinization (intravenous administration of 5,000 U of heparin), side-biting clamping of
the subclavian artery in the VA ostium region was performed using a Satinsky vascular clamp. The clamp was placed on the VA 2 cm distal to the VA deformity region. The VA was dissected from the subclavian artery in the ostium region with subsequent suturing of the ostium with Prolene 6.0 suture and removal of the clamp from the subclavian artery. An atherosclerotic plaque was seen in the VA lumen, narrowing the lumen by 85—90%; the artery wall was dysplastic, especially in the region of the ostium and septal kinkings. A 1 cm segment of the altered VA was excised; additionally, eversion endarterectomy from the VA was performed.

At the next stage, carotid occlusion was performed. The CCA was cut transversely in the bifurcation region; a heterogeneous dense calcified atherosclerotic plaque was found in the bifurcation, narrowing the artery lumen by 75%. The atherosclerotically altered distal segments of the CCA were resected together with the plaque for a length of 2 cm, with straightening of the existing C-shaped bend in the proximal third of the left CCA (Fig. 3a). After this, a temporary intraluminal shunt was placed into the lumen of the ICA and CCA. The duration of carotid occlusion before starting blood flow through the shunt was 3 min. After placement of the shunt, recovery of the linear blood flow velocity in the left MCA, up to 40 cm/s, and an increase in CO to the baseline values were observed. The shunt was fixed with a tourniquet in the proximal CCA — up to the region of a planned carotid-vertebral anastomosis (Fig. 3b). At this level, a 7 mm longitudinal incision of the CCA, extended up to the VA ostium size, was performed. The end-to-side anastomosis between the carotid artery and the VA was performed with continuous suturing using a 6.0 suture (Fig. 3b). After restoring blood flow in the VA and confirming tightness of the anastomosis, the proximal end of the temporary intraluminal shunt was tightened and fixed with a tourniquet distal to the carotid-vertebral anastomosis. Therefore, direct blood flow in the VA was started (Fig. 3c). The proximal third of the CCA (up to the tourniquet) and the VA were well pulsating. According to the CO data, after restoration of blood flow in the VA, the maximum elevation of CO from 87 to 95% (baseline value, 65±2%) was observed, which confirmed good functioning of the anastomosis.

At the next stage, DeBakey eversion endarterectomy was performed from the CCA bifurcation and ostia of the internal and external carotid arteries. Additionally, eversion endarterectomy from the distal CCA was performed for a length of 5 cm (Fig. 3c).

After removal of atherosclerotic plaques from the arteries, weak retrograde blood flow from the ICA (according to direct measurement of retrograde pressure, less than 30 mm Hg) and good blood flow from the external carotid artery (ECA) were detected. An end-to-end anastomosis was performed between the proximal and distal ends of the CCA. Before stitching the artery was finished, the temporary shunt was removed. The duration of carotid occlusion in the absence of a shunt was less than 10 min. Clamps were successively removed from the ECA, CCA, and ICA. Good arterial pulsation in the wound and the absence of kinks were noted.

To monitor the quality of reconstruction, intraoperative fluorescence angiography was performed using an OPM 900 operating microscope (Carl Zeiss, Germany) in the infrared (IR800) mode after intravenous administration of 10 mg of indocyanine green (ICG-Pulsion). Rapid anterograde contrast filling of the CCA, including its bifurcation, VA, and region of the carotid-vertebral anastomosis, was observed since the 15th second from the

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**Fig. 2. Intraoperative bifrontal cerebral oximetry.**
moment of administration (Fig. 4), which indicated good functioning of the reconstructed arteries.

After performing hemostasis, soft tissues were closed in layers. The duration of VA occlusion was 17 min; the duration carotid occlusion was 51 min. According to
TCD, the linear blood flow velocity in the left MCA after reperfusion of the arteries was restored to 90—95 cm/s. In the early postoperative period, the patient noted an improvement, mainly in the form of regression of cerebral and cerebellar symptoms. The neurological status was assessed at day 7 and at 3 months after surgery: a NIHSS score of 0 and a Rankin scale score of 1.

On the 3rd postoperative day, control CT angiography of the brachiocephalic arteries was performed, which confirmed good functioning of the reconstructed arteries (Fig. 5).

Discussion

The presented variant of surgical correction of the vertebrobasilar arterial territory pathology belongs to extra-anatomical reconstructions where restoration of blood flow in the affected artery is achieved through a change in the normal anatomical structure of the vascular system. The idea of similar interventions was first proposed by C. Lyons in 1957. In 1967, I. Dietrich performed first successful subclavian-carotid transposition surgery in a patient with occlusion of the first segment of the subclavian artery [6]. Since then, extra-anatomical bypass grafting has become the “gold standard” in reconstructive surgery of the subclavian and vertebral arteries, even despite the active development of X-ray endovascular treatment techniques.

Along with classical CEA, extra-anatomical reconstructive interventions on the VA are also used in patients with combined lesions of the carotid and vertebrobasilar arterial territories. For example, according to A. Abu Rahma et al. [6], 18% of patients with multifocal atherosclerosis underwent carotid-subclavian bypass grafting simultaneously with CEA on the ipsilateral side. There were reported cases of one-stage transposition of the VA to the CCA and CEA on the ipsilateral side, but all of them were performed without the use of a temporary intraluminal shunt [7]. The reason for this was careful pre-operative selection of patients for these interventions when the presence of an incomplete arterial circle of Willis was a contraindication to transposition to the CCA. In these patients, preference was given to anatomical reconstruction of the VA in the form of endarterectomy from the artery ostium as well as to transposition of the VA to the subclavian artery or thyrocervical trunk, which avoided temporary occlusion of the CCA and associated ischemic complications [7].

However, there are situations where it is advisable to perform one-stage CEA and extra-anatomical reconstruction of the VA, even in patients with intolerance to temporary occlusion of the CCA. For example, the VA lesion in the analyzed case was represented by a marked excess of the artery length with formation of two septal stenoses and signs of dysplasia of the vascular wall and vertebral and subclavian arteries. In addition, there were the topographic anatomical features: deviation of the VA from the posterior wall of the subclavian artery and multiple branching of the thyrocervical trunk. These findings technically complicated reconstruction of the first segment of the VA with its subsequent transposition to the subclavian artery [7]. In similar cases, transposition of the VA to the CCA provides the best technical results of reconstruction and is considered by many specialists to be the surgery of choice [7, 8]. However, a severe septal kinking in the proximal third of the CCA complicated performing a carotid-vertebral anastomosis, and further would promote its subsequent deformity with a high risk of early thrombosis in the reconstruction area. Therefore, we decided to use one-stage DeBakey eversion endarterectomy to eliminate stenosis and CCA deformity and to provide favorable conditions for performing a carotid-vertebral anastomosis.

The feature of performed surgery is one-stage reconstruction of the vertebral and carotid arteries in the patient with intolerance to temporary carotid occlusion.

Fig. 4. Intraoperative images.

a — overall view of reconstruction in the wound (1 — the region of a carotid-vertebral anastomosis, 2 — the region of reconstruction of the common carotid artery bifurcation); b — intraoperative fluorescence angiography (IR800) visualizes good functioning of the carotid-vertebral anastomosis (indicated by an arrow).
Application of CEA in similar cases is combined with the use of a temporary intraluminal shunt for brain protection in 18% of cases [5]. However, an analysis of the domestic and foreign literature did not reveal publications on the use of a temporary intraluminal shunt in extra-anatomical shunt surgery.

An adapted algorithm for using a temporary shunt, which was applied during the main stage of reconstruction, provided good compensation of the cerebral circulation during the entire period of CCA occlusion (51 min) and enabled implementation of all planned vascular reconstruction procedures. Of particular importance is the use of intraoperative neuromonitoring techniques (cerebral oximetry and ultrasound dopplerography), which enabled timely detection of signs of cerebral circulation and metabolism decompensation associated with temporary carotid occlusion, which was the reason for placing a temporary intraluminal shunt. In our opinion, the use of intraoperative neuromonitoring techniques (cerebral oximetry and ultrasound dopplerography), which enabled timely detection of signs of cerebral circulation and metabolism decompensation associated with temporary carotid occlusion, which was the reason for placing a temporary intraluminal shunt. In our opinion, the use of neuromonitoring in vascular extra-anatomical surgery is as reasonable as in CEA and can significantly affect the intraoperative choice of a technique for reconstruction or brain protection at the main stage of surgery.

To assess the quality of reconstruction, we used near-infrared (800 nm) fluorescence angiography after intravenous administration of indocyanine green. The technique has been extensively and successfully used for visualization of cerebral vessels [9—11], but the possibility of its use for visualization of extracranial arteries possessing a different type of the vascular wall structure requires additional study. In the analyzed case, the experience of using this technique for visualization of carotid-vertebral reconstruction was successful: rapid anterograde contrast filling of the arteries in the anastomosis region was observed, which was confirmed by a postoperative angiographic examination and prolonged functioning of the anastomosis throughout the follow-up period. These facts allow us to recommend intraoperative fluorescence angiography in particular for evaluating the quality of extra-anatomical reconstruction of neck vessels.

**Conclusion**

Vertebral-carotid transposition and CEA on the surgery side can be successfully performed simultaneously in patients with combined lesions of the carotid and vertebrobasilar territories. In patients with insufficient collateral circulation and intolerance to temporary carotid occlusion, these procedures are performed with the use of a temporary intraluminal shunt. These procedures should be accompanied by intraoperative neuromonitoring of the function, blood supply, and metabolism of the brain for early detection and prevention of intraoperative cerebral ischemia.

**Authors declare no conflict of interest.**

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**Fig. 5. Postoperative SCT angiography.**

a — 3D reconstruction of the brachiocephalic arteries; b — multiplanar reconstruction of the brachiocephalic arteries: postoperative anastomoses in the area of the vertebral artery ostium and internal carotid artery are patent: 1 — common carotid-vertebral anastomosis; 2 — the region of reconstruction of the common carotid artery bifurcation.
The article presents a clinical case of surgical treatment of a patient with disseminated atherosclerotic disease of the brachiocephalic arteries, which manifested as cerebrovascular insufficiency both in the carotid and vertebrobasilar territories. In this situation, the authors performed successful radical surgery on the carotid and vertebral arteries, which led to restoration of adequate blood flow in the affected territories.

The presented publication will be of interest to a wide range of specialists — vascular neurosurgeons and vascular surgeons.

V. N. Dan (Moscow, Russia)
Diencephalic cachexia (DC) or Russell’s syndrome is a rare disorder caused by tumor lesion of the hypothalamic region. Its prevalence in the population is unknown. Since the first description of the syndrome by the English pediatrician A. Russell in 1951, it is considered to be found exclusively in infants [1—3].

A specific feature of the disease is the development of pronounced cachexia despite adequate nutrition and satisfactory physical and mental state. There is often a case of a lack of weight gain with preserved linear growth rates in children. Psychiatric disorders and changes in the behavior noticeable for others often appear in these patients. They become excessively communicative, disinhibited and euphoric. Despite of expressed exhaustion, well-being and motor activity are preserved in patients. As the tumor grows, a set of neurological symptoms often appear in the clinical picture due to the compression of the surrounding brain structures by the tumor [1—6].

It should be noted that a progressive weight loss with almost complete atrophy of subcutaneous fat can be the leading and, as a rule, the only manifestation of the disease in the early stages. This significantly complicates the timely diagnosis of the tumor until the moment when neurological symptoms appear. Regression of cachexia can be noted in association with a decrease in the tumor volume after surgical treatment, as well as after radiation therapy and/or chemotherapy [7—10]. In case if no treatment is applied, most patients die within 1—2 years [2]. DC develops in suprasellar tumors of the anterior regions of the hypothalamus, as well as of chiasm and optic nerves compressing the bottom of the third ventricle. Among the variety of tumors described in the literature [10—16], astrocytomas and other types of gliomas prevail. Germinoma and craniopharyngioma (CP) were found to cause DC much rarely [17, 18]. The age of the disease onset in children ranges from a neonatal period to 4 years with a peak in the first 2 years of life [2—6]. In adults, this syndrome is extremely rare: 4 cases of tumor lesion to the hypothalamus with the development of DC: 2 cases are due to CP, while 2 others are caused by astrocytoma [19—22]. This disorder is more often described as “diencephalic syndrome” in the foreign literature [1—6, 8—11, 14, 15, 18—23]. Here we present a rare case of DC in a 24-year-old female with papillary craniopharyngioma.

Clinical case

Patient P, 24 years of age, (age of birth, 1991) sought medical attention at Burdenko Neurosurgical Institute in August 2015 with complaints of progressive weight loss, thirst, lack of amenorrhea, decreased vision, and headache.

Analysis of medical history showed that growth and development was normal. Previous diseases included chronic pyelonephritis due to hereditary congenital renal duplication. She had no injuries and had never undergone surgeries. The patient is married, has 2 children (two normal pregnancies ended in deliveries at term in 2009 and 2013, the children are healthy). Amenorrhea persisted after the second birth. However, the patient did pay any attention to this and did not sought medical help.

The patient started noticing weight loss despite adequate nutrition in January 2015. Thirst, decrease in vision, headache, memory loss appeared in March 2015. The patient had a gradual loss in body weight by 20 kg (from 48 to 28 kg). Magnetic resonance imaging (MRI) of the brain was performed in May of the same year, which revealed tumor of the chiasmatic-sellar region (CSR) extended onto the third ventricle. The patient was referred to Burdenko Neurosurgical Institute for clarification of the diagnosis and selection of the method of treatment.

Upon admission, the patient’s condition was relatively satisfactory. Her height was 161 cm, and her weight was 28 kg, body mass index (BMI) equaled 11.5. Magnetic resonance imaging of the brain and lumbar puncture were performed that showed an increase of intracranial pressure to 260 mm H2O.

Surgical treatment was performed in September 2015 by a transsphenoidal approach. The main pathological finding was a large tumor growth at the level of the suprasellar region, communicating with the third ventricle and the ventricular system up to the frontal horns of the lateral ventricles. Pathological examination of the tumor confirmed the diagnosis of CP. The tumor volume was 80 cm3. The tumor was removed partially, and a small residuum of the tumor was left.

Postoperative period was uneventful. The patient was discharged in good condition on October 1, 2015. During follow-up, the patient was healthy and the neurological examination revealed no abnormalities.

Keywords: craniopharyngioma, diencephalic cachexia, Russel syndrome, hypothalamic tumor.
10.9 kg/m² (normal range, 18—25 kg/m²). The patient looks older than her age. Complete absence of subcutaneous adipose tissue is noted (Fig. 1b, c).

Skin and visible mucous membranes are pale and of normal moisture content. Teeth and fingers have no signs of systemic “vomiting” behavior. Blood pressure is 80/60 mm Hg; heart rate is 50 bpm. Defecation pattern is normal; no dysuria is noted. Thyroid gland is not enlarged, soft, painless, nodal formations are not palpable.

ECG data are as follows: sinus rhythm, heart rate is 45 beats/min, normal position of the electrical axis of the heart, disturbed AVL repolarization.

Examination by a neurologist revealed visual abnormalities in the form of a chiasmatic syndrome; VISOD is 0.6; VISOS is 0.9. Hemianopia is bitemporal. Examination of the fundus showed blanching in the temporal region of the optic nerve discs with clear boundaries. There were no focal otoneurological symptoms.

Examination by psychiatrist showed that the patient is active, makes her own decision on visiting doctors, she takes interest in her condition. An apparent decrease in criticism draws attention: the patient does not take the situation into consideration, does not keep distance (enters the doctor’s office to ask for tea, to take a look through the window, and etc.). In addition, she actively talks about her life and disease specifying all of the details and drawing attention to insignificances. The patient presents numerous complaints without identifying the main ones. Complains of a significant memory loss, which occurred simultaneously with weight loss, appear only during questioning.

Emotional background is significantly elevated and accompanied by a hint of euphoria. The patient orient in time, place and personal situation. She shows interest in the upcoming surgery and her future but at the same has no particular concern and worry both about the surgery and its possible outcomes. According to relatives, this manner of behavior and style of communication were not typical for the patient earlier.

Here we present laboratory analysis data.

Clinical analysis of blood findings were as follows: hemoglobin level is decreased to 108 g/L (112—153), erythrocyte level is decreased to 3.56 (3.80—5.15 10·12/L); left deviation in the white blood cell count: 8% (1—6) stab neutrophils; 29% (47—72) segmented neutrophils, 57% (19—43) lymphocytes, 3 mm/h (2—15) ESR.

Clinical and biochemical analysis of morning urine showed the following data: SC is decreased to 1004; 148.3 (135—145) mmol/L sodium, 649 mOsm/kg (>300 mOsm/kg) osmolality.

Biochemical analysis of blood was without electrolyte disorders, it indicated 286 mOsm/kg H2O (275—295) blood osmolality, GPT increased to 80 U/L (up to 60), 32 g/L (35—52) hypoalbuminemia, serum iron level decreased to 10.4 μmol/L (10.7—25), the remaining parameters are unchanged. The level of glycated hemoglobin (HbA1c) was 4.7% (<6.1%).

The data of hormonal blood test are presented in the Table; they indicate the presence of secondary hypothyroidism, hyperprolactinemia, secondary hypogonadism. There are no convincing data for secondary adrenal insufficiency and diabetes insipidus. High level of growth hormone...
hormone (GH) in association with reduced insulin-like growth factor-1 (IGF-1) is observed. The latter change is characteristic of DC. However, alongside with the above-mentioned disorders, it is not the cause of weight loss.

Brain MRI performed with a series of tomograms in three planes and using T1, T2, DWI and FLAIR modes before and after intravenous administration of a contrast agent reveals cystic and solid formation of the CSR with endo-suprasellar growth. A solid part of the tumor intensively accumulates contrast agent corresponding in its location to the altered pituitary stalk and filling the space from the adenohypophysis to the hypophyseal stalk. There are cystic cavities around the solid component of the tumor (above it and around it). The ventricular system is neither expanded nor displaced (Fig. 2).

A surgery involving transcranial resection of CP localized in infundibular stalk with basal frontotemporal access was performed on September 2, 2015 (surgeon, RAS academician A.N. Konovalov). An “anterior” type of a chiasm with short optic nerves was found. The tumor was resected through the opticocarotid triangle. A dense tissue of grayish-yellow color with a tuberous surface and thin capsule that extends into the cavity of the third ventricle and resemble papillomatous CP was found directly above the sella turcica. Its resection was carried out mainly by ultrasonic suction. Large cysts were emptied during tumor resection, arterial branches of the cyst capsule were preserved. The walls of the capsule were mostly excised. Residues of the pituitary stalk were observed in the posterior sections of the capsule. The tumor was resected almost completely with exception for the capsule fragments spreading into the cavity of the third ventricle. A computed tomography (SCT) of the brain was performed immediately after surgery, which confirmed high completeness of tumor resection with preservation of small residues in the infundibular region of the third ventricle (Fig. 3).

The histological diagnosis of papillary craniopharyngioma was made. Postoperative therapy included administration of hydrocortisone (100 mg per day I.M. for 7 days, then 25 mg per day orally), thyroid hormone preparations (L-thyroxin at a dose of 25 μg orally). The signs of diabetes insipidus in the form of thirst and polyuria up to 4000 mL daily, hypernatremia (sodium, 147—149 mmol/L) appeared on the second day after surgery. Desmopressin (minirin at 0.05 mg orally 3 times a day) was included in the treatment program.

An increase in the severity of emotional and personality disorders (euphoria, relief, lack of criticism) were observed in the early postoperative period. In association with this, optical illusions sporadically occurred that co-incided with water-electrolyte disturbances. The “sleep-wake” cycle was inversed. Visual hallucinations regressed, and a night sleep recovered by the time of discharge. The patient was discharged with emotional and personality disorders and cognitive impairments with the same degree of manifestation as before surgery. Neuro-ophthalmologic examination showed that vision was maintained at the preoperative level. The patient began actively gaining weight after surgery. By the time of discharge (12 days after surgery), the patient gained 14 kg and her body weight was 42 kg (Fig. 4a). Hormonal examination diagnosed panhypopituitarism, moderate hyperprolactinemia (prolactin, 1005 mU/L) was preserved

### Patient’s blood hormone analysis results before and after surgery for craniopharyngioma (explanations are given in the text)

<table>
<thead>
<tr>
<th>Test</th>
<th>Prior to the first surgery</th>
<th>Day 8 after the first surgery</th>
<th>6 months after the first surgery</th>
<th>Prior to the second surgery</th>
<th>Reference interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolactin</td>
<td>4081</td>
<td>1005</td>
<td>2884</td>
<td>853 mE/L</td>
<td>59—619 mE/L</td>
</tr>
<tr>
<td>Somatotropin</td>
<td>23</td>
<td>2.01</td>
<td>0.27</td>
<td>0.33</td>
<td>&lt;8.00 ng/mL</td>
</tr>
<tr>
<td>IGF-1</td>
<td>53.7</td>
<td>73.6</td>
<td>66.6</td>
<td>63.0</td>
<td>116.0—358.0 ng/mL</td>
</tr>
<tr>
<td>Cortisol</td>
<td>329</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>119—618 nmole/L</td>
</tr>
<tr>
<td>Thyrotropin</td>
<td>1.41</td>
<td>0.19</td>
<td>1.63</td>
<td>0.01</td>
<td>0.40—4.00 mE/L</td>
</tr>
<tr>
<td>Lutropin</td>
<td>&lt;0.1</td>
<td>—</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>Follicular phase: 1.9—12.5 E/L</td>
</tr>
<tr>
<td>FSH</td>
<td>0.6</td>
<td>—</td>
<td>0.1</td>
<td>0.1</td>
<td>Follicular phase: 2.5—10.2 E/L</td>
</tr>
<tr>
<td>Estradiol</td>
<td>70</td>
<td>—</td>
<td>58</td>
<td>—</td>
<td>Follicular phase: 72—529 nmole/L</td>
</tr>
<tr>
<td>Free thyroxine (free T4)</td>
<td>10.7</td>
<td>8.2</td>
<td>5.6</td>
<td>22.5</td>
<td>11.5—22.7 nmole/L</td>
</tr>
<tr>
<td>Free triiodothyronine (free T3)</td>
<td>2.73</td>
<td>1.96</td>
<td>—</td>
<td>—</td>
<td>3.50—6.50 nmole/L</td>
</tr>
<tr>
<td>Testosterone</td>
<td>0.0</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0.5—2.6 nmole/L</td>
</tr>
<tr>
<td>Leptin</td>
<td>0.6</td>
<td>—</td>
<td>5</td>
<td>—</td>
<td>1.7—28 ng/mL</td>
</tr>
<tr>
<td>Insulin</td>
<td>18</td>
<td>—</td>
<td>31</td>
<td>—</td>
<td>22—180 nmole/L</td>
</tr>
<tr>
<td>Free b-HCG</td>
<td>&lt;2.0</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>&lt;2.0 ng/mL</td>
</tr>
<tr>
<td>Parathyroid hormone</td>
<td>2.70</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1.48—7.63 nmole/L</td>
</tr>
</tbody>
</table>

The patient was discharged in a satisfactory condition with recommendations to continue substitution therapy for secondary adrenal insufficiency (cortef, 10 mg in the morning and 5 mg after lunch), secondary hypothyroidism (L-thyroxine, 50 μg), diabetes insipidus (minirin, 0.1 mg twice daily). For the period of 3 months, her body weight was increased by 4 kg followed by its stabilization within the range of 45—46 kg.

Control examination of the patient was conducted 6 months after surgery. Examination performed on January 18, 2016 showed that her condition was satisfactory, consciousness was clear. Body weight is 46 kg, BMI is 16.89 kg/m² (see Fig. 4b).

Examination of mental status showed that euphoric tone of mood, relaxed behavior, disinhibition, and lack of criticism were preserved. However, the existing significant emotional and personality disorders did not affect the patient’s “quality of life”. Hormonal examination (18.01.16), showed preserved panhypopituitarism, diabetes insipidus and hyperprolactinaemia (see Table). Substitution therapy was corrected: the dose of L-thyroxine was increased to 125 μg in the morning, administration of cortef and minirin was recommended at the previous doses, gonadal hormones were administered after gynecological examination. MRI performed on January 18, 2016 (Fig. 5) and SCT conducted after surgery (see Fig. 3) revealed residual tumor in the pituitary stalk and the bottom of the third ventricle. In connection with this, the patient was recommended to undergo stereotactic radiation, which was scheduled for September 2016.

The patient’s condition remained stable from January to May 2016. However, she started experiencing headache, weakness, memory impairments, and occasional involuntary urination in May 2016. Further deterioration in the condition in the form of increased drowsiness, weakness in the right limbs, weight loss, weakened control of pelvic functions were noted during this month. The level of wakefulness was gradually decreasing, the patient ceased to move independently, did not speak, sleep for the most part of the day. It is known that she did...
not stop taking substitution therapy (cortef, 15 mg, L-thyroxine, 125 μg, minirin, 0.1 mg 2 times a day); while substitution therapy with gonadal hormones was not received.

She was hospitalized due to progressive deterioration of the condition on the 1st of April in 2016. Examination revealed the following symptoms: severe condition, the level of consciousness corresponds to lightheadedness. Skin covers and visible mucous membranes are pale and of normal moisture content. Blood pressure is 80/50 mm Hg, heart rate is 60 bpm. Muscular strength in the right limbs is reduced to 34 points. She has no control over pelvic function. There were no other significant abnormalities in the patient’s condition.

Vision has no obvious deterioration signs: VIS OD=0.9; VIS OS=0.9. Hemoanopia is bitemporal. Examination of the fundus showed blanching in the temporal region of the optic nerve discs with clear boundaries.

Clinical analysis of blood showed a decrease in the level of hemoglobin to 111 g/L (112—153), biochemical blood test revealed a decrease in creatinine to 45 μmol/L (50—115), albumin was decreased to 34 g/L (35—50); sodium level was 144 mmol/L (135—145), other parameters were without deviations. Hormonal blood test demonstrated panhypopituitarism (secondary hypothyroidism and hypocorticism were medically compensated) and moderate hyperprolactinemia (prolactin, 853 mE/L) (see Table).

MRI of the brain revealed a relapse, mainly in the form of a giant multi-cameral cyst extending into the third ventricle (Fig. 6).

The second surgery, which included transcranial resection of CP of the third ventricle and sella turcica from the combined transcalloid and right-sided subfrontal access with endoscopic assistance, was performed on August 4, 2016 (surgeon, RAS academician A.N. Konovalov). The resection was first performed from the transcallosus access on the right. A tumor cyst wall was found in the region of the right Monro foramen, which was then perforated (immediate histological examination revealed no tumorous tissue in it). A tumor of yellow-grayish color was found in the region of the anterolateral wall of the third ventricle on the right. It was separated from its walls...
and resected. Tumor sac was present in the basal sections of the third ventricle, which spread onto its bottom and had no clear borders. Next, the remaining basal part of the tumor, including the wall of the cyst extending into the sella turcica, was resected using the right-sided subfrontal access through the opticocarotid triangle. Then, all fragments of the suprasellar sac, where tumor proliferation sites were observed, were incised during repeated transclavicular access, where there were visible tumor growths.

A histological examination confirmed the diagnosis of papillary CP.

Control SCT performed on the day of surgery showed complete tumor resection with the presence of small fragments of hemostatic materials in its bed (Fig. 7).

Episodes of psychomotor agitation with confused consciousness associated with hypernatremia (sodium, 147—163 mmol/L) was observed on day 2 after surgery. At the same time, the patient was roughly disoriented in place and time, always tended to go somewhere, talked to herself, did not succumb to persuasion. She manifested dysphoricism, aggressiveness towards relatives taking care of her, resisted medical procedures. Night sleep was disruptive. These symptoms regressed significantly after correction of water-electrolyte disorders, sedation and psychotropic therapy.

At the time of discharge, visual functions were preserved at the same level as before surgery. Clear positive changes were noted in the psychoneurological condition with restoration of consciousness and orientation, complete regression of right-sided hemiparesis, restoration of control over pelvic functions. The patient was discharged on day 14 after surgery.

The patient underwent a course of stereotactic radiotherapy (Fig. 8) with a hypofractionation mode of 5 fractions of 5.5 Gy each two months after the second surgery in the period from 17.10 to 21.10.16. The total focal dose was 27.5 Gy. The patient’s condition remained stable during the treatment.

The patient’s condition was satisfactory 2 months after the course of stereotactic radiotherapy. MRI data showed no relapse. Hormone blood test revealed no significant differences from ones listed in the table. She is active, has no complaints due to substitution therapy. The body weight is 50 kg (Figs. 9, 10).

The patient’s hormonal status was studied during the entire treatment course (see Table).

Discussion

Weight loss is a common occurrence in the pathogenesis of many diseases (chronic heart and kidney failure, diabetes mellitus, Addison’s disease, rheumatoid arthritis, Alzheimer’s disease, malignant neoplasms, and etc.). Regardless of the etiology, cachexia is a serious medical problem. Even a slight decrease in a patient’s body weight determines unfavorable prognosis of the disease and is a powerful predictor of high mortality [24—26]. Loss of more than 40% of the ideal body weight is the most dangerous condition for life [26, 27]. Since the ancient times, the term “cachexia” (originating from Greek word “kachexia”, kakos meaning “bad” + hexis meaning “condition”) was synonymous with a rapid death. Hippocrates wrote that “The flesh is consumed... the shoulders, clavicles, chest, and thighs melt away. The illness is fatal” [28]. The novel “A living relic”, written by I.S. Turgenev in 1846, describes a case of cachexia in a young
woman who first came as “the greatest beauty in all our household — that tall, plump, pink-and-white...” “Before me lay a living human being; but what sort of a creature was it? A head utterly withered, of a uniform coppery hue — like some very ancient holy picture, yellow with age; a sharp nose like a keen-edged knife; the lips could barely be seen — only the teeth flashed white and the eyes; and from under the kerchief some thin wisps of yellow hair straggled on to the forehead. At the chin, where the quilt was folded, two tiny hands of the same coppery hue were moving, the fingers slowly twitching like little sticks... the face, far from being ugly, was positively beautiful, but strange and dreadful” [29].

Despite the fact that the first description of cachexia was made more than 2,000 years ago, the issues concerning its pathogenesis in various diseases are still the subject of discussions and scientific studies. Weight loss in CSR tumors still remains to be unexplained. Here we describe a rare case of diencephalic cachexia in a young woman with CP.

CPs are benign epithelial tumors (WHO I) originating from residuary embryonic cells of the Rathke’s pouch located along the pharyngeal pituitary pouch. The incidence of CP in adults is approximately 2.1—4.6% of all intracranial neoplasms [30—32].

There are two main types of CP that can be distinguished histologically: adamantine-like and papillomatous CPs. The papillomatous type occurs predominantly in adults. CPs are characterized by the presence of a solid and cystic component, which is detected in about 80% of the cases [33, 34]. Development of papillomatous CP, in contrast to adamantine-like CP, is associated with epithelial cell metaplasia. Papillomatous CPs are predominantly localized in the region of the third ventricle; papilloma of the third ventricle is one of the names for these tumors.
Embryogenesis and topography of CP determine high incidence of endocrine and metabolic disorders. Damage to the hypothalamic region can result in imbalanced energy homeostasis leading to obesity or cachexia. CP is known to be often associated with the development of diencephalic (hypothalamic) obesity [35, 36]. DC is less common and represented only by isolated cases. For instance, a large retrospective study among children with CP revealed only 7 patients with DC out of 485 cases [37]. Unlike in case of hypothalamic region compression, development of obesity or cachexia in CP is assumed to be associated with invasive tumor growth [6, 37]. The pathophysiology of DC still remains unknown. Modern concept on the central mechanisms of metabolic control suggest that weight loss in DC is due to dysfunction of hypothalamic neurons involved in regulation of energy homeostasis and body weight. The lack of clinical and laboratory data on the secondary hypofunction of peripheral glands, especially hypocorticism, clearly demonstrates different mechanisms of weight loss in DC and Simmonds’ and Sheehan’s syndromes.

Weight loss is a key symptom and the main reason for seeking medical help. The first stage of examination of such patients is aimed at excluding malnutrition, anorexia nervosa and conditions associated with malabsorption (impaired absorption of nutrients in the small intestine). Further, the diagnostic search should be aimed at eliminating organic pathology of the brain, even in the absence of cerebral or focal neurological symptoms.

In our clinical observation, manifestation of the disease coincided with the postpartum period; secondary amenorrhea was not regarded by the patient as a motive for seeking medical help. It was only the rapid weight loss that led to her examination by doctors, while neuro-ophtalmologic symptoms in the form of chiasmatic syndrome played a crucial role in making an indication for brain MRI.

By the time of tumor diagnosis, the body mass deficit was about 20%. It achieved the value of 40% of initial body weight (which was a life-threatening condition for the patient) by the time of hospitalization.

Fig. 9. Brain MRI with contrast enhancement in the sagittal (a) and frontal (b) planes 3 months after radiotherapy.

Fig. 10. General appearance of the patient 4 months after the second surgery and 2 months after radiotherapy.
Such patients require constant nutritional support until the stage of surgical treatment or if it is considered to be impossible. To date, there is no generally accepted pharmacological therapy for the treatment of cachexia of any etiology.

An increase in the basal level of STH typical for DC and associated with a decrease in IGF-1 was noted in the laboratory analysis data. Similar changes can be observed in cachexia of any etiology, for example, in anorexia nervosa [38].

The patient also had a significant increase in prolactin level, which had not been previously described for DC. This change is most likely due to the blockade of the dopaminergic system in case of suprasellar localization of tumor. Secondary hypogonadism was confirmed by laboratory analysis. There were no other clinically significant biochemical abnormalities. All of these changes are not the cause of weight loss, but secondary events.

We would like to note that, despite the pronounced body mass deficit, the patient maintained well-being and physical activity, experienced euphoric mood, which contrasted to her physical appearance. Euphoric mood and even euphoria itself was often described in children with DC by the authors of previously published cases.

This clinical case is of interest also because of the fact that DC is typical for children of the first 2—3 years of life, while it is extremely rare in adults. DC often causes astrocytomas of the diencephalic region of various degrees of malignancy. Other types of tumors, including CP, which is the case in our patient, are rather an exception than a rule. Development of cachexia is rather a sign of stimulation of the preserved hypothalamic structures, since the symptoms regressed after surgery.

Surgery remains to be the main method to treat CP. Anatomical proximity of the tumor to vital structures (bottom of the third ventricle, optic nerves and chiasm, the main vessels of the basal brain surface) determines great complexity of surgical treatment and creates difficulties for their complete removal [39—44]. CP resection mostly leads to exacerbation of neuroendocrine disorders [44, 45]. In the current observation, the patient experienced additional impairments after the first surgery: diabetes insipidus, central hypocorticism and hypothyroidism, persisted secondary hypogonadism (see Table). The patient required lifelong replacement therapy with L-thyroxine, hydrocortisone, desmopressin and gonadal steroids. However, it is important to emphasize that the patient began rapidly gaining weight despite the presence of tumor residues in the region of the third ventricle bottom. Thus, we can assume a significant role of compression but not the destruction of diencephalic structures in the development of cachexia in the observation described by us.

To date, monitoring of tumor growth after incomplete CP resection remains to be an unresolved problem [46]. This tumor is characterized by a high incidence of recurrence reaching 30% within the period of 10 years after complete resection [34, 39, 47].

Incomplete CP resection is a risk factor for tumor recurrence and determines indications for stereotactic radiation [39]. Our case is demonstrative in this respect. The continued growth of tumor was detected in the patient 8 months after the incomplete surgery. According to the brain MRI data, the size of the recurrent tumor was higher than that of the initial tumor, which characterizes CP as an aggressive tumor. Taking into account tumor localization, treatment of such patients is aimed not only complete tumor resection but prevention of severe complications associated with damage to the hypothalamus as well. Such surgeries should be conducted in institutions with an interdisciplinary team of specialists, including a neurosurgeon, a neurologist, a radiologist, an endocrinologist, a psychiatrist, and an ophthalmologist.

Thus, the treatment strategy is to be determined individually in each case based on the nature of tumor growth and its histology, as well as the patient’s age and condition. Often, only partial resection or biopsy of the tumor with subsequent application of non-surgical methods is possible. In such cases, radiation therapy and/or chemotherapy can be the only hope of saving the patient [8, 9, 48, 49]. It is difficult to explain why, but even partial resection of tumor can lead to cachexia regression, which took place in our observation. Sometimes, there is a recovery of body weight followed by obesity [8, 23]. A detailed study of the mechanisms controlling energy exchange can elucidate the pathogenesis of these disorders and determine a purposeful approach in the treatment of patients with metabolic disorders.

All photographs are posted with the patient’s written consent.

Authors declare no conflict of interest.
The subject of discussion in the presented work is a rather rare pathology: diencephalic cachexia (DC), the pathogenesis of which still remains obscure. The article presents a unique clinical case of DC in a young woman with papillary craniopharyngioma. A detailed presentation of clinical manifestations, laboratory and MRI data clearly demonstrates the primary role of diencephalic lesion in the weight loss and development of cachexia. A long follow-up period endows this observation with extrinsic value. It is important to emphasize that cachexia regression after surgery is, apparently, due to compression of diencephalic structures only but not their deterioration. The authors also consider the questions of etiology, clinical picture, and diagnosis of DC in association with various tumors of the chiasmatic-sellar region and modern approaches to their treatment based on the analysis of literature. The authors emphasize that weight loss can be the first manifestation of craniopharyngioma. The rapid course of the disease with the development of cachexia, the lack of effective therapeutic strategies emphasize the importance of early diagnosis and timely surgical treatment, as well as the need for a multidisciplinary approach in the treatment of such severe patients. All this determines the exceptional relevance of this problem (article).

Commentary

The subject of discussion in the presented work is a rather rare pathology: diencephalic cachexia (DC), the pathogenesis of which still remains obscure. The article presents a unique clinical case of DC in a young woman with papillary craniopharyngioma. A detailed presentation of clinical manifestations, laboratory and MRI data clearly demonstrates the primary role of diencephalic lesion in the weight loss and development of cachexia. A long follow-up period endows this observation with extrinsic value. It is important to emphasize that cachexia regression after surgery is, apparently, due to compression of diencephalic structures only but not their deterioration. The authors also consider the questions of etiology, clinical picture, and diagnosis of DC in association with various tumors of the chiasmatic-sellar region and modern approaches to their treatment based on the analysis of literature. The authors emphasize that weight loss can be the first manifestation of craniopharyngioma. The rapid course of the disease with the development of cachexia, the lack of effective therapeutic strategies emphasize the importance of early diagnosis and timely surgical treatment, as well as the need for a multidisciplinary approach in the treatment of such severe patients. All this determines the exceptional relevance of this problem (article).

The article is written in a good literary language; it is interesting to read it.

L. Ya. Rozhinskaya (Moscow, Russia)
Epileptic seizures developing for the first time after a neurosurgical intervention (de novo seizures) are a challenge for choosing an optimal treatment. The pathogenesis of these seizures is often associated with factors that become inactive in the early postoperative period. When seizures are absent in history, prophylactic anticonvulsant therapy is not currently prescribed [3]. Therefore, epileptic seizures that develop for the first time after neurosurgical operations (de novo seizures) are a particular challenge. These seizures can be provoked by an operation itself and independently cease without anticonvulsant therapy. However, they can be a debut of symptomatic epilepsy, which requires long-term medical therapy. There is no single decision-making algorithm in such situations. Some authors suggest starting anticonvulsant therapy in any case [4, 5]. Others recommend onset of treatment only after the diagnosis of “symptomatic epilepsy”, in accordance with the standards of epileptology [3].

It is obvious that unreasonable use of anticonvulsant therapy significantly reduces the quality of life of a patient. If epileptic seizure developing for the first time after surgery is a manifestation of symptomatic epilepsy then absence of therapy will cause complications and worsen the prognosis [2, 3]. Videoelectroencephalographic monitoring (video EEG monitoring) can help in decision-making.

We present two clinical cases in which video EEG monitoring influenced the choice of algorithm for further management of patients.

Case report 1. A female patient aged 70 years old developed weakness in the left extremities that aggravated, memory for current events deteriorated, and criticism of own condition decreased 2 months before hospitalization. Magnetic resonance imaging (MRI) diagnosed an intracranial tumor of the right temporal lobe with a zone of perifocal edema (Fig. 1).

The tumor was glioblastoma (Grade IV) by histology and was resected on February 02, 2016. After the surgery, the patient was transferred to post anesthesia care unit of the intensive care unit, where secondary generalized seizure developed in 4.5 h (2 h after extubation) that lasted for about 2 minutes. The seizure was stopped by intravenous bolus administration of diazepam 10 mg and valproic acid (convulex) 500 mg. Emergency CT scan revealed postoperative changes in the right temporal lobe and absence of surgical complications (Fig. 2).

This patient on the first day after surgery underwent video EEG monitoring, which revealed deceleration of biopotentials in the right frontotemporal region and disorganization of the cortical rhythm (Fig. 3). For the next 13 hours of recording, 7 electroencephalographic patterns with duration of 2 to 4 minutes were recorded, which were accompanied by the appearance of epileptiform potentials in the form of acute—slow wave complexes in the right frontal centrotemporal region (Fig. 4). Six of the seven episodes were not clinically apparent. In 1 case, paroxysmal symptoms manifested as short-term (about 5 sec) tonic tension of the neck muscles and head rotation to the right.

Taking into account the data of video EEG monitoring, anticonvulsant therapy was prescribed in the form of intravenous administration of valproic acid (convulex)
through a perfusor at a dose of 1500 mg/day. On the second postoperative day, epileptiform activity on EEG was stopped; the patient was transferred to the clinical department, where anticonvulsant therapy with valproic acid (Convulex) in a tablet form at a dose of 2000 mg/day was continued. In 11 days postoperatively, the patient in a satisfactory condition was discharged from the hospital and recommended to continue intake of valproic acid at 1,500 mg/day under control of EEG and circulating drug concentration.

**Case report 2.** A female patient aged 64 years 10 months had been operated and underwent combined treatment for glioblastoma (Grade IV) of the left frontal lobe before present hospitalization. During the entire period of the disease, seizures with impaired consciousness or other paroxysmal disorders were not observed. Anticonvulsant therapy had not been received. Control MRI 3 weeks before hospitalization revealed an increase in tumor size. The decision on repeated surgery was made. After surgery on March 14, 2016, the patient was transferred to post anesthesia care unit, where a secondary generalized seizure developed in 1.5 hours during recovery from anesthesia, which independently stopped during 1 minute. CT scans revealed postoperative changes and the absence of surgical complications (Fig. 5). Diffuse changes of biopotentials in the form of moderate disorganization of cortical activity and absence of typical epileptiform potentials were revealed in daily video EEG monitoring (Fig. 6). It was decided against anticonvulsant therapy and to observe the patient for a day in the intensive care unit. No clinical seizures or other paroxysmal manifestations were noted and no epileptiform activity was recorded during video EEG monitoring. After transferring the patient to the clinical department, seizures were neither observed. Eight days after the surgery, the patient was discharged in satisfactory condition and continued chemotherapy at the place of residence.

**Discussion**

The first epileptic seizures (de novo) are divided into early (acute postoperative seizures) and late ones according to the period when they develop after surgery [6, 7]. Early seizures typically include those that occur within 48 hours after the operation, but some authors believe that early epileptic seizures should include all seizures that occur in the first week after surgery [8]. The rate of early new seizures after resection of a brain tumor varies in different case series from 4.3 to 23.6% [7, 9] and depends on the location, histological diagnosis, resected tumor volume, intensity of edema, hemorrhagic brain imbition, pneumocephalus and presence of complications [6, 9]. It is generally believed that the likelihood of epileptic seizures is 5—10% after removal of a hemispheric tumor [7, 9].

The pathogenesis of epileptic seizures that first appeared in the early postoperative period has not been finally established. One of the mechanisms can be irritation of the cerebral cortex by blood components and hemoglobin degradation products. It is also possible that peroxide compounds accumulating in the lesion reduce the concentration of gamma-aminobutyric acid, which inhibits the neuronal activity in the cortex and thalamus [6]. Finally, transmembrane transport of water and ions is disturbed in ischemic peritumoral brain tissue due to reduced levels of ATP synthetases, changing cell membrane potential [11]. In any case, the pathogenesis of new early postoperative seizures is mediated by mechanisms...
that typically become inactive in the early postoperative period. Therefore, such seizures, especially single ones, are not a reason to diagnose symptomatic epilepsy and should be regarded as a brain reaction to surgery [6, 8].

Several studies [6, 11] have shown that early de novo postoperative seizures do not enhance the risk of symptomatic epilepsy and are not a reason for initiating anticonvulsant therapy. A less common belief is that seizures in the early postoperative period increase the risk of postoperative symptomatic epilepsy [12].

The prophylactic administration of anticonvulsants after neurosurgical manipulations was widely practiced in the twentieth century and today it is routine in many Russian

\[ \text{Prophylactic use} \] is prescription of drugs, including following seizures in the early postoperative period, when new early postoperative seizures are not the onset of “symptomatic epilepsy”
and foreign clinics. The issue of preventive use of anticonvulsants is still debatable. A review of the American Association of Neurosurgeons (AANS) for 2005 showed that neurosurgeons practicing for long-term more often indicate anticonvulsants for prophylaxis [13]. Some authors [14] propose anticonvulsant medications in the first week after surgery for the prevention of early seizures. The Quality Standards Committee of The American Academy of Neurology (AAN) in its recommendations of 2000 advises against continuing anticonvulsant therapy for more than one week after surgery, since medical therapy is ineffective against late seizures [15].

The literature reports that a total of five randomized controlled trials of three antiepileptic drugs have been performed [17]: phenytoin, phenobarbital and valproates. The difference between the effect of these drugs and placebo in terms of preventing the first seizure in patients with brain tumors was not revealed. Moreover, in one study the results in the group of patients with prophylactic therapy using phenytoin were worse than in the placebo group (10 and 8% of early postoperative seizures, respectively), and adverse effects were noted in 18% of patients receiving phenytoin [17]. It is emphasized that studies with the highest level of evidence have been performed only for the three drugs mentioned, and there is no reason to anticipate a similar result in the study of new anticonvulsants.

The literature [17, 18] is dominated by a view that adverse effects of prophylactic anticonvulsant therapy prevail over possible benefits and definitely reduce the quality of life of patients. It is obvious that in certain situations, early postoperative seizures are the first manifestation of symptomatic epilepsy and delayed prescription of appropriate therapy can have negative sequelae. The differential diagnosis between early postoperative seizures arising as a brain reaction to injury and early seizures, which are the debut of symptomatic epilepsy, is difficult and an unambiguous algorithm for decision-making in such a situation is absent in the modern literature.

Video EEG monitoring is a method that helps to make the correct decision. Continued video EEG monitoring is more informative compared to routine EEG recording [3, 19]. We used the recommendations of ESIEM (European Society of Intensive Medicine) for video EEG monitoring in neurosurgical intensive care units [19]. In accordance with these recommendations, video EEG monitoring was performed immediately after the detection of seizure.

Currently, our hospital uses standard therapy for prolonged epileptic seizure and epileptic status [18]: the first-line drug (of those registered in Russia) is benzodiazepines (diazepam 0.1—0.3 mg/kg). The second line drugs can be valproic acid or levetiracetam. Valproic acid

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**Fig. 5. Case report 2. CT in the first hours after removal of a tumor from the left frontal lobe. Postoperative changes with an area of perifocal edema, accumulation of air and an insignificant area of blood imbibition in a surgical region.**

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**Fig. 6. Case report 2. A fragment of EEG-monitoring.**
A moderately disorganized rhythm, with dominant slow forms of activity and acute potentials in the fronto-anterior temporal region, more on the right.
... is given by intravenous bolus injection at a dose of 15 mg per 1 kg of body weight and then in 30 minutes through a perfusor at a dose of 1 mg/kg/h (no more 2500 mg/day). Leviteracetam (Keppra) is administered in an intravenous bolus injection at a dose of 30 mg/kg/day; the dose is divided into three doses (no more than 3000 mg/day). Video EEG monitoring is performed for a single epileptic seizure, even when it independently stops. Based on the results of monitoring, anticonvulsant therapy is prescribed to some patients for a period of at least 1 year under the control of EEG and MRI. Another part of patients without evident epileptic activity, according to EEG-monitoring, is discharged and is followed-up by a neurologist without prescription of anticonvulsant therapy under the control of MRI and EEG in dynamics. In case of recurrent seizures, anticonvulsant therapy is prescribed.

**Conclusion**

Based on the analysis of the literature data, the development of epileptic seizures de novo after neurosurgical interventions is a frequent event that requires not only a rapid reaction of a doctor to stop seizure, but also requires understanding the situation in terms of further management of a patient. The development of symptomatic epilepsy can deteriorate the outcomes of surgical treatment, raise mortality, and enlarge the patient’s hospital stay. However, unreasonable use of antiepileptic drugs when a single seizure is a brain reaction to surgical injury significantly reduces the quality of life of the patient in the future. The current discussion in the literature confirms that these issues have not been solved (this also applies to prophylactic use and selection of a specific antiepileptic drug and periods of use).

Our clinical cases reflect different treatment options for new epileptic seizures in patients after resection of an intracranial tumor. In our opinion, an important criteria for making a decision to indicate anticonvulsant therapy today is the data of video EEG monitoring, which is necessary to perform after a single epileptic seizure in the first week after surgery.

**Authors declare no conflict of interest.**

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This paper is focused on an urgent issue — management algorithm of patients with de novo epileptic seizures after removal of intracranial tumors. Management of patients with “acute symptomatic seizures” has been the subject of intense debate in recent years. It seems that the things are simple: long-term administration of antiepileptic drugs is necessary in case of epileptic seizures in patients with brain injury. However, this is not true for all cases.

The authors cite two clinical cases. Both female patients developed bilateral tonic-clonic epileptic seizures after resection of malignant brain tumors. In the first case, video EEG monitoring (VEM) revealed regional deceleration, epileptiform activity and multiple EEG patterns of focal seizures. In the second case, there was only a single seizure with no epileptiform activity on EEG. In the first case, the authors recommended long-term administration of antiepileptic drugs, in the second case — only observation.

Thus, the main advantage of this paper is a differentiated and complex approach to this category of patients. On the basis of anamnesis, clinical presentation, neuroimaging, and VEM in the early postoperative period, the authors define a group of patients with high risk of epilepsy and recommend long-term therapy and a group with low risk for observation without treatment. This approach helps to avoid unreasonable long-term administration of potentially toxic antiepileptic drugs.

This article is written in a good scientific language and concerns an urgent issue; both patients were examined using modern methods and the conclusions are adequate. The authors present a review of modern foreign literature on this subject.

The only wish concerning this work is to conduct at least minimal follow-up of patients.

K. Yu. Mukhin (Moscow, Russia)
Topical Respiratory Strategies in Neurocritical Care

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Management of the respiratory tract and maintenance of adequate gas exchange are the basic goals of critical care. Injury to the nervous system is often accompanied by development of respiratory disorders. On the other hand, changes in the gas composition of arterial blood can cause brain damage. In addition, approaches to the patient with respiratory failure, which are used in general critical care and neurocritical care, may differ. The presented literature review is devoted to modern respiratory strategies used in neurocritical care.

Keywords: respiratory failure, neurocritical care, tracheal intubation, tracheostomy, protective artificial ventilation, extracorporeal decarboxylation, extracorporeal membrane oxygenation.

Abbreviations:
PaO₂ — partial pressure of arterial oxygen
PaCO₂ — partial pressure of arterial carbon dioxide
PbrO₂ — partial pressure of brain tissue oxygen
SvjO₂ — jugular venous bulb hemoglobin oxygen saturation
APTT — activated partial thromboplastin time
HF MV — high-frequency mechanical ventilation
MV — mechanical ventilation
NIMV — non-invasive mechanical ventilation
PEEP — positive end-expiratory pressure
PDT — puncture-dilated tracheostomy
RDS — respiratory distress syndrome
SAH — subarachnoid hemorrhage
US — ultrasound
ECMO — extracorporeal membrane oxygenation
ECPR — extracorporeal cardiopulmonary resuscitation

Neurocritical patients often belong to the most serious groups of intensive care patients. Neurocritical care is a part of anesthesiology and intensive care and it is guided by the general principles and rules of critical care. However, neurocritical care include specific factors and conditions influencing the choice of treatment strategy for respiratory failure and respiratory support. Neurocritical situations, which necessitate making a decision on the beginning of respiratory support and methods of its implementation, are often specific and differ from general critical care approaches. The incidence of respiratory disorders in patients with acute brain injury is higher than that in other groups of intensive care patients [1]. Furthermore, if respiratory failure occurs in a neurocritical patient, it is significant in 57% of cases and necessitate respiratory support as early as the prehospital stage [2, 3]. There is a significant correlation between the abnormal blood gas composition and respiratory disorders in neurocritical patients during prehospital and hospital care, on the one hand, and neurological and general outcome, on the other hand [3, 4]. This literature review focuses on the current respiratory strategies in neurocritical care.

Goals and objectives of respiratory support. Indications for endotracheal intubation and mechanical ventilation.

Maintenance of the adequate parameters of arterial blood gas composition is the primary objective of intensivists regardless of the intensive care patient profile. Parenchymal lung injury is the most common cause of its disturbance. Thorough evaluation and timely correction of disturbed respiratory drive and dysphagia is another, no less important, objective that should be solved by a neurocritical care specialist, because these disorders often develop during acute nervous system injury [3, 5, 6]. Hypoxemia significantly worsens neurological outcome in neurocritical patients [7]. PaO₂ level should be no less than 80 mm Hg, and some protocols recommend maintaining even higher values, about 100 mm Hg [8, 9]. However, higher levels of oxygen tension are not indicated in neurocritical patients, since hyperoxia leads to
excessive production of free radicals, further brain damage, and poorer outcomes [10].

Partial pressure of arterial carbon dioxide should be maintained within narrow limits in neurocritical patients, because carbon dioxide has a significant effect on cerebral blood flow [11]. In the absence of intracranial hypertension, normocapnia (PaCO₂, of 35–45 mm Hg) should be maintained. In the case of intracranial hypertension, transient episodes of controlled hypocapnia PaCO₂ (28–34 mm Hg) are allowed [1]. Hypocapnia below 28 mm Hg should be avoided, since this carbon dioxide tension results in the development of cerebral ischemia and intracranial hypertension, which worsens both neurological and general outcomes in neurocritical patients [12]. Monitoring of the partial pressure of brain tissue oxygen (PbrO₂) or oxygen saturation of blood flowing from the brain (SvO₂) during hyperventilation minimizes the risk of ischemic brain injury [13, 14].

There are scarce publications on the effectiveness of hypercapnia in patients with severe vasospasm that developed after aneurysmal subarachnoid hemorrhage (SAH). Thus, T. Westermaier et al. [15] demonstrated that maintaining PaC level of 50—60 mmHg in patients with severe cerebral vasospasm leads to significant increase in cerebral blood flow and cerebral tissue oxygenation. However, it should be remembered that hypercapnia can lead to severe intracranial hypertension and unpredictable consequences [16]. The use of hypercapnia in the intensive care of patients with SAH and vasospasm is currently the subject of research. This method in no case should be used in routine clinical practice until reliable evidence of its safety is obtained.

Specific features of respiratory failure, which differ between neurocritical and general intensive care patients, include altered state of consciousness, respiratory drive disorders, dysphagic disorder, and weakness of respiratory muscles. Consciousness impairment leads to changes in the respiratory drive and, therefore, minute pulmonary ventilation and carbon dioxide level. Loss of consciousness, as well as damage to neural and supranuclear structures of bulbar cranial nerves lead to dysphagia, which, in turn, can be the direct cause of aspiration and sputum evacuation disorders. Polyneuromyopathy involving the diaphragm and intercostal respiratory muscles leads to reduced minute pulmonary ventilation, hypoxemia, hypercapnia, and impaired sputum evacuation due to reduced effectiveness of cough impulse.

Parenchymal respiratory distress with a respiratory index (the ratio of arterial oxygen tension to the oxygen fraction in the inhaled mixture) of less than 200, coma, falling back of tongue, severe dysphagia with impossible swallowing and sputum evacuation, and pronounced weakness of the respiratory muscles with inability to make a complete breath are the absolute indications for mechanical ventilation [17—20]. In this situations, there is an undoubted need for tracheal intubation and mechanical ventilation. The situation when the patient is conscious and has no dysphagic disorders, while oxygenation index exceeds 300, is also simple to determine the tactics of respiratory tract management. These patients require neither respiratory tract protection nor mechanical ventilation. As a rule, they stay at neurocritical care department for a short time and then are transferred to a relevant department. However, the situations when there are no absolute indications for respiratory tract protection and mechanical ventilation in neurocritical patients, but there are various combinations of consciousness disorders, hypopharynx innervation disorders, and parenchymal lung injury are quite common. These states are the so-called “gray zone”, where there are no absolute indications for endotracheal intubation and it is difficult to objectify the indications for respiratory tract protection and mechanical ventilation. In these situations, the decision-making is mostly subjective and depends on personal experience and opinions of the resuscitator. K.A. Popugaev et al. [21, 22] developed the respiratory disorder scale, estimating the level of consciousness and the severity of dysphagic disorders and parenchymal lung injury, for objectification of the decision-making process as for the need for respiratory tract protection and initiation of artificial ventilation. The scale is easy to use and does not require additional and time-consuming diagnostic techniques. It was validated for neurosurgical patients with complicated early postoperative period and recently published in the Springer guide.

Approach to the respiratory tract. Non-invasive and invasive mechanical ventilation

MV should be initiated in the case of respiratory failure and ineffective oxygen insufflation. It can be carried out through the face mask, laryngeal mask, endotracheal tube, or tracheostomy cannula. Laryngeal mask can be used in neurocritical care at the prehospital phase or in a hospital in the case of difficult intubation. Ventilation through the face mask is a non-invasive mechanical ventilation (NIMV), which is widely used in general intensive care and cardiac intensive care patients. Technical improvements of masks and nasal cannulae makes NIMV more convenient and safe tool [23, 24]. However, the practical use of NIMV in neurocritical care is limited, since prerequisites for safe ventilation through the face mask include adequate cooperation between the patients and medical staff, the absence of dysphagia, and potential reversibility of the causes that led to respiratory failure within a short period of time [25, 26]. Acute nervous system disorders typically lead to the development of impaired consciousness, dysphagic disorders, and it is extremely difficult to predict the recovery rate of the full-scale effective spontaneous breathing function. Therefore, the use of NIMV in neurocritical care is only limited to a population of patients with obstructive sleep apnea syndrome and, possibly, a small cohort of patients with
across development of impaired neuromuscular transmission, e.g. due to myasthenic crisis [27—30].

Therefore, invasive MV, which necessitates orotracheal intubation, is the method of choice for respiratory support in neurocritical care. Nasotracheal intubation is associated with many complications, severe pain, and now should not be used in clinical practice.

Prolonged mechanical ventilation is an indication for tracheostomy regardless of intensive care patient profile, since prolonged action of transaryngeal endotracheal tube on laryngeal structures leads to edema and mucosal damage [17, 26—28, 31]. Depression of consciousness and dysphagic disorders are the specific indications for tracheostomy in the population of neurocritical patients. Tracheostomy reduces discomfort and the need for sedation, facilitates oral and tracheobronchial care, and the patient can receive physiological feeding through the mouth and communicate with others [32—34].

The optimal timing of tracheostomy is still a matter of debate [35]. Despite the fact that the terms “early” and “late” are commonly used as applied to tracheostomy, there are no clear time criteria for these terms. However, most authors consider a tracheostomy as early, when it is carried out on day 3—10, and late, when it is carried out on day 10—15 of mechanical ventilation [36]. The results of multicenter studies, meta-analysis, and data from Cochrane Library suggest that tracheostomy should be carried out 7—10 days after mechanical ventilation in the population of general intensive care patients and on day 3—7 in neurocritical patients [37, 38]. “Early” tracheostomy significantly reduces the need for sedation and time of MV and patient’s stay in the intensive care unit [39]. As a result, “early” tracheostomy reduces the economic costs of treatment [40]. However, the timing of tracheostomy does not affect the incidence of nosocomial infections, including pneumonia, and do not affect the outcome of the disease [41]. The “late” tracheostomy enables extubation of a certain percentage of patients, who would undergo tracheostomy, if the “early” tracheostomy strategy was implemented. This results in higher incidence of complications directly associated with tracheostomy and inserted tracheostomy cannula [42]. Complications of tracheostomy can be divided into early perioperative (hemorrhage, pneumothorax, tracheal separation, esophageal injury) and late (tracheal stenosis, tracheoesophageal fistula, arrosive hemorrhage, infection of paratracheal tissues and mediastinum) complications. In this connection, the method of tracheostomy, the choice of the cannula, and subsequent care for a tracheostome are extremely important.

Special non-rigid plastic, which is used to produce modern tracheostomy cannula, low-pressure and large-volume cuffs, and the possibility to aspirate the contents of the supra-cuff space made tracheostomy tubes comfortable and safe for long-term use [43]. Implementation of puncture-dilated tracheostomy (PDT) in the routine practice of intensive therapy resulted in almost complete replacement of open surgical tracheostomy operation [44]. This reduced the incidence of perioperative bleeding, tracheal stenosis, and infections of soft tissue and mediastinum [45]. It should be remembered that PDT must be carried out only under bronchoscopic assistance and ultrasound control. This improves the safety of the procedure and minimizes the risks of perioperative complications [46, 47]. All current PDT methods (Ciglia, Griggs, and Frova) are safe and can be successfully used in neurocritical patients. However, rotary PDT techniques should be preferred in neurocritical care [48] for two reasons. First, rotary techniques do not involve compulsory hyperextension of the neck, which is especially important for patients with intracranial hypertension [49]. Second, the incidence of perioperative bleeding is the lowest when using Frova technique [48]. This is especially important, because neurocritical patients have an extremely high risk of thromboembolic complications, and they almost always receive antithrombotic therapy at the time when PDT is indicated, on day 3—7 [2, 5, 6].

Blood gas composition correction strategies in respiratory distress syndrome

Respiratory distress syndrome (RDS) is an acute bilateral damage to the lower respiratory tract of various etiologies leading to acute respiratory failure [50]. In 2012, diagnostic criteria of RDS were revised and the so-called Berlin definitions were formulated: 1) acute onset; 2) bilateral infiltrates on chest radiograph; 3) no heart failure and fluid overload as potential causes of respiratory failure. There are three RDS severity levels depending on the oxygenation index: 1) mild (oxygenation index of 200—300); 2) moderate (oxygenation index of 100—200); 3) severe (oxygenation index of less than 100) [51].

Severe RDS is significantly less common in neurocritical patients compared to general intensive care patients. In neurocritical patients, it is mainly caused by neurogenic pulmonary edema and lung injury associated with concomitant injury and polytrauma [52, 53]. However, if a neurocritical patient develops RDS, it significantly worsens patient’s condition and outcome [54]. The studies on RDS in general intensive care patients showed that the following therapeutic options significantly improve disease outcomes: 1) protective mechanical ventilation; 2) prone position; 3) the use of muscle relaxants [55]. Along with this, there are quite aggressive hypoxemia correction methods, which were not proved to be effective, but nevertheless they are used in severe RDS: 1) high-frequency mechanical ventilation (HF MV); 2) nitric oxide inhalation [56]. In recent years, extracorporeal gas exchange techniques are increasingly more popular in general intensive care. Some therapeutic strategies for hypoxemia correction that were proved to be effective in general intensive care practice are successfully used in neurocritical care in the case of RDS, whereas the other therapeutic options cannot be used in...
patients with brain damage or their use is significantly limited [57].

**The protective MV.** On the one hand, MV is a life-saving procedure in patients with RDS. On the other hand, MV itself can damage lung tissue, which is particularly important in RDS patients, when even the standard MV parameters can cause barotrauma, volutrauma, atelectrauma, or biotrauma of the lungs [58]. Therefore, so called protective MV should be carried out in RDS patients, which involved pressure restriction in the respiratory tract, while maintaining plateau pressure below 30 cm of water column, the tidal volume of 6—8 mL/kg of the ideal body weight, positive end-expiratory pressure (PEEP) above 10 cm of water column [18—20]. This MV strategy proved to be effective in general intensive care patients despite the high incidence of hypercapnia. Treatment outcomes of RDS patients significantly improved when using protective MV compared to those patients, where respiratory tract pressure, PEEP, and tidal volume were not controlled [59]. The design of studies that proved the efficacy and safety of protective MV excluded neurocritical patients.

Hypothetically, high PEEP and hypercapnia may have a negative effect on intracranial situation in patients with brain damage and intracranial hypertension. In actual clinical practice of management of neurocritical patient with RDS, PEEP have almost no negative effect on intracranial situation. Earlier studies examining the effect of PEEP on the intracranial pressure found no significant increase in intracranial pressure in the case of the correct elevated position of the head end of the patient and PEEP below 15—17 cm of water column [60]. In addition, protective MV assumes monitoring of the plateau pressure in the respiratory tract, and therefore increase in PEEP is compensated by decrease in tidal volume and/or inspiratory pressure. Therefore, no fundamental changes in the intrapleural pressure, central venous pressure, parameters of venous outflow from the cranial cavity, and, consequently, intracranial pressure occur during the protective MV regardless of the absolute PEEP values [61].

Another situation takes place with hypercapnia, which often develops during protective MV [62]. From the viewpoint of general intensive care, it is a so-called permissive hypercapnia, but in the case of neurocritical care, it is a prohibitive hypercapnia, since its value often reaches 60 mm Hg and higher. This level of hypercapnia usually leads to intracranial hypertension in patients with brain injury [63, 64].

Therefore, protective MV strategy should be regarded as effective and safe in neurocritical RDS patients as long as there is no hypercapnia. Management of these patients should include monitoring of arterial and end-expiratory carbon dioxide, as well as multimodal neuromonitoring, which is a standard for neurocritical situation. In the case of hypercapnia, either aggravating or leading to intracranial hypertension, the level of carbon dioxide should be immediately normalized. This can be done using body temperature control or extracorporeal carbon dioxide elimination. However, correction of carbon dioxide level usually begins with increasing minute ventilation, which can create conditions for further lung injury due increase in tidal volume and/or plateau pressure in the respiratory tract [65].

**Muscle relaxants** were conclusively shown to be effective in the treatment of RDS in the population of general intensive care patients [66—69]. Furthermore, muscle relaxants are included in intracranial hypertension correction protocols [3]. Based on these facts, these drugs should be used in neurocritical patients with RDS to correct hypoxemia and prevent MV-associated lung injury.

**Prone position.** i.e. MV in patient’s prone position. This improves drainage and oxygenizing lung function due to recruitment of alveoli and improvement of ventilation-perfusion ratios [67, 68]. However, prone position is only effective if it is used for a long time, at least 12—18 hours per day [69]. Due to this fact, the use of prone position is limited and complicated in most neurocritical patients because patient’s horizontal prone position causes intracranial hypertension and reduces cerebral perfusion pressure [70, 71].

**High-frequency MV.** Application of HF MV in general intensive care patients with RDS enhances blood oxygenation. However, this neither reduces mortality no improves disease outcome [72—74]. HF MV is used in routine general intensive care only in the case of refractory hypoxemia [75]. HF MV is associated with faster development and greater severity of hypercapnia compared to protective MV. Actually, it is hypercapnia that causes major limitations in the use of this technique in neurocritical patients.

Inhalation of nitric oxide leads to dilatation of pulmonary circulation arteria and correction of pulmonary hypertension [76]. However, nitric oxide has antiaggregatory and immunomodulatory effects due to platelet receptor blockade, influence on T-helpers, increased production of IL-4, as well as direct bacteriostatic and virus-static effect [77, 78]. Nitric oxide is routinely used in neonatology in the case of neonatal respiratory distress syndrome [79, 80]. The use of inhalable nitric oxide in adult patients with severe RDS and refractory hypoxemia increases oxygenation indices, but the studies have failed to demonstrate reduced mortality and improved outcomes in the population of general intensive care patients [81, 82]. No studies on the efficacy of nitric oxide were carried out in neurocritical patients with RDS. At the same time, the effects of inhaled nitric oxide as a neuroprotectant were investigated in neurocritical patients with isolated brain damage [83], and very interesting and promising results were obtained. In this regard, nitric oxide therapy in neurocritical patients with RDS should be subject to clinical trials, and this strategy could become a promising area of intensive care in the future.
Body temperature control is an artificially achieved and maintained normothermia (induced hypothermia: 33—35°C) or normothermia (induced normothermia: 36—37.5°C) [84]. Decrease in body temperature reduces body metabolism and, therefore, reduces the need for oxygen and carbon dioxide production. This reduces minute volume ventilation. Thus, the body temperature control strategy can be an effective complement of protective MV and HF MV strategies, if the patient develops hypercapnia. Given the fact that induced hypothermia and normothermia have neuroprotective effects and it is one of the most effective options of intracranial hypertension correction, body temperature control should be regarded as one of the most effective additive respiratory strategies in neurocritical care. However, it should be kept in mind that body temperature control, in particular therapeutic hypothermia, is an aggressive technique of intensive therapy, and therefore the decision whether to use it should be taken carefully and after careful consideration [85, 86]. However, when fever occurs in a neurocritical patient during the acute phase of the disease complicated by the development of RDS with hypercapnia, it should be stopped as quickly as possible.

Extracorporeal decarboxylation allows extracorporeal elimination of carbon dioxide [87, 88]. The method is based on the use of a pumpless arteriovenous system, where blood flow occurs due to pressure gradient [89, 90]. For this purpose, femoral artery and vein are cannulated. Blood flow is about 1 L/min. The use of extracorporeal decarboxylation together with normalization of carbon dioxide level results in improvement of blood pH [89]. The use of anticoagulants, usually heparin, are required for adequate system functioning in order to achieve and maintain PTT of 45—60 s or activated clotting time (ACT) of 140—160 s [91, 92]. The cases of RDS, wherein oxygenation was normalized, but severe hypercapnia developed, are the application point for extracorporeal decarboxylation [93].

Despite the obvious advantages and efficacy of extracorporeal decarboxylation in the population of general surgical patients, this technique is not widely used in neurocritical care. First of all, this is due to the extremely high risk of intracranial hemorrhagic complications during prolonged use of heparin. Additionally, if a neurocritical patient develops RDS accompanied by severe hypercapnia, then this patient almost always has hypoxemia, and this condition necessitate extracorporeal membrane oxygenation.

Extracorporeal membrane oxygenation (ECMO) is a technique based on patient’s blood perfusion through the extracorporeal oxygenator, where gas exchange occurs, and then returns to the bloodstream. There are two ways to connect the system: venous ECMO, where blood is taken from the inferior vena cava and returns to the superior vena cava, and veno-arterial ECMO, where blood is returned to the aorta. Typical volumetric flow rate during ECMO is 3—4 L/min, but it may be increase to 7—8 L/min, if necessary [94]. Almost all values of PaO₂ and PaCO₂ can be obtained by varying the ECMO parameters. ECMO in the only effective method of blood gas normalization in the case of severe RDS accompanied by drug-resistant hypoxemia and hypercapnia. Furthermore, ECMO significantly reduces the aggressiveness of MV parameters, which creates favorable conditions for recovery of damaged lung [95].

Predicted mortality of RDS patients who have indications for ECMO is almost 100%. When ECMO is used in this population of patients, mortality is 29—43%, and therefore more than a half of the patients have a chance for favorable outcome [96, 97]. The time of ECMO initiation is one of the most important modifiable risk factors that affect the outcome in RDS patients with ECMO. When ECMO was started 7 days after initiation of MV in RDS patients with aggressive parameters, the outcomes remain the same as without ECMO [98]. Therefore, timely initiation of ECMO is extremely important.

ECMO is almost the absolute prerogative in general critical conditions. This applies both to the routine practice and clinical studies [99]. The literature reports only individual cases, where ECMO was used in neurocritical care [100—103], except for the patients with cardiac arrest, where ECMO was started during resuscitation, when it was ineffectiveness for 10—15 minutes [104]. This is a so-called extracorporeal cardiopulmonary resuscitation (ECPR), which is significantly and obviously superior to conventional CPR [105].

The risk of intracranial hemorrhage complications, which occur in 2—12% of cases even in general intensive care patients with intact brain, is the main reason for the lack of experience in using ECMO in neurocritical care [106, 107]. The need for using relatively high doses of heparin increases the risk of these complications in neurocritical patients [108]. Some authors experienced in using ECMO in neurocritical patients suggest that ECMO can be used without heparin [109]. Modern ECMO circuits are covered with a special biomaterial, which actually reduce thrombogenesis upon contact with blood, and virtually no blood clots are formed in the circuit during 2—3 days [110]. However, clots may form on the outer surface of the cannula and the oxygenator, and therefore heparin-free ECMO technique can be used only in exceptional cases and for a short time [111]. Some authors recommend to use anticoagulation in the same way as in general intensive care patients, maintaining of the activated clotting times of 180—220 s [110]. However, this strategy is extremely dangerous, and it is advisable to avoid it in neurocritical patients. Our personal experience with ECMO in patients with subarachnoid hemorrhage after endovascular occlusion of the anterior cerebral artery aneurysms with underlying invasive multimodal neuromonitoring shows that the tactics of using low heparin dose, while maintaining the activated clotting time of 120—140 s and with strict hemostatic system control,
is effective and can be safe [112]. Despite the difficulties arising during ECMO in neurocritical patients, it is obvious that this aggressive, but life-saving procedure will be increasingly used in neurocritical care in the near future.

Conclusion

Arterial blood gas control became a fundamental of resuscitation. Neurocritical care, as a part of intensive care, is characterized by specific features due to pathophysicsology of nervous system damage. These features, on the one hand, make adjustments to the algorithms of respiratory strategies that are conventionally used in general intensive care patients. On the other hand, brain damage places special demands on the respiratory system, so as to prevent the development of secondary brain injury. Thus, favorable outcome in the treatment of serious patient is impossible unless the neurosurgeon understands both modern general critical respiratory strategies and cross impact of brain injury and respiratory strategies.

Authors declare no conflict of interest.

REFERENCES


Respiratory therapy is currently one of the main treatments for patients in critical condition. Dozens of books and thousands of publications focus on this problem. Why do we need another review on this issue, while there are so many publications? And yet it is absolutely necessary. The authors of the article clearly and efficiently structured the problem of respiratory therapy in patients with brain damage and represented the results in a condensed form. It is without equal in the Russian literature published during the last 10 years.

At the beginning of the article, the authors present a number of basic points that explain the special urgency of respiratory problems for neurological patients: on the one hand, the incidence of respiratory disorders in patients with brain damage exceeds that in all other surgical patients; on the other hand, the presence of pronounced respiratory disorders in neurocritical patients significantly reduce survival and worsens neurological outcomes. Third, the repertoire of respiratory intensive care techniques has changed and considerably increased over the last few years. The tactics of the use of various modalities of respiratory intensive care and possible place of new techniques necessitate analysis and discussion.

The paragraph “Goals and objectives of respiratory support” is discussed by the authors in quite unusual way despite the obviousness of the material. The possibility to change the tone of cerebral arterioles and thus affect the cerebral blood flow and the intracranial blood volume by changing partial pressure of arterial CO2 has long been known. This phenomenon forms the basis for the use of therapeutic hyperventilation to reduce the intracranial pressure (ICP); hyperventilation — hypocapnia — spasm of cerebral arterioles — decrease in the intracranial blood volume — reduced ICP. However, the authors present another interesting information on the therapeutic use of hypocapnia (PaCO2 = 50—60 mmHg) in patients with cerebral vasospasm: hypocapnia — dilation of cerebral arterioles — increase in cerebral blood flow.

The terms “respiratory drive” (respiratory activity), “respiratory index” (RI = PaO2 (mmHg)/FiO2 (conv. units), “respiratory tract management”, and “respiratory tract protection” (management and protection of respiratory tract) used by the authors in the text of the review may seem to be a certain innovation at the first glance. However, these are well-established and approved concepts in the lexicon of intensivists.

The author’s attitude toward non-invasive mechanical ventilation in neurosurgical patients reflects a global trend: the use of noninvasive MV is contraindicated in patients with neurological disorders, especially in the case of reduced level of wakefulness.

The question of the timing of tracheostomy in neurosurgical patients is still a subject of debate. And although there is a series of publications emphasizing the advantages of early tracheostomy, its superiority over late tracheostomy in terms of the incidence of nosocomial infections and outcomes of treatment still remains unproved.

The section describing respiratory distress-syndrome clearly lists and reviews all the modern therapeutic options of both first and second order.

The author correctly noted that the therapeutic option “patient’s body temperature control” must also be considered and used in respiratory therapy, since mild induced hypothermia and normothermia are accompanied by decrease in oxygen consumption and CO2 production.

In addition to all these advantages, the section on decarboxogenization and ECMO is of particular interest. I am impressed by the authors’ rationally cautious approach to the ECMO procedure, which is now experiencing the peak of clinical popularity in patients with brain damage. This is probably due to the fact that the authors have their own experience in this field. I believe that there are good reasons to publish this article in the neurosurgical journal. One more remark. In English, there are two implicitly different concepts: “information” and “knowledge”. While information is only information, knowledge is at least information passed through the mind of practicing professionals. In my opinion, this review article clearly represents the second case.

A.Yu. Lubnin (Moscow, Russia)
Indications for surgical treatment of prolactin-secreting pituitary adenomas

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Abstract

Prolactinomas account for about 40% of all pituitary adenomas. The main treatment for prolactinomas is undoubtedly therapy with dopamine agonists (DAs). However, prolonged conservative treatment (for many years or even throughout life) that is necessary for permanent control of the disease makes some patients refuse pharmacological treatment for various reasons. In addition, not all prolactinomas respond to DAs therapy. Sometimes, the patient is not able to continue treatment because of the severity of side effects. Along with tumor resistance to therapy and patient intolerance of DAs, complications (liquorrhea, hemorrhage in the tumor) may occur during conservative treatment. In these cases, surgery is necessary.

The paper analyzes the modern literature on various treatment options for prolactin-secreting pituitary adenomas and defines the indications for surgical treatment.

Keywords: prolactinomas, prolactin-secreting pituitary adenomas, pituitary adenomas, transsphenoidal surgery, hyperprolactinemia, dopamine agonists, cabergoline, bromocriptine, liquorrhea, resistance, hemorrhage.

Abbreviations:
DAs — dopamine agonists
PRL — prolactin
Cab — cabergoline
Brc — bromocriptine

Prolactinoma is a hormonally active pituitary tumor originating from lactotroph cells of the adenohypophysis and characterized by excessive production of prolactin (PRL). Prolactinomas accounts for about 40% of adenomas and 50–60% of hormonally active pituitary adenomas [1–3]. Prolactinomas are six-fold more common in females than in males [4].

The clinical picture is determined by hyperprolactinemia and usually presents with decreased libido, erectile dysfunction in males, amenorrhea and galactorrhea in females, and infertility in both sexes. Large tumor may cause cerebral symptoms (usually in the form of headache), as well as visual and oculomotor disorders; occlusive-hypertensive symptoms may develop as a result of tumor propagation into the ventricular system [3, 5, 6].

Any treatment for prolactinoma is aimed at reducing clinical manifestations associated with excessive secretion of PRL, reducing tumor size, and preventing of disease recurrence or progression.

Since late into the 19th century and until the mid-20th century, surgery was the main treatment for prolactinoma. Transcranial or transsphenoidal tumor resection was carried out depending on the size, growth pattern, and surgeon preferences [7].

Since the second half of the 20th century, treatment for prolactinomas with dopamine agonists (DAs) was the standard and basic method of treatment [8, 9]. Bromocriptine (Brc), which is used since 1968, is the most common DA; cabergoline (Cab) is a modern and the most effective drug [10].

Biomechanism of DA action is targeted at reducing the size of lactotroph cells due to binding to the type 2 dopamine receptors and degeneration of the endoplasmic reticulum and Golgi apparatus. Additionally, cell proliferation is inhibited [11, 12].

Cab is the most selective and long-acting drug product. It selectively acts only on D2-receptors of normal and tumorous pituitary lactotrophes [13–15].

The efficacy DAs is determined by decrease in blood level of PRL, dynamics of decrease in tumor size, and resolution of clinical symptoms. Some authors carried out comparative studies of the efficacy of Brc and Cab. Thus, M. Molitch [16] analyzed the data of 1022 patients treated with Brc and reported that remission occurred in up to 76% of cases; in patients treated with Cab (612 patients), remission was achieved in 89% of cases.

A multicenter comparative study of the efficacy of Cab and Brc demonstrated normalization of PRL level in 48 (65%) out of 74 females who received Brc and in 66 (92%) out of 72 patients who received Cab [17]. V. Pascal-Vigneron et al. [18] reported decrease in PRL level only in 27 (48%) out of 58 females who received Brc and in 56 (93%) out of 60 females who received Cab. Ono M. et al. [19] studied the effect of Cab in 150 patients, who received the drug at a dose of less than 2 mg/week: 78.8% of patients demonstrated decrease in PRL blood level.

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The study of L.I. Asta’eva [9], focusing on the treatment of macroadenomas with Cab, demonstrated positive dynamics in the form of significant decrease in PRL level or its normalization in 76% of patients and decrease in tumor size in 84.6% of patients.

Despite the high efficacy of DAs in the treatment of prolactinomas, several studies reported recurrent hyperprolactinemia after discontinuation of the drug. Recurrence was observed in 3 to 9.6 months after drug withdrawal [20—25].

Despite the fact that current international standards recommend DAs as the first-line therapy for prolactinomas, some patients prefer primary surgical treatment since they are afraid of potential negative effects of long-term pharmacotherapy and want to avoid prolonged conservative treatment.

There are several studies [26—29] demonstrating good results of surgical treatment of small non-invasive prolactinomas, where normalization of PRL blood level and restoration of reproductive function was observed. At the same time, there were almost no surgical complications.

Resistance and intolerance of dopamine agonists

PRL-secreting pituitary adenomas demonstrate various levels of sensitivity to various DAs. The resistance to DAs manifests as the absence of normalization of PRL blood level and at least 50% decrease in tumor size, when using high doses of DAs for 3 to 6 months [16, 30—32]. The use of high doses of Cab is limited due to its side effect, cardiac valve insufficiency as exemplified by the cases of patients with Parkinson’s disease, who were administered with Cab at a dose of more than 3 mg/day [33, 34].

Insensitivity of some prolactinomas to DAs can be due to various reasons. Decrease in the number of D2-receptors on the membranes of tumorous lactotroph cells, which prevents the effect of dopamine on these cells, is considered as a possible factor [35].

According to the literature [35], resistance of prolactinomas to Brc and Cab is 15—25 and 3—12%, respectively.

According to L.I. Asta’eva [9], tumors were partially or totally drug-resistant in 25% of patients (of these, 105 patients received pharmacotherapy as a primary treatment and 52 patients received DAs after surgery).

Sometimes, treatable tumors become drug-resistant after some time. E. Delgrange et al. [36] suggested that delayed development of resistance is a negative prognostic factor, since it can be indicative of malignant transformation of prolactinomas.

The article of D. McCall et al. [37] reports two cases of secondary resistance of a prolactinoma to Cab and significant increase in tumor size, which necessitated surgical treatment, while histological examination revealed no malignant transformation. Thus, the mechanism of delayed or secondary resistance to DAs is still not fully understood [38].

Apart from resistance, intolerance of DAs is also possible. Intolerance presents with a set of side effects that occur in patients receiving DAs. Common side effects include headache, drowsiness, and dizziness. Gastrointestinal symptoms include dyspepsia, reflux esophagitis, nausea, vomiting, and abnormal stools. There are psychiatric disorders, such as psychosis and mania, especially in the postpartum period [39, 40]. The incidence of Brc and Cab intolerance is 12 and 3%, respectively [40]. Adverse effects can be avoided by reducing the dose to tolerable value [41].

Surgical treatment of prolactinomas

Surgical treatment is used in patients with DA-resistant tumors. DA intolerance, complications arising during treatment with DAs, as well as patients who refuse long-term administration of DAs [42].

The effectiveness of surgical treatment for prolactinomas is assessed in terms of postoperative remission parameters, the incidence of postoperative complications, and recurrence rate [43].

According to many researchers [44—47], patients who did not receive conservative treatment with DAs are more likely to normalize PRL blood level after surgery. Thus, the study by Z. Gnjidic [27] demonstrated that PRL blood level was normalized in more than 90% of patients who underwent primary operation, whereas in patients who were preoperatively treated with DAs, PRL blood level was normalized only in 40% of cases.

Tumor size also affects the likelihood of disease remission [43]. Thus, according to Z. Gnjidic et al. [27], postoperative decrease in PRL blood level was observed in 98% of patients with microprolactinoma. M. Babey et al. [29] reported long-term remission in 22 (91%) of 24 patients with microprolactinoma after surgery. J. Kreutzer et al. [48] observed remission after resection of microprolactinoma in 91.3% of patients.

Similar results were obtained after transsphenoidal operations for microprolactinomas were reported in a number of international publications [28, 47, 49, 50].

R. Salvatori [26, 45, 46, 48, 49, 51-54] analyzed papers published in 2008—2013, reporting the results of surgery for 627 microprolactinomas. In total, normalization of PRL level in the early postoperative period was observed in 522 (83.2%) of 627 patients.

The results of surgical treatment for macroadenomas were somewhat worse. Thus, in V. Primeau et al. [45] reported stable postoperative remission in 60% of cases (12 of 20 patients).

P.L. Kalinin [7, 55] report the results of surgical treatment of 34 patients with macroadenomas. Of these, normalization of PRL level was achieved in 22 (67%) patients.

L.I. Asta’eva [38] have shown that the results of surgical and medicinal treatment of endosellar macrop-
lactinomas are substantially similar: normalization of PRL level was achieved in 67% of cases after surgery and in 71% of cases during pharmacotherapy.

Y. Song et al. [56] conducted a retrospective study (184 patients with prolactinomas) and concluded that the probability of total tumor resection (and therefore, the probability of PRL level normalization) is inversely proportional to adenoma size.

Patient’s age may be one of the factors affecting the outcome of surgical treatment of prolactinomas. According to K. Sinkunas et al. [47], young patients are more likely to normalize PRL levels than older patients.

Tumor invasion into the skull base structures and adenoma invasion to cavernous sinus reduce the likelihood of total tumor resection and, therefore, the probability of postoperative normalization of PRL level [44, 47, 57].

The article of M. Chen et al. [58] reflected the relationship between Ki-67 index and postoperative recurrence rate: the likelihood of recurrence is significantly higher ($p<0.01$) in the case of Ki-67>3. Thus, relapses were observed only in 3 (3.9%) out of 83 patients with Ki-67<1%; in 4 out of 54 patients with Ki-67 of 1—3%; in 9 (35.0%) out of 29 patients with Ki-67 3—5%; in 10 (58.3%) of 18 patients with Ki-67>5%.

Some authors [48, 59] reported that surgical treatment of cystic prolactinomas results in better outcomes compared to solid tumors.

The incidence of postoperative complications depends on the type of health care facility, the number of transsphenoidal operations carried out in this institution per year, and personal experience of the surgeon. The centers where more than 25 resections of various pituitary tumors per year is carried out demonstrate mortality rate of 0.2% [60]. Most articles show a direct correlation between the results of surgical treatment and surgeon’s experience: the best outcomes were observed in the study that included patients operated on by one surgeon [28, 30, 57].

Mortality and the incidence of postoperative complications directly correlate with tumor size. Thus, surgical treatment of large and giant prolactinomas is associated with lethality of 3.3 to 31.2% [41]. At the same time, according to P.L. Kalinin [7, 55], lethality after endoscopic transsphenoidal operations for small tumors tends to zero.

H. Ikeda et al. [57] operated on 138 females with prolactinomas (21 microadenomas and 117 macroadenomas) and reported that there were neither deaths nor postoperative complications, while PRL level was normalized in 76% of patients (105 patients). The authors found a correlation between the possibility of adenoma capsule resection and probability of PRL level normalization.

Transient postoperative diabetes insipidus is very common irrespective of the adenoma size, but irreversible diabetes insipidus was observed only in 1% of patients (usually with large and giant tumors) [61].

The so-called secondary surgery is carried out in patients who developed complications during therapy with DAs, mostly intra-tumor hemorrhage and spontaneous nasal liquorrhea [62—64].

L.I. Astaf’eva [65] reported 3 out of 176 cases, where there was bleeding into the prolactinoma during therapy with DAs, 2 of these patients were operated on.

Nasal liquorrhea is a rare but potentially serious complication. G. Lam et al. [62] analyzed 29 scientific papers published in 1980—2011, which reported 42 cases of nasal liquorrhea in patients with prolactinomas who received DAs. In these cases, the main treatment included transsphenoidal reconstruction of fistulas using autologous materials and allomaterials.

Recurrence of hyperprolactinemia

Possible duration of DA administration is specified by the International consensus on the treatment of hyperprolactinemia as of 2011:

— drug withdrawal is possible, if the patient maintains normal level of PRL for 2 years and neuroimaging (MRI, CT) shows no evidence of tumor;

— oral contraceptives are recommended to postmenopausal patients or patients who are not planning pregnancy [8].

After drug withdrawal, the patient should be further followed to monitor for disease recurrence. There is a high risk of recurrence, 26 to 69%, within the first year after drug withdrawal [20, 23]. Continuous monitoring of PRL blood level and clinical condition of patients is required after cessation of therapy; control MRI studies are indicated in the case of increase in PRL blood level or recurrent clinical manifestations of the disease.

The incidence of recurrent hyperprolactinemia after surgical treatment of prolactinomas and after withdrawal of DAs are quite comparable. Thus, according to J. Kreutzer et al. [48], recurrence was observed in 18.7% of cases after resection of prolactinomas and in 7.1% of cases after removal of microprolactinomas. According to A. Colao et al. [22], the incidence of recurrent hyperprolactinemia after withdrawal of DAs is 30—36%, depending on tumor size.

Prolactinomas and pregnancy

International Endocrinology Society drew up the guidelines for the treatment of pregnant females with prolactinomas. Withdrawal of DAs during pregnancy is recommended in patients with small prolactinomas. In the case of macroadenomas not subjected to surgery and radiation therapy, characterized by invasive growth, and affecting the visual pathways, it is recommended to continue treatment with DAs. If there are clinical signs of increase in tumor size (visual and oculomotor disorders) or resistance/intolerance of DAs, it is necessary to decide whether surgery is appropriate, irrespective of gestational age [8].
Given the existing risk of increase in tumor size during pregnancy, the pros and cons of the surgery should be evaluated at the stage of planning for pregnancy.

In the case of increase in tumor volume, emergency operation during pregnancy results in 1.5-fold higher risk of threatened abortion in the first trimester and five-fold higher risk in the second trimester [66, 67].

H. Ikeda et al. [57] summarized the materials from several studies and reported that 66 (39%) of 171 patients with macroadenomas had symptoms associated with increase in tumor volume (worsening of headache, visual deterioration) during pregnancy. The authors concluded that planning for pregnancy in patients with macroadenomas is advisable only after transsphenoidal tumor resection.

Z. Yan et al. [68] carried out quite interesting retrospective study on the efficacy of surgical treatment of prolactinomas in females of reproductive age (68 microadenomas and 31 macroadenomas). Total resection of the tumor was carried out in 88 cases, subtotal — in 9 cases, and partial — in 2 cases. The incidence of postoperative remission was significantly higher (80.9%) in females with microadenomas than in patients with macroadenomas (51.6%). Full recovery of menstrual cycle was observed in 23.5% of cases (irregular menstrual cycle or the need for DA administration), 10% of patients retained amenorrhea. Fourteen of 17 patients who planned for pregnancy got pregnant.

The economic aspect of the treatment of prolactinomas

The financial aspect should be considered when discussing the advantages or disadvantages of a certain method of treatment and its availability in different social strata.

P. Jethwa et al. [69] concluded that surgical resection carried out by an experienced surgeon (using microscopic or endoscopic technique) is a more cost-effective treatment of young patients than conservative treatment with expected DA administration time of more than 10 years. In addition, transsphenoidal endoscopic surgery is superior to microscopic one.

L.I. Astaf’eva [9] obtained similar results when studying the costs of medical and surgical treatment.

Conclusion

There is no doubt that administration of DAs has become the first-line treatment for prolactin-secreting pituitary adenomas over the last 30 years. However, there are groups of patients, who can undergo surgery, providing the results comparable to those of conservative treatment. Surgery is a serious alternative to pharmacotherapy in patients with microprolactinomas and small endosellar tumors. In these cases, the operation can be carried out with minimal complications and provides stable remission as evidenced by long-term postoperative follow-up.

In addition, surgical treatment in carried out in patients intolerant or refractory to AD therapy and patients who had complications during treatment (nasal liqueorrhea and intra-tumor hemorrhage).

Recent advances in endoscopic technique and the experience of neurosurgeons working in large specialized clinics improve the effectiveness of transsphenoidal interventions and provide high probability of postoperative remission with a minimum incidence of complications.

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The literature review focusing on the indications for surgical treatment of pituitary prolactinomas is a very important and timely work. The detailed analysis of the effectiveness of various pharmaceuticals used to treat prolactinomas suggests that surgical treatment is required in a certain part of patients. Primary resistance to therapy and delayed development of resistance, as well as idiosyncrasy of dopamine agonists dictate the use of more aggressive (from the viewpoint of surgery) approach to the treatment of prolactinomas. The review illustrates the efficacy of surgical treatment for prolactinomas and provides comparative evaluation of the results in various clinics, including the author’s own experience. This work shakes the beliefs that only pharmacotherapy is appropriate to treat prolactinomas and emphasizes the importance of endoscopic interventions, whose effectiveness is comparable to that of dopamine agonists.

Publication of this review seems to be important and necessary, since it will allow endocrinologists and neurosurgeons experienced in endoscopic interventions to make adequate correction of treatment strategy in patients with prolactinomas. Familiarity with the modern approach to the treatment of prolactin-secreting pituitary adenomas, which is based on the increasing role of surgical techniques, is also a necessary step in the education and professional development of young specialists involved in the treatment of pituitary tumors.

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The article focuses on the topical problem of selecting the optimal treatment of patients with prolactinomas. According to existing guidelines, pharmacotherapy with dopamine agonists is the method of choice in patients with tumor-related hyperprolactinemia. However, in some cases, there is the need for surgical treatment of patients with prolactin-secreting pituitary adenomas. This literature review describes in detail clinical situations, when surgical treatment is an advantageous option, even in the case of microprolactinoma. The detailed analysis of original papers studying this problem was carried out. Almost 30% of 69 literature sources have been published within the last 5 years.

The article is written in good literary language, it’s terminology is clear and understandable for the target audience and broadly covers the current state of the problem. The summary accurately reflects the structure of the literature review and the main issues discussed in the article.

The last part of the article discusses the economic aspects of the treatments for prolactinomas used in practice. The article cites the study carried out by P. Jethwa et al. [69], which assesses the cost-effectiveness of conservative and surgical treatment using the decision tree method. Similarly to other studies using the mathematical modeling methods, this study has several limitations, which were discussed by the authors in detail, in particular, the fact that the model may differ from the actual clinical practice and that the model is based on the costs in the United States, which also may differ significantly from the costs in other countries, etc. Since the cited study is one of the few currently available studies evaluating the cost-effectiveness of different treatment options, this aspect could be discussed in more detail.

The article deals with the topical problem of endocrinology and is of practical interest.

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