BURDENKO'S JOURNAL OF NEUROSURGERY

№1 * 2018 * vol. 82

Founded in 1937.

Media Sphera
Burdenko Neurosurgical Institute, Moscow, Russia
Official journal of the Association of Neurosurgeons of Russia

«Zhurnal voprosy neirokhirurgii imeni N N Burdenko» (Burdenko's Journal of Neurosurgery) is a bimonthly peer-reviewed medical journal published by MEDIA SPHERA Publishing Group. Founded in 1937.

Sponsored by fund «Neuro»

Journal is indexed in RSCI (Russian Science Citation Index), Web of Science (Russian Science Citation Index — RSCI), Scopus, PubMed/Medline, Index Medicus, Ulrich’s Periodicals Directory, Google Scholar.

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Art and Layout: MEDIA SPHERA Publishing Group

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- Professional satisfaction of neurosurgeons working in the Russian Federation
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- Spinal cord epidermoids

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.
The study purpose was to develop a technique for intravitral visualization of the brainstem reticular formation fibers in healthy volunteers using magnetic resonance imaging (MRI). Material and methods. The study included 21 subjects (13 males and 8 females) aged 21 to 62 years. The study was performed on a magnetic resonance imaging scanner with a magnetic field strength of 3 T in T1, T2, T2-FLAIR, DWI, and SWI modes. A CSD-HARDI algorithm was used to identify thin intersecting fibers of the reticular formation. Results. We developed a technique for reconstructing the reticular formation pathways, tested it in healthy volunteers, and obtained standard quantitative indicators (fractional anisotropy (FA), apparent diffusion coefficient (ACD), fiber length and density, and axial and radial diffusion). We performed a comparative analysis of these indicators in males and females. There was no difference between these groups and between indicators for the right and left brainstem. Our findings will enable comparative analysis of examination results in patients with brain pathology accompanied by brainstem injury, which may help predict the outcome. This work was supported by a grant of the Russian Foundation for Basic Research (№16—04-01472).

Keywords: reticular formation, ascending activating system, consciousness, tractography, CSD-HARDI, magnetic resonance imaging.

Long-term brain researches have shown that recovery of consciousness, cognitive functions and emotional response is determined by severity of cerebral dysfunction as a result of direct structural damage (trauma, ischemia, hypoxia) as well as neurochemical and metabolic disorders. It is known that consciousness is ensured by ascending reticular activating system (ARAS) of the brainstem which includes ventral and dorsal pathways. The first one passes through the hypothalamus and basal parts of forebrain (histamine-, choline-, dopamine-, glutamatergic systems). Dorsal pathway activates cortex through the thalamus (mainly dopamine-, serotonin-, noradrenaline-, cholinergic systems) (Fig. 1). ARAS is not only a part of brain stem reticular formation from pons to thalamus, but also nuclei set of different neurotransmitter systems [1]. ARAS injury is followed by decreased number of afferent projections of many neurotransmitter systems to cerebral cortex including those activating and maintaining consciousness.

Neuroimaging is very important to investigate mechanisms of cerebral functions restoration in current neuroscience. It is able to determine in vivo focal and diffuse cerebral lesion, impaired blood flow in certain structures, qualitatively and quantitatively assess conductive paths by using of 3D-reconstruction, to analyze local or diffuse biochemical changes (MR-spectroscopy) [2—6]. In recent years, special attention has been paid to MR-tractography allowing 3D-reconstruction of various cerebral conductive pathways with creation of so-called connectome. Well-equipped projects "Human Brain Connectome" in the USA and "Human Brain Project" in the countries of the European Union confirm relevance of human conductive pathways research [7, 8].

Patterns of multivariate brain cleavage with degeneration of commissural (interhemispheric), associative (hemispheric) and corticospinal conductive pathways have been previously shown on diffuse axonal damage model [9, 10]. At the same time, MR-tractography of reticular formation is under relatively little attention mainly due to difficult visualization of fine intersecting fibers of this structure. The first works for visualization of fibers and nuclei of reticular formation have been started recently [11—14]. Previous publications are based on posthumous cerebral examination of three patients with severe brain damage and several healthy volunteers. In these works, the authors used deterministic method of tractography on MR-tomograph (3 T) with Constrained Spherical Deconvolution—High Angular Resolution Diffusion Imaging (CSD-HARDI) algorithm. The advantage of this method is visualization of two or more axonal beams intersecting in different directions.

Currently, prognosis and treatment of severe cranio-cerebral trauma (CCT) has become particularly relevant due to socio-economic importance of the problem, since trauma is the leading cause of disability among employable persons. Definition of probability and grade of mental activity recovery is the key to assessing rehabilitation potential. However, domestic and foreign clinical criteria for unconscious states assessment do not always allow us to interpret correctly patient’s consciousness. Recent studies have shown that about 40% of patients with clinical picture of vegetative status have signs of higher level of
At present time correction of impaired consciousness and other mental functions are aimed at changing of neurotransmitter systems’ functions. Recently, US Department of Defense have published review of 12 the most perspective pharmacological agents for treatment of CCT patients: 5 of them directly affect neurotransmitter systems, and another 5 indirectly modulate their activity [16]. It is important that there are still no objective guidelines for neurotransmitter disorders detecting. Clinical syndromes of glutamatergic, dopaminergic, cholinergic neurotransmitter systems dysfunction have been determined [17]. However, their instrumental confirmation with MR-spectroscopy and MR-tractography is absent. By the way these methods are useful for intravital evaluation of cerebral neurotransmitter systems.

The purpose of this study is to obtain the normative data of MR-tractography of reticular formation (fractional anisotropy-FA, diffusion coefficient, fiber density and length, axial and radial diffusion), their comparative analysis in men and women for subsequent comparison with similar data in patients with severe brain damage followed by primary or secondary brain stem injury.

**Material and methods**

The study included 21 healthy volunteers (13 men and 8 women) aged 21 to 62 years (mean 31.3±9.6 years). All of them had higher education, one was left-handed. Informed consent to participate in the study was obtained from each volunteer.

**CSD-HARDI MR-tractography:** Scanning was carried out on 3.0 T MRI scanner General Electric Signa HD (GE Healthcare) with 8-channel head coil. Following protocols were used in the study: T1 FSPGR BRAVO with an isotropic voxel 1×1×1 mm and zero gap, axial T2 with cut-off thickness 5 mm and gap between slices 1.5 mm, axial T2-FLAR with cut-off thickness 5 mm and gap 1 mm, DWI ASSET with cut-off thickness 5 mm and gap 1 mm, spectroscopy (single voxel, 2D CSI and 3D MRS), and HARDI protocol. HARDI data were obtained by using of SE DWI EPI sequence with the following parameters: TR=12,000 ms, TE-min, pixel bandwidth 3,906.25 Hz, 256×256 or 128×128 matrix, the number of slices is 30, 32, 34 or 36. Zero gap was established between slices, cut-off thickness was 2.5 mm, FOV=22×22, 24×24, 25×25 or 26×26 cm², b-factor was 2,000, 3,000 or 4,000 s/mm², the number of diffusion gradient directions — 120 or 110 with corresponding quantity of non-diffusion volumes (b=0 s/mm²): 1 or 11. In the second case non-diffusion volumes scanning was performed in every 10 directions of diffusion gradients. Overall time of scanning for HARDI algorithm was 24 min 25 s. Then diffusion images obtained were interpolated to voxel size of 1×1×2.5 mm.

Pre-processing of diffusion images was carried out by using of FSL 5.0 (http://fsl.fmrib.ox.ac.uk/fsl/) and ExploreDTI (http://www.exploredti.com/) software. Tracks were constructed in ExploreDTI program.

Paxinos and Huang atlas was used to identify the zone of interest (brain stem cholinergic nuclei localization — pedunculopontinous and laterodorsal tegmental) [18]. Image of such zone near 28 mm² is shown in Fig. 2. All quantitative parameters were measured: mean FA and diffusion coefficient over entire length of fibers, number and length of fibers, axial and radial diffusion.

Statistical processing was carried out by using of Statistica 8.0 software (Statsoft, USA). In all cases nonparametric criteria were used. Spearman rank correlation coefficient and Mann-Whitney test were used to estimate correlations and to compare two independent samples, respectively. Differences were considered significant at p<0.05.

**Results**

We have developed the technique for visualization and quantitative assessment of fine intersecting fibers of brain stem reticular formation (ARAS) by using of MRI CSD-HARDI algorithm (Fig. 3). Group of healthy volunteers of middle age was selected and analyzed for this purpose.

For each healthy volunteer two-sided 3D-reconstructions of ascending tracts were performed. They started from dorsolateral pons at the level of two closely located cholinergic nuclei (pedunculopontinous and laterodorsal tegmental) (Fig. 4). It can be seen that in all cases fibers are represented by two main bundles which pass through mesencephalon and divide into smaller beams extending to thalamic (dorsal tegmental tract) and...
hypothalamic nuclei, basal parts of frontal lobes (ventral tegmental path) (Fig. 3c).

Quantitative characteristics including FA, diffusion coefficient, length and number of fibers, axial (L1) and radial (L2) diffusion for left (Table 1) and right (Table 2) tracts were obtained. It was shown that all these variables do not depend on the side of tract (left or right) and gender.

Thus, we have obtained control normal quantitative characteristics for evaluation of bilateral tracts of reticular formation arising from cholinergic nuclei in young employable men and women.

Discussion

For the first time we have developed the technique of brain stem ARAS formation in healthy volunteers. We obtained averaged quantitative data for pons fibers of reticular formation where cholinergic nuclei are localized (FA, diffusion coefficient, fibers density and length, axial and radial diffusion). The last will allow further comparative analysis of reticular formation state in patients with brain injury by using of statistical processing. Firstly, ARAS visualization with CSD-HARDI and deterministic processing was demonstrated in 2 pathoanatomical cases and one healthy volunteer [11]. Also there were attempts to visualize fibers via formation through two target points (brain stem and thalamus/hypothalamus) in healthy volunteers [19, 20]. However, these trials were performed on tomograph 1.5 T without CSD-HARDI algorithm, interesting zone included entire region of reticular formation rather separate nuclei. So, it was shown that fibers of reticular formation are mainly projected onto certain areas of prefrontal cortex (lateral and ventromedial), quantitative variables of reticular formation are similar for both hemispheres and in males and females [19, 20].

Currently, there are more and more publications [21—25] confirming relationship between impaired
consciousness and other mental functions including emotions with injury of some brain stem neurotransmitter systems. It is known that cholinergic system participates in short-term memory, attention, emotions regulation, wakefulness level.

Acetylcholine is produced in following cerebral nuclei: pontine reticular formation nuclei (pedunculopontine (PPN) and laterodorsal (LDT) tegmental, interneurons of neostriatum and basal forebrain (Meynert nucleus, medial septal nucleus and Brock’s diagonal strip which are together forming substantia innominate). PPN and LDT fibers as a part of paramedian pontine reticular formation are associated with vestibular nuclei, locus coeruleus, cerebellum, thalamus and giant–cell preoptic nucleus [26].

Cholinergic nuclei of basal forebrain are more active in wakefulness than in sleep, while cholinergic neurons of PPN nucleus are predominantly activated during rapid eye movement sleep (REM-sleep) and are responsible for pontine-geniculo-occipital EEG complexes. It is considered that PPN neurons provide decreased muscles tone during REM-sleep through activation of glycinegic inhibitory systems [27].

Near 85—90% of brain stem cholinergic afferents are involved into innervation of various (specific and non-specific) thalamic nuclei. The most pronounced cholinergic nuclei are the following: subicular, entorhinal, insular, cingulate, prefrontal, supplementary motor areas, infralimbic, agranular, parahippocampal cortex, anterior cingulate, medio-orbital, orbitofrontal cortex, basal forebrain including Meynert nucleus, and adjacent septopallidal nuclei (medial septal nucleus, nucleus accumbens, olfactory tubercle). It is worth noting that afferents of basal forebrain, cholinergic neurons of which are located in the Meynert nucleus, innervate large areas of the neocortex including frontal, parietal, temporal, and occipital cortices [28].

Footnote. Here and in Table 2: FA — fractional anisotropy; L1 — axial diffusion index; L2 — radial diffusion index.
ergic innervation (from pontine PPN and LDT nuclei) is obtained by anterior intralaminar nuclei and additional paralaminar areas of thalamus, which are key for wakefulness regulation [28]. Cholinergic afferents to thalamic nuclei have a double effect on their activity. On the one hand, they inhibit GABAergic neurons of thalamic reticular nucleus through M-cholinergic receptors. These neurons inhibit activating neurons of front intralaminar nuclei. So, cortex is activated. On the other hand, direct cholinergic projections activate front intralaminar nuclei via nicotinic receptors (N-cholinoreceptors) [28]. Brainstem cholinergic fibers also activate anteroventral thalamic nucleus that has projections to retrosplenial cortex (part of posteromedial cortex) [29]. Increased metabolic activity of this cortex is one of the neuroimaging markers of consciousness recovery onset. Thus, concomitant activation of brainstem and forebrain cholinergic projections during wakefulness and REM-sleep ensures integrative thalamic function and can modulate conscious processes. It is evidenced by some trials which have shown that cholinergic neurons of basal forebrain are responsible for cognitive evoked P300 potentials [30].

Besides the thalamus, brainstem cholinergic neurons innervate other cerebral structures providing wakefulness, in particular glutamatergic (reticular formation of mesencephalon, pontine oral nucleus), cholinergic (basal forebrain) and prefrontal cortex [31]. It is important to note that cholinergic system is able to maintain active cerebral state without activation of monoaminergic (catecholaminergic, serotonergic) systems [32], but with obligatory activity of glutamatergic system [30].

Thus, we have obtained reticular formation tracts originating from dorsolateral pons where cholinergic nuclei are localized. Our data correspond to concept of anatomical connections of this structure. Further evaluation of cholinergic system in brain lesions may be important to predict consciousness and cognitive functions recovery. In general, non-invasive diagnosis of structural and metabolic biomarkers reflecting damage of various neurotransmitter systems in severe cerebral injury may be key to assess recovery of consciousness, intellectual-mnestic functions and emotional-volitional disorders. The last is necessary to develop personalized therapeutic-predictive model.

Limitations of HARDI should be considered. Identical diffusion characteristics of all cerebral fibers are accepted to simplify calculations [33]. CSD–HARDI method is sensitive to noise on the image [34, 35] and can give erroneous information about the tracts within grey matter and cerebrospinal fluid [36]. Tractography depends on various methodological factors: scanning parameters such as b-factor and the number of diffusion gradients directions [37], and post-processing of data including noise and artifacts correction. It cannot be ruled out that pathways constructed can contain both descending and ascending fibers since ARAS is polysynaptic structure with many internal and external associations.

The work is supported by RFFI grant No. 16–04–01472.

Acknowledgment to radiologist A.S. Tonoyan for participation in MR-tractography variables selection.

Authors declare no conflict of interest.

**Table 2. Quantitative features of right-sided tracts of reticular formation from pontine cholinergic nuclei**

<table>
<thead>
<tr>
<th>Variable</th>
<th>All sample (n=21)</th>
<th>Males (n=13)</th>
<th>Females (n=8)</th>
<th>p (Mann-Whitney test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FA</td>
<td>0.33—0.48</td>
<td>0.33—0.48</td>
<td>0.33—0.48</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Diffusion coefficient</td>
<td>0.46—0.94·10⁻³</td>
<td>0.46—0.82·10⁻³</td>
<td>0.47—0.94·10⁻³</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>(0.62±0.13·10⁻³)</td>
<td>(0.58±0.12·10⁻³)</td>
<td>(0.68±0.15·10⁻³)</td>
<td></td>
</tr>
<tr>
<td>Length of fibers, mm</td>
<td>35.3—64.4</td>
<td>35.3—64.4</td>
<td>38.2—57.1</td>
<td>0.97</td>
</tr>
<tr>
<td></td>
<td>(48.2±8.3)</td>
<td>(48.4±9.6)</td>
<td>(47.9±6.1)</td>
<td></td>
</tr>
<tr>
<td>Density of fibers, U</td>
<td>15—35</td>
<td>17—35</td>
<td>15—34</td>
<td>0.86</td>
</tr>
<tr>
<td></td>
<td>(27.3±5.8)</td>
<td>(27.5±5.8)</td>
<td>(27±6.1)</td>
<td></td>
</tr>
<tr>
<td>L1</td>
<td>0.67—1.2·10⁻³</td>
<td>0.67—1.2·10⁻³</td>
<td>0.67—1.3·10⁻³</td>
<td>0.21</td>
</tr>
<tr>
<td></td>
<td>(0.9±0.2·10⁻³)</td>
<td>(0.84±0.19·10⁻³)</td>
<td>(0.98±0.2·10⁻³)</td>
<td></td>
</tr>
<tr>
<td>L2</td>
<td>0.38—0.84·10⁻³</td>
<td>0.38—0.7·10⁻³</td>
<td>0.41—0.84·10⁻³</td>
<td>0.14</td>
</tr>
<tr>
<td></td>
<td>(0.5±0.1·10⁻³)</td>
<td>(0.5±0.095·10⁻³)</td>
<td>(0.58±0.13·10⁻³)</td>
<td></td>
</tr>
</tbody>
</table>
Modern technique of CSD-HARDI for visualization of conductive fibers passing through pontine cholinergic nuclei (pedunculopontinosus and laterodorsal tegmental) is used in healthy volunteers. The authors obtained quantitative data about pontine reticular formation fibers where their cholinergic nuclei are localized. These data may be later used for comparative analysis of patients with brain stem injury and impaired consciousness. The article follows organically from previous literature for this issue and greatly advances our knowledge in this field. There are single works about this problem in the world literature at present time.

A.I. Kholodniy (New York, USA)
Endocrine Disorders Prior and After Surgery for Pituitary Stalk Lesion With Suprasellar Tumors


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The pituitary stalk (PS) is a relatively thin bundle connecting the hypophyseal stalk to the pituitary gland; it consists of both axons of the hypothalamic nuclei (terminating in the neurohypophysis) and the system of portal vessels. Compression of the PS by a space-occupying lesion or its transection (forced or intended) during surgery may lead to the development of endocrine disorders: hypopituitarism, diabetes insipidus, and hyperprolactinemia. The modern literature lacks studies evaluating the severity of endocrine disorders depending on the PS condition before and after surgery.

Purpose. The study purpose was to investigate endocrine disorders in patients with sellar region (SR) tumors and the PS that was compressed before surgery and preserved or transected during a neurosurgical intervention.

Material and methods. The study included 139 patients with various SR tumors. In 82 patients, a preoperatively compressed PS was preserved (41 patients with hormonal inactive adenoma (HIA) and 41 patients with suprasellar meningioma); in 57 patients, the PS was transected during surgery (46 patients with pituitary stalk craniopharyngioma and 11 patients with hormonally inactive endosuprasellar pituitary adenoma). The hormonal status (PRL, TSH, LH, FSH, fT4, cortisol, testosterone, or estradiol) was examined in all patients before and after surgery.

Results. Hyperprolactinemia was preoperatively detected in 37% of patients with tumors compressing the PS. Elimination of PS compression (tumor resection) led to normalization of the PRL level in most patients and was not accompanied by aggravation of hypopituitarism symptoms. Transection of the PS caused panhypopituitarism in 100% of patients and diabetes insipidus in 93% of cases. After transection of the PS, hyperprolactinemia did not develop in 59% of patients with craniopharyngiomas (CPs) and 82% of patients with HIA.

Conclusions. Given the difference in symptoms associated with compression and surgical transection of the PS, we believe that these two concepts should be clearly distinguished. The PS compression syndrome includes primarily hyperprolactinemia (37% of cases); elimination of PS compression leads to normalization of the PRL level in most patients and is not accompanied by aggravation of hypopituitarism symptoms. The PS transection syndrome in patients with CP and HIA led to the development of panhypopituitarism in all patients and permanent diabetes insipidus in most of them. The causes of the absence of hyperprolactinemia in many patients with PS transection require further research. The surgeon planning intraoperative PS transection to increase the radicality of surgery should be well informed about the consequences of this procedure for the patient’s endocrine status.

Keywords: pituitary stalk, pituitary stalk compression, pituitary stalk transection, diabetes insipidus, prolactin.

Abbreviations:
PA — pituitary adenoma
ADH — antidiuretic hormone
ACTH — adrenocorticotropic hormone
HIA — hormone-inactive adenoma
CP — craniopharyngioma
LH — luteinizing hormone
DI — diabetes insipidus
PRL — prolactin
Fr.T4 — free thyroxine
PS — pituitary stalk
TSH — thyroid stimulating hormone
FSH — follicle-stimulating hormone
CSR — chiasmatic-sellar region
PSIS — pituitary stalk interruption syndrome (congenital absence of pituitary stalk)

So-called intersected PS syndrome can occur in various cases: compression with suprasellar tumors (PA, meningioma, CP, etc.), intraoperative iatrogenic intersection, traumatic rupture, PSIS.

Despite similar symptoms (hyperprolactinemia, DI, hypopituitarism) treatment and prognosis are significantly different depending on the pathogenesis.

Moreover, attitude of many neurosurgeons to PS is often incorrect due to unclear understanding of its function.

We have compared endocrine disorders in patients with PS compression by tumor and/or its intraoperative intersection.
The aim of the study was an analysis of pre- and postoperative endocrine disorders in patients with suprasellar CSR tumors followed by PS lesion.

Material and methods

Retrospective study included 139 patients with CSR tumors who have undergone surgery at the Institute of Neurosurgery from 2000 till 2016.

Patients were divided into 4 groups depending on tumor histology, its localization, pituitary gland state, and also whether PS was intraoperatively intersected (Fig. 1):

— group 1: 46 patients with CP of stalk (surgery was carried out via transcranial approach). In these cases, initial place of tumor growth was PS per se that required its intersection. Pituitary gland was intact prior to and after surgery;

— group 2: 11 patients with hormone-inactive endonasal transsphenoidal approach). Tumor’s capsule was not excised, pituitary gland was anatomically altered before and after surgery;

— group 3: 41 patients with hormone-inactive endonasal transsphenoidal approach). Tumor’s capsule was not excised, pituitary gland was anatomically altered before and after surgery;

— group 4: 41 patients with suprasellar meningioma followed by PS compression, stalk was intraoperatively preserved. Pituitary gland remained anatomically intact before and after transcranial procedure in these patients.

PRL, TS, LH, FSH, Fr.T4, cortisol, testosterone or estradiol have been analyzed prior to surgery and after transcranial procedure in these patients.

Results

So, there were four groups of patients with different state of PS and pituitary gland before and after surgery. Outcomes are presented in the Table.

CP removal followed by PS intersection was accompanied by panhypopituitarism in all patients of the 1st group.

DI was noted in 43 patients (11 of them had DI prior to surgery). Herewith, DI was not observed in 3 patients from this group despite PS intersection.

All patients of the 1st group needed for postoperative hormonal replacement therapy (glucocorticoid, thyroid, sex hormones, desmopressin).

Postoperative hyperprolactinemia occurred in 19 (41%) patients. At the same time, 5 out of 19 patients with increased PRL level prior to surgery had its postoperative normalization and 5 patients with normal preoperative PRL level had hyperprolactinemia after surgery. Maximum postoperative PRL level was 3,600 IU/l. 2 patients had hypoprolactinemia (35 and 50 IU/l).

The same outcomes were observed in the 2nd group (transcranial removal of hormone-inactive PA followed by PS intersection).

All 11 patients had hypopituitary disorders de novo or their aggravation. DI developed in 10 out of 11 patients. All patients in this group needed for postoperative hormone replacement therapy.

Moderate preoperative hyperprolactinemia was observed in 4 cases. PA excision followed by PS intersection of SG was associated with increased level of PRL only in 2 patients. Hypoprolactinemia occurred in 1 patient (33 IU/L).

In group 3 (transnasal PS-sparing PA excision) some patients with preoperative hypopituitary symptoms had their regression after surgery: sexual function recovery was observed in 5 (15%) out of 33 patients, hypothyroidism relief — in 3 (21%) out of 14 cases, and hypocorticism regression — in 2 (18%) out of 11 patients.

In this group incidence of hypopituitary disorders in patients without previous ones was relatively small: hypogonadism developed in 1 (12.5%) case, hypocorticism — in 1 (3%), hypothyroidism — in 1 (4%) patients. There were no cases of DI. Moderate preoperative hyperprolactinemia was detected in 16 (39%) cases; tumor excision was followed by decrease of blood PRL in majority of cases.

In 13 (32%) patients with CSR meningiomas (group 4) preoperative hyperprolactinemia was detected; maximum PRL level was 4050 IU/l. Moderate postoperative hyperprolactinemia occurred in 2 (15%) out of 13 patients with increased preoperative level of PRL.

Surgery for suprasellar meningiomas without PS intersection in our sample was practically not accompanied by occurrence/aggravation of hypopituitary disturbances. Hypogonadism was observed in 1 case, DI remained in 1 (2%) patient, DI de novo was absent.

Discussion

Pituitary stalk is anatomical part consisting of portal vessels and hypothalamic nuclei axons which terminate in posterior pituitary lobe (Fig. 2).

Current ideas about anatomy and pathophysiology of hypothalamic-pituitary system were comprehensively described by I.I. Dedov, I.G. Akmanyev, A.A. Voitkevich, V.N. Babichev [1—4] and some other domestic and foreign authors.

It is known that pituitary gland supply is provided by small branches of internal carotid artery — superior and inferior pituitary arteries [5]. Superior pituitary arteries enter median hypothalamic eminence and form capillary network (Figs. 2 and 3). These capillaries have a contact with axons of neurosecretory hypothalamic cells and...
then gather in portal veins descending to adenohypophysis through PS. In pituitary gland they are again divided into capillary network. Thus, blood is enriched with releasing hormones in hypothalamus and then passes into adenohypophysis. Blood outflow with pituitary hormones saturated occurs through venous system to venous sinuses of dura mater. Portal supply to pituitary gland with descending blood flow from hypothalamus is a morphofunctional component of neurohumoral control of tropic pituitary functions. Pituitary hormones secretion depends on interaction of hypothalamus, portal vessels and secreting cells of adenohypophysis.

Inferior pituitary arteries participate in neurohypophysis blood supply, contact with neurosecretory axons of large-cell hypothalamic nuclei and are located below sellar diaphragm (Fig. 3).

PRL secretion is under inhibitory effect of dopamine produced by hypothalamus. All other pituitary hormones are under stimulating effect of hypothalamic releasing hormones.

It is believed that PS rupture or mechanical compression of portal vessels disrupts transport of dopamine and releasing hormones. The last is followed by reduced hypothalamic control over pituitary hormones secretion and leads to hyperprolactinemia and impaired secretion of all other pituitary hormones.

Besides vessels PS consists of axons of supraoptic and paraventricular neurons of hypothalamus which are responsible for antidiuretic hormone (ADH) secretion. Complexes of ADH and neurophysin protein are transported along these axons to neurohypophysis which is reservoir for ADH. Therefore, ADH release into blood flow is observed (Fig. 2). Damage of these axons is associated with DI [6].

Patients with congenital pituitary stalk interruption syndrome (PSIS) are described in the world literature [7]. There are no PS and posterior pituitary lobe on MRI scans in these cases. Similar phenomenon is interpreted by scientists as neurohypophysis ectopy and PS agenesia due to embryogenesis disorders or rupture within birth trauma. Rare mutations of HESX1, LH4, OTX3 and SOX3 genes may be also the cause of PSIS [8, 9]. Clinical picture is characterized by pituitary dwarfism. Large-scale trial of 55 children with PSIS syndrome revealed somatotropic hormone deficiency in all patients, hypogonadotropic hypogonadism in 95.8%, ACTH deficiency in 81.8% and secondary hypothyroidism in 76.3% of patients. Hyperprolactinemia was noted only in 36.4% of cases [10].

Some researches [11—15] reported impaired secretion of pituitary hormones due to PS compression by different CSR tumors including pituitary adenoma, meningioma, CP, germinoma, glioma, inflammatory processes (tuberculosis, sarcoidosis), metastases, carotid artery aneurysms. Patients with PS and portal vessels compression have moderate hyperprolactinemia and impaired release of pituitary hormones. PRL level in such cases usually does not exceed 2,000 IU/l [16—18].

B. Arafah et al. [19] reported increased intrasellar pressure and consequently impaired blood flow through portal vessels as important mechanism of hyperprolactinemia and hypopituitarism. Intrasellar pressure is near 28.8±13.5 mm Hg in patients with pituitary adenoma (normal intracranial pressure 10—15 mm Hg); herewith
Patients' characteristics and endocrine disorders before and after surgery

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
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<tr>
<td>Pituitary compression</td>
<td>Stalk CP followed by PS intersection</td>
<td>Pituitary adenoma with PS intersection</td>
<td>Pituitary adenoma without PS intersection</td>
<td>Suprasellar meningioma without PS intersection</td>
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<tr>
<td>PS compression</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>–</td>
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<tr>
<td>Number of patients</td>
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<td>18—57 (45)</td>
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<td>185—1085 (500)</td>
<td>140—1980 (550)</td>
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<tr>
<td>Hypothyroidism, n (%)</td>
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<td>14 (34)</td>
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<td>10 (91)</td>
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</table>

Footnote. * — transient postoperative DI followed by regression within 6 months was not taken into account in analysis. ** — in groups 2 and 3 preservation of pituitary gland (compressed? atrophied?) is not exactly known. Moreover, it could be additionally damaged during surgery.

higher PRL level is associated with higher intrasellar pressure. Pituitary function recovery after adenomectomy may be caused by not only pituitary compression elimination but also normalization of intrasellar pressure and restoration of portal blood flow.

Persistent postoperative pituitary dysfunction may be associated with ischemic necrosis followed by circulatory disturbances in portal system [19, 20].

In our sample preoperative hyperprolactinemia was observed in 52 (37%) patients. In most cases PRL level did not exceed 2,000 ml/l and only in 2 cases (CP and meningioma) reached 3,000 and 4,050 IU/l, respectively.

23% of patients with CP followed by partial PS destruction (group 1) had DI due to interrupted ADH transport or death of hypothalamic ADH-secreting cells.

PS compression in patients with pituitary adenomas and suprasellar meningiomas (groups 2, 3, 4) did not lead to DI. PS-sparring removal of neoplasm (groups 3 and 4) obviously led to restoration of dopamine and hypothalamic releasing hormones transport. This is evidenced by normal PRL level in most cases and regress of hypopituitarism in some patients (Table).

Similar data were presented by H. Zaidi et al. [21] in analysis of pituitary function in 276 patients undergoing transphenoidal surgery. Normal PRL level was noted in 72 (77.8%) patients with preoperative hyperprolactinemia.

P. Nomikos et al. [22] reported improved pituitary function in 50% of patients with HIA and hypopituitarism prior to transsphenoidal surgery. Moreover, it was proved that elevated preoperative PRL is a predictor of postoperative restoration of pituitary function. Partial or complete regression of pituitary disorders was noted in 80% of patients with PRL over 500 IU/l, in 52.3% with PRL 100 to 500 IU/l and only in 30% with PRL less than 100 IU/l.

There are small number of reports in the world literature for pituitary stalk interruption syndrome; experimental works are also limited.

There is severe atrophy of adrenal glands, gonads, thyroid gland, DI in animals with pituitary stalk interruption. This syndrome is followed by impaired somatic growth in young specimens [23]. L. Vaughan et al. [24] analyzed hormone secretion in 20 monkeys with experimental PS intersection. It was accompanied by increased PRL level in most cases throughout follow-up (3 years).

J. Hume Adams [26] reported advanced necrosis of anterior lobe of pituitary gland after PS intersection in animals due to injury of portal vessels. However, glandular pituitary tissue was partially preserved due to blood
Fig. 2. Scheme of the structure and function of “hypothalamus-pituitary gland-peripheral endocrine glands” system (explanations in the text).
supply via inferior pituitary arteries. The same author in 1966 reported 21 patients who underwent transcranial intersection of PS (article in the journal *J Neurol Neurosurg Psychiat*). There were 20 cases of breast or prostate gland cancer and 1 case of diabetic retinopathy. In 50s and 60s of the 20th century hypophysectomy and/or PS intersection were used for advanced breast and prostate cancer, as well as in patients with progressive diabetic retinopathy. It was believed that PS intersection was followed by regression of pain syndrome and inhibited tumor growth. All those patients died within 30 hours — 11 months after surgery. Morphological survey revealed infarctions in adenohypophysis (large as a rule) but complete necrosis of adenohypophysis has been never noted. Posterior pituitary lobe remained intact but decreased in dimensions [26].

J. Honegger [27] analyzed endocrine disorders after CP removal; it was shown that PS intersection was associated with panhypopituitarism and DI in all cases. Those after partial intersection of PS had lower risk hypopituitarism and DI. However, PRL level was not analyzed in this work.

In our study PS intersection in preserved or compressed pituitary gland (CP in group 1 or HIA in group 2) led to panhypopituitarism in all patients and DI in most cases. At the same time, there was no DI in 4 (7%) patients from these groups. It is possibly caused by normal ADH secretion and its release into systemic circulation bypassing neurohypophysis. Ectopic neurohypophysis within proximally enlarged PS cannot be also excluded. This phenomenon is described in patients with PS intersected close to sellar diaphragm. DI regression is unlikely if PS intersection occurs near hypothalamus [28, 29].

PS intersection in our patients did not cause expected apparent hyperprolactinemia. In pituitary adenoma it may be explained by intraoperative damage of residual adenohypophysis, but occurrence of this phenomenon in CP with preserved pituitary gland is unclear. Pituitary ischemia and necrosis may be assumed. However, it would be more likely to expect hypoprolactinemia due to pituitary cells death including lactotrophic cells in this case that was not noted in our study. Hypoprolactinemia was detected only in 3 cases. It cannot be ruled out that dopamine transport to adenohypophysis occur not only through PS vessels or partial revascularization of intersected vessels is possible.

**Conclusion**

As a result of our research, it is worthwhile to distinguish two concepts: "PS compression syndrome" and "surgically intersected PS syndrome".

*PS compression syndrome* implies pressure by neoplasm and includes hyperprolactinemia as a rule (37%); incidence of hypopituitarism and DI is low in preserved pituitary gland. Hyperprolactinemia is usually asymptomatic but may be followed by hyperprolactinemic hypogonadism in some cases. Therapy with cabergoline leads to regression of hyperprolactinemia and restores sexual function. Tumor excision eliminates PS compression and normalizes PRL level. The last is accompanied by physiologic dopamine transport. Compression of PS

![Hypophysis blood supply and vascular injury in PS intersection](image)
and pituitary gland (in pituitary adenoma with suprasellar growth) is associated with hypopituitarism besides hyperprolactinemia. Hyperprolactinemia is also regressed after adenoma removal. Surgical elimination of PS and pituitary gland compression repairs pituitary function in 15—21% of cases. Other patients have partial or total hypopituitarism due to possible atrophy of hormone-secreting pituitary cells.

Surgically intersected PS syndrome is manifested by panhypopituitarism in 100% of cases, DI — in 93%, hyperprolactinemia — in 37% of cases. Thus, the role of PS in transfer of hypothalamic hormones through vessels and axons of secretory nuclei from hypothalamus to adeno- and neurohypophysis is confirmed. At the same time, expected increase of PRL level after PS intersection was not observed. On the contrary, incidence of hyperprolactinemia decreased in pituitary adenoma and was the same in CP. So, comprehensive analysis of hyperprolactinemia in patients with CSR tumors is required.

Following conclusion is the most relevant for neurosurgeons: PS intersection is followed by appearance or progression of panhypopituitarism in all patients and DI in most patients. PS should be preserved in patients with pituitary adenoma if it is possible.

In patients with CP this question is individually solved depending on intraoperative features, age and consideration that risk of recurrence will be increased in this case.

Authors declare no conflict of interest.

REFERENCES

Authors’ work is devoted to analysis of pre- and postoperative endocrine disorders in patients with CSR tumors followed by compressed, preserved or forcibly intersected pituitary stalk during neurosurgical procedure. Neuroendocrine secretion depending on tumor growth features and surgical effect on PS, adeno- and neurohypophysis have been assessed. The role of PS in transfer of hypothalamic hormones through vessels and axons of secretory nuclei from hypothalamus to adeno- and neurohypophysis was confirmed. Moreover, the authors have analyzed hormonal secretion in different patients depending on grade of injury of PS, adeno- and neurohypophysis. The research is interesting for neuroendocrinologists, neurosurgeons and fully corresponds to the journal’s profile.

The authors have evaluated hormonal secretion in 57 patients with PS intersection during surgery and compared these results with group of PS compression. The results determine the significance of this work.

Patients who underwent surgery for CSR tumors were divided into 4 groups depending on effect of tumor and subsequent surgery on PS, adeno- and neurohypophysis. Data are presented as quantitative and percentage dynamics of secretory function. Conclusions are based on these findings.

There are 29 references including 5 domestic and 24 foreign. Seven of them are not more than 5 years old that emphasizes work’s relevance.

Statistical analysis is limited in some ways for reliable conclusions. However, it does not detract relevance and quality of the work. The work will be interesting for a wide range of physicians, in particular neurosurgeons and endocrinologists.

A.Yu. Grigoriyev (Moscow, Russia)
Efficiency of Intraoperative Monitoring of Motor Evoked Potentials in Predicting Early Postoperative Neurological Status in Patients With Cervical Spinal Cord Tumors

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Aim. The study aim was to evaluate the effectiveness of intraoperative monitoring of motor evoked potentials (MEPs) for predicting changes in the neurological status of patients with cervical spinal cord tumors in the early postoperative period.

Material and methods. The study included 74 patients with intradural cervical spinal cord tumors who were operated on using motor evoked potential monitoring in the period from 2013 to 2016. There were 29 (39%) males and 46 (61%) females. Group 1 included 26 (35%) patients with intramedullary tumors; group 2 included 48 (65%) patients with intradural extramedullary tumors. The neurological status was assessed by using a six-grade muscle power MRC scale; a modified McCormick scale was used to evaluate the functional status. Transcranial electrical stimulation of the precentral gyri was performed. Recording electrodes were located in the peripheral target muscles of the upper and lower limbs. Total intravenous anesthesia with propofol and fentanyl was used.

Results. In Group 1, MEPs decreased in 19 (73%) of 26 patients; MEPs remained unchanged in 7 (27%) patients. Among the patients with decreased MEPs, 14 (74%) patients had postoperative deterioration of the neurological status; 6 (32%) patients had a preoperative severe neurological deficit; 4 (21%) patients had no changes in the neurological status. The sensitivity and specificity of MEPs from the upper limb muscles were higher than those from the lower limb muscles. In Group 2, improvement of the neurological status occurred in all 48 patients. There was no case of a true positive decrease in the MEP amplitude.

Conclusions. 1. Registration of MEPs is a highly sensitive and highly specific method for diagnosing corticospinal tract dysfunction in patients with intramedullary tumors of the cervical spinal cord. The sensitivity and specificity of MEPs recorded from the upper limbs are higher than those from the lower limb muscles.
2. The sensitivity of MEPs in patients with extramedullary intradural tumors was 0%, the diagnostic effectiveness of MEPs amounted to 86% from the upper limb muscles and 93% from the lower limb muscles.
3. When the MEP amplitude in patients with extra- and intramedullary tumors of the cervical spinal cord decreases, a change in the surgeon’s approach may reduce or completely eliminate surgically-induced damage to the spinal cord.

Keywords: cervical spinal cord, motor evoked potentials, intradural extramedullary tumors, intramedullary tumors.

Intraduillary tumors are rare and account for about 2—8.5% of all tumors of central nervous system (CNS) and 15% of all primary intradural spinal cord tumors [1—4]. Extramedullary tumors are observed in 10—12% among all CNS tumors and outnumber intramedullary neoplasms as 4:1 [4—7].

Surgery is the main treatment of spinal cord tumors. Intraduillary tumors are the least favorable for their surgical excision although they are benign with slow growth as a rule [8]. Treatment of malignancies is usually limited by biopsy and radiotherapy [1, 9].

There are several methods of intraoperative neurophysiological monitoring of spinal cord functions: somato-sensory evoked potentials (SSEP), motor evoked potentials (MEP) — muscle response registration (actually MEP) and responses from spinal cord surface (D-wave). Changes of SSEP is not currently criterion determining the need for cessation of surgical excision of intramedullary tumors [10]. MEP method allows to assess functional state of corticospinal tract and to observe the first signs of surgical injury of spinal cord. The last makes it possible to carry out appropriate measures to prevent or reduce postoperative neurological disorders [10, 11].

The aim of the work was to evaluate an effectiveness of intraoperative monitoring (IOM) of MEP for predicting early postoperative neurological status in patients with cervical spinal cord tumors.

Material and methods

There were 74 patients including 28 (38%) men and 46 (62%) women aged 49±12 years who underwent MEP-controlled surgery at the Federal Center for Neurosurgery (Novosibirsk) for intradural tumors and other neoplasms of cervical spinal cord for the period from 2013 till 2016. Histological diagnosis was established in view of criteria of WHO classification (2007) of CNS tumors [12]. Schwannoma was observed in 24 (33%) cases, meningioma — in 18 (24%), ependymoma — in 15 (20%), neurofibroma — in 6 (8%), astrocytoma — in 1 (1%), hemangioblastoma — in 4 (6%), cavernous angioma — in 4 (6%), mature teratoma — in 1 (1%), dermoid cyst — in 1 (1%).

Neurological status was evaluated by using of 6-point scale of muscle strength (MRC-scale), patient’s functional state — with McCormick modified scale [13—15].
All patients underwent contrast-enhanced magnetic resonance imaging (MRI) prior to surgery to assess tumor’s dimensions and location and within the 1st postoperative day to analyze surgical effect.

Surgical approach, bone resection type, patient’s position on the operating table were planned taking into account MRI data about solid tumor. All patients were operated under rigid head fixation in Mayfield bracket. Removal of intradural tumor was accompanied by MEP monitoring.

We performed transcranial electrical stimulation of precentral gyrus in order to obtain MEP, recording electrodes were placed in peripheral target muscles. Triceps and biceps shoulder muscles, tenar and hypotenar muscles, quadriceps femoris muscle, anterior tibial muscle and gastrocnemius muscle were selected for this purpose. Bilateral monitoring was applied in all patients. Stimulation parameters were various: strength 400—800 V, length of stimulus 0.5—0.75 ms, number of stimuli 4 to 9, interval between stimulation 2 ms. Stimulating electrodes were placed in C3/C’1 and C4/C’2 by 10—20 international system [16].

Baseline transcranial MEP were recorded after muscle relaxants’ end effect before skin incision, prior to and after dura mater dissection. Later, intraoperative stimulation was continued regularly as often as it was possible in surgical situation. Responses were recorded every 2—10 minutes as a rule. Any significant decrease (> 50%) of MEP amplitude was recorded, these data were reported to surgeon.

Nicolet Viking and Cadwell Cascade Elite systems were used for monitoring. General intravenous anesthesia with propofol and fentanyl was administered in all cases.

Sensitivity, specificity, prognostic value of positive and negative results and diagnostic effectiveness were analyzed to assess MEP efficacy. Above-mentioned variables were evaluated separately for arms and legs muscles. Sensitivity included proportion of truly positive results among patients with decreased MEP, specificity — proportion of truly negative results among patients with unchanged postoperative neurological status. Prognostic value of positive result was assessed as probability of neurologic disorders in decreased MEP, prognostic significance of negative result — probability of absent neurologic changes in unchanged amplitude of MEP. The Number of true results obtained by using of MEP determined diagnostic efficiency. True positive (TP) result was defined as postoperative deterioration of neurological status with intraoperative decrease of motor evoked response (MER), true negative (TN) — unchanged MER followed by normal postoperative neurological status. False positive (FP) result implied normal postoperative neurological status with decreased intraoperative MER, false negative (FN) — postoperative neurological disorders with normal intraoperative amplitude of MER. Following formulas were used to calculate these values:

\[ \text{sensitivity} = \frac{\text{TP}}{\text{TP} + \text{FN}} \times 100; \ \text{specificity} = \frac{\text{TN}}{\text{TN} + \text{FP}} \times 100; \ \text{positive predictive value (PPV)} = \frac{\text{TP}}{\text{TP} + \text{FP}} \times 100; \ \text{negative predictive value (NPV)} = \frac{\text{TN}}{\text{TN} + \text{FN}} \times 100; \ \text{diagnostic effectiveness} = \frac{\left( \text{TP} + \text{TN} \right)}{\left( \text{TP} + \text{TN} + \text{FP} + \text{FN} \right)} \times 100 \ [16].

All patients were divided into two groups: group 1 with intramedullary tumors: 26 (35%) patients aged 45±11 years, 12 (46%) men and 14 (54%) women; group 2 with extramedullary tumors: 48 (65%) patients aged 50±12 years, 15 (31%) men and 33 (69%) women.

**Results**

In group 1 tumor’s mean transverse size was 12±4 mm, tumor spread along 1—2 vertebrae in 10 patients, in 7 cases — 3—4 vertebrae and in 5 patients — along 6—7 vertebrae. Ependymoma was observed in 15 (58%) cases, hemangioblastoma — 4 (15%), cavernous angioma — 4 (15%), astrocytoma — 1 (4%), mature teratoma — 1 (4%), dermoid cyst — 1 (4%). Mean postoperative MRC-score was 4.5±0.2, McCormick modified scale value — 2.5±0.9.

Patient’s position on operating table depended on tumor’s location: sitting position in 19 (73%) patients, lateral decubitus position in 5 (19%) ones, prone position in 2 (8%) patients. Mean time of surgery was 240±53 min; mean blood loss — 115±57 mL.

Mean postoperative MRC-score was 3.6±0.1. Deteriorated neurological status by this scale was noted in 15 (58%) patients who had tumor’s transverse size 4—23 mm. Further improvement of neurologic state was observed in 3 (8%) patients with tumor’s transverse dimension 9—18 mm. Unchanged neurological status compared to that prior to surgery was in 6 (27%) patients (tumor’s transverse size 5—12 mm). Mean postoperative McCormick modified score was 2.9±1. Deteriorated, unchanged and improved functional outcome was noted in 12 (46%), 11 (42%) and 3 (12%) patients, respectively.

Decrease of MEP amplitude was revealed in 19 (73%) out of 26 patients, unchanged MEPs — in 7 (27%) ones. 14 (54%) patients with decreased MEP had also deterioration of postoperative neurological status, 6 (23%) of them had severe preoperative neurologic disturbances, and 4 (15%) patients had not any neurological disorders. Ependymoma was histologically predominant in these patients (14 cases). Hemangioblastoma was detected in 3 patients, cavernous angioma in 1 and diffuse astrocytoma Grade II in 1 patient.

Neurosurgeon made intermission as soon as MEPs were decreased, changed tumor’s dissection side, applied irrigation of dissection area with warm saline, reduced tumor’s volume or administered methylprednisolone. As a result, deterioration of neurological status within only 1—2 scores was observed.

Informational values of MEP for the 1st group are presented in Table 1. Sensitivity and specificity of MEP
registered from the arms were higher compared with leg muscles.

According to contrast-enhanced MRI of cervical spine within the 1st postoperative day there was no abnormal contrast accumulation. So, tumors were radically removed.

Case report

**Patient Sh.**, 35 years old, was hospitalized at the neurosurgery department №2 with the diagnosis of "C2 intramedullary tumor", complaints of weakness and numbness in right hand.

Neurological status: paresis of flexor and extensor of the right hand (3 scores), flexors and extensors of the right forearm (4 scores).

McCormick scale — 2 scores. Contrast-enhanced MRI of cervical spine revealed intramedullary postero-lateral tumor at the level of C2-vertebra (Fig. 1).

Laminectomy of C2-vertebra, intramedullary tumor removal under neurophysiological control were carried out. There was sitting position of patient on the operating table with head fixed in Mayfield bracket. Before and after dura mater dissection unchanged MER was obtained from all target muscles.

Severe deterioration of MER amplitude from the right hand’s muscles (by 90%) and disappearance of MER from the right leg’s muscles were observed in 7 minutes after tumor dissection onset (19:10) (Fig. 2). These data could indicate impaired right-sided motor conduction through anterior and lateral spinal cord columns due to surgical injury of corticospinal tract. At 19:15 irrigation of the wound with warm saline, methylprednisolone (1000 mg) administration and change of tumor dissection side were applied.

During hemostasis after tumor removal (19:30) recovery of MER amplitude from the right leg’s muscles was observed, at 19:39 — restoration of MER amplitude from the right hand’s muscles. Preserved MER was obtained from all target muscles at the end of hemostasis (Fig. 3).

Thus, there was a marked transient decrease of MER from the right hand and leg during tumor removal that can indicate surgical injury of spinal cord.

In early postoperative period aggravation of right hand paresis followed by decreased muscle strength up to 2 scores was noted, also there was mild paresis of left hand associated with impaired muscle strength up to 4 scores (initially 5 scores), McCormick score — 3.

Contrast-enhanced MRI of cervical spine within the 1st postoperative day confirmed radical tumor excision (Fig. 4).

Positive in-hospital dynamics of neurological status was noted: muscle strength recovery in left hand up to 5 scores, in right hand — up to 3 scores, McCormick score — 2. Patient was discharged in 8 days after surgery. Histological conclusion: hemangioblastoma, Grade I.

In group 2 mean transverse dimension of tumors was 17±6 mm, tumor spread along 1—2 vertebrae was in 31 patients, 3 vertebrae — in 9 ones and 6—7 vertebrae — in 7 cases. Schwannoma, meningioma and neurofibroma were diagnosed in 24 (50%), 18 (38%) and 6 (12%) cases, respectively. Mean preoperative MRC-score was 4.6±0.1, McCormick score — 2.15±0.9. Patient’s position on the operating table depended on tumor’s lateralization: 37 (77%) patients were operated in decubitus position, 5 (11%) — in sitting position and 6 (12%) in prone position. Mean time of surgery and blood loss were 296±113 min and 417±350 mL, respectively.

There was significantly improved postoperative MRC-score in all 48 patients, mean muscle strength score — 4.8±0.1. Modified McCormick score was 2±0.8 after tumor removal. Unchanged functional status was observed in 38 (79%) patients, improved — in 8 (17%), aggravated — in 2 (4%) patients due to decreased sensitivity of limbs. Intraoperative impaired MEP amplitude from hands’ muscles was recorded in only 6 (13%) patients, from legs — in 3 (6%) ones. In other cases, MEP amplitude was the same. Among all patients with decreased MEP schwannoma Grade I was in 5 cases (tumor’s transverse size 5, 16, 20, 21 mm), meningioma Grade I — in 3 (transverse dimensions 8, 12 mm), neurofibroma — in 1 (transverse size 10 mm).

During intradural extramedullary tumor excision surgeon’s actions were aimed at reducing spinal cord traction via enlarged bone approach, use of ultrasonic destructor for debulking, methylprednisolone administration, irrigation with warm saline.

There were no cases of true positive decrease of MEP in group 2. In 9 (19%) patients with decreased MEP amplitude normal postoperative muscle strength was observed. The last was considered false positive result, so sensitivity of MEP monitoring is 0%. MEP monitoring variables are presented in Table 2.

Contrast-enhanced MRI in the first postoperative day confirmed radical tumor dissection in this group.

Case report

**Patient T.**, 60 years old, was hospitalized at the neurosurgery department №2 with the diagnosis of C1—C4 intradural extramedullary tumor, type II by K. Sridhar et al. [17].

At admission: complaints of pain in cervical spine, weakness and numbness in hands and legs.

Neurological examination: spastic tetraparesis (3 scores) conductive hypoesthesia from C3 level. Preoperative McCormick score 4. Contrast-enhanced MRI of spine cord: intradural extramedullary tumor at C1—C4 level with right-sided lateralization occupying most of vertebral canal (Fig. 5).

Surgery included C1—C4 laminectomy, intradural tumor dissection under neurophysiological control. Patient’s position is left decubitus with head fixed in May-
Table 1. Diagnostic efficacy of intraoperative MEPs monitoring for intramedullary tumors

<table>
<thead>
<tr>
<th>Method</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>Positive predictive value, %</th>
<th>Negative predictive value, %</th>
<th>Diagnostic efficacy, %</th>
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<td>100</td>
<td>80</td>
<td>92</td>
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<tr>
<td>Foot MEPs</td>
<td>83</td>
<td>14</td>
<td>45</td>
<td>50</td>
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</tbody>
</table>

Fig. 1. Contrast-enhanced MRI-scan of cervical spine in patient Sh., sagittal and axial planes.

There is intramedullary tumor at the level of C2-vertebra (arrows) in posterior regions with right-sided lateralization. Sagittal size — 6.5 mm, frontal — 8 mm.

Fig. 2. Intraoperative MER from target muscles and variables of transcranial electrical stimulation of motor cortex in patient Sh.

Here and in Fig. 3, 6, 7: impaired or disappeared MER is marked with oval. Signatures of channels (superiorly in columns): AP L — left hand: tenar and hypotenar; AP R — right hand: tenar and hypotenar; Brah L — left shoulder: biceps and triceps; Brah R — right shoulder: biceps and triceps, Tib L — left leg: anterior tibial and gastrocnemius muscles; Tib R — right leg: anterior tibial and gastrocnemius muscles. Time of MER registration is indicated on the right from each channel (chronologically). Initial MEPs amplitudes prior to tumor removal are presented under all traces. Arrows indicate the time of MER deterioration.
field bracket. Before and after dura mater dissection unchanged MER was obtained from all target muscles.

At 19:07 severe deterioration of MER amplitude from the right hand’s muscles (by 90%) was recorded (Fig. 6), that could indicate impaired right-sided motor conduction through anterior and lateral spinal cord columns due to surgical injury of corticospinal tract. At 19:08 irrigation of the wound with warm saline, methylprednisolone (1,000 mg) administration and change of tumor dissection side were applied.

At 19:11 recovery of MER amplitude from the right hand’s muscles was recorded. At the end of hemostasis...
normal MER was obtained from all target muscles (Fig. 7).

Contrast-enhanced MRI within the first postoperative day confirmed radical removal of tumor (Fig. 8).

Improvement of neurological state in early postoperative period was observed: tetraparesis up to 4 scores (initially 3 scores), McCormick score 3. Patient was discharged in 7 days after surgery. Histological conclusion: schwannoma, Grade I.

**Discussion**

According to V. Deletis and F. Sala [18], unfavorable outcome after spinal cord surgery is associated with ischemic disorders and prolonged intraoperative traction. MEPs reflect normal motor function, useful for intraoperative assessment of conductive function of spinal cord and to determine possibility of further surgical dissection and excision of tumor. In our trial surgeon changed surgical tactics if aggravation of MEPs occurred: change of tumor dissection side, waiting for MEPs recovery, irrigation of the wound with warm saline, debulking and methylprednisolone administration. F. Sala et al. [18—23] reported recovery of potentials and possible following tumor dissection after temporary discontinuation of manipulations if significant decrease or disappearance of MEPs occurred. Tumor dissection despite aggravation of MEPs may be followed by irreversible neurological disorders. In our study in both groups this approach led to MEPs recovery followed by radical excision of tumor with preserved movements in limbs. The last confirms high diagnostic efficiency of the method in group 1 (MEP of hand — 92%, MEP of leg — 46%) and in group 2 (MEP of hand — 86%, MEP of leg — 93%).

F. Sala et al. [19] reported similar early postoperative functional outcomes after surgery with/without intraoperative monitoring. In early postoperative period impaired functional status was noted in 10 patients with severe neurological disorders prior to surgery (McCormick 3 and 4). However, long-term functional outcome (>3 months) was significantly better in group of intraoperative monitoring. In our sample impaired neurological status in early postoperative period was noted in patients with intramedullary tumors (14 out of 26) and intraoperative decrease of MEPs. Long-term neurologic state was not assessed in these patients. Histologically ependymoma was predominant (9 cases), hemangioblastoma (3), cavernous angioma (1) and astrocytoma (1) were less common. In patients with intradural extramedullary tumors impaired neurological status was not detected in either case.

### Table 2. Diagnostic efficacy of intraoperative MEPs monitoring for extramedullary tumors

<table>
<thead>
<tr>
<th>Method</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
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<th>Negative predictive value, %</th>
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<td>Foot MEPs</td>
<td>0</td>
<td>93</td>
<td>0</td>
<td>100</td>
<td>93</td>
</tr>
</tbody>
</table>

*Fig. 5. Contrast-enhanced MRI-scan of cervical spine in patient T., sagittal and axial planes.*

There is intradural extramedullary tumor occupying almost entire vertebral canal with right-sided lateralization (arrows). Sagittal size — 49 mm, transverse size — 22 mm.
S. Peker et al. [24] reported tumor’s transverse dimension as a predictor of pre- and postoperative neurologic disorders. Length of tumor affects postoperative dysesthesia. There was more severe neurological status in patients with large tumors in pre- and postoperative period. P. Velayutham et al. [25] showed that spinal cord tumor had not effect on postoperative functional status. In our trial deterioration of neurologic state was noted in patients with tumor’s transverse size 4—23 mm that can indicate absent correlation between these variables. However, such data may be associated with small sample size and heterogeneity.

E.A. Burkova [26] concluded that intraoperative MEP monitoring in 41 patients with intramedullary tumors was highly sensitive method to diagnose disturbances of motor activity. Our data also confirm high sensitivity and specificity that justifies MER registration in spinal cord surgery.

P. Velayutham et al. [25] argued that early intraoperative correction of surgical manipulations for decreased MEP prevent severe postoperative deterioration of motor functions of limbs. The authors observed postoperative neurological deficit in muscles with intraoperative impairment of MEP. Complete disappearance of MEP was followed by 3-fold augmentation of the incidence of neurologic disorders. Tumor’s placement (intramedullary, extramedullary) did not influence predictive value of MEP monitoring which had high sensitivity (100%) and specificity (98.1 %) in patients with both intra- and extramedullary tumors.

Fig. 6. Intraoperative MER from target muscles and variables of transcranial electrical stimulation of motor cortex in patient T.

Fig. 7. Postoperative MER from target muscles and variables of transcranial electrical stimulation of motor cortex in patient T.
MEP monitoring during intradural tumors excision is associated with opportunity to correct surgical tactics in accordance with intraoperative situation. Evaluation of early postoperative neurological status is useful to determine rather intraoperative information is objective for surgeon.

**Conclusions**

1. MEP monitoring is highly sensitive and specific method to diagnose corticospinal tract dysfunction in patients with intramedullary tumors of cervical spinal cord. Sensitivity and specificity of MEPs from hands are higher than those from lower extremities.

2. Sensitivity of MEPs in patients with extramedullary intradural tumors is 0%, diagnostic efficiency for hands’ muscles — 86%, legs’ muscles — 93%.

3. Correction of surgical tactics for impaired MEPs in patients with intramedullary and extramedullary tumors of cervical spinal cord makes it possible to reduce or completely exclude surgical injury of spinal cord.

Authors declare no conflict of interest.

**REFERENCES**


The problem of surgical treatment of intramedullary spinal cord tumors is extremely important for current medicine since disease is characterized by aggressive course, often affects young and middle age people and followed by severe disability in most cases. Currently, intraoperative monitoring (IOM) is obligatory in surgery for intramedullary tumors. At the same time there are still no data about efficacy of this approach in national literature as well as clear algorithm of monitoring that makes this publication interesting.

Yu.V. Kushel, J. Klekamp, J. Brotchi have shown that intramedullary tumors should be operated only at specialized clinics where at least 20—30 procedures per year are performed by one surgeon. Fewer number of interventions is followed by advanced morbidity while technical inaccuracies can lead to severe disability. According to J. Klekamp surgeons with experience of more than 70 surgeries for intramedullary tumors made total removal in 95 (88.8%) out of 107 cases. At the same time total removal was achieved in 19 (61.3%) out of 31 cases in less skilled surgeons with experience less than 20 surgeries.

At present time MEPs monitoring is one of routine methods for spinal cord functions control although it is necessary to remember shortcomings of this method. One of them is high variability in MER amplitude from study to study that makes it difficult to determine clear criteria of impaired and complete absence of responses. Moreover, sensitivity of these potentials to spinal cord ischemia is high. As a result, false-positive results will be more common in MEPs monitoring alone. Therefore, qualitative changes should be considered during monitoring rather quantitative disorders. So, MEP with spinal D-wave registration is advisable to assess motor pathways of spinal cord. D-wave (direct wave) reflects direct axonal activation of spinal cord and functional integrity of fast-moving neurons of corticospinal tract. According to Morota (1997), D-wave is one of the best predictors of favorable functional outcome along with preoperative status of patient. At the same time, MEP monitoring significantly improves long-term outcomes and predicts motor disorders at the end of surgery. The last is also noted by the authors.

In our opinion, authors’ statement about ineffectiveness of somatosensory evoked potentials (SSEP) for IOM seems unfounded. There are confirmations that MEP and SSEP should be used together. Thus, S. Hyun and S. Rhim reported higher sensitivity and positive predictive value for simultaneous MEP and SSEP monitoring rather their separate application.

Thus, it is difficult to disagree with authors that neurophysiological IOM prevents early postoperative neurological disorders after surgery for intramedullary tumors of cervical spinal cord. It is especially true for preoperative mild and moderate neurologic deficit.

In our data preserved M-response amplitude up to 50% by the end of surgery is predictor of unchanged muscle strength, M-response 65—70% in preoperative period is predictor of adverse long-term outcome. Combination of monitoring (MEP, SSEP, D-wave) is appropriate. In our opinion, IOM for extramedullary tumors of cervical spinal cord may be only used to ascertain excessive spinal cord compression. Adequate surgical approach and technique should prevent neurologic deficit in surgery for extramedullary neoplasms.

A.O. Gushcha (Moscow, Russia)
Ventral Decompression in Patients With Traumatic and Non-Traumatic Atlanto-Axial Dislocations

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Compression of the caudal medulla oblongata and ventral portions of the spinal cord is the most dangerous complication of atlanto-axial dislocation (AAD).

Objective. The study objective was to improve surgical management of patients with ventral compression of the spinal cord in the setting of AAD of various genesis.

Material and methods. We analyzed treatment outcomes in 250 patients with C1 and C2 injuries and diseases for the period between 2002 and 2016. Persistent ventral compression of the neural structures in the setting of AAD was detected in 34 (13.6%) patients. Anterior or posterior dislocation was in 21 patients, vertical dislocation occurred in 7 patients, and mixed (anterior and vertical) occurred in 6 cases. The causes of AAD included odontoid fractures (21 patients, 61.8%), Jefferson fractures (6 patients, 17.6%), atlas transverse ligament rupture (1 patient, 2.9%), rheumatoid arthritis (4 patients, 11.8%), and nonspecific spondylitis (2 patients, 5.9%).

Results. All dislocations were divided into Halo-tractable and Halo-intractable ones. In 24 cases, ventral decompression was achieved due to Halo reposition. Additional resection of a compressing substrate was performed through the submandibular approach in 4 patients, through the transoral approach in 5 patients, and through the transnasal approach in 1 case. In the postoperative period, complications in the form of pharyngeal edema developed in 1 patient after transoral decompression. In the other cases, there were no postoperative complications. All patients had improvement in their condition in the form of regression of a neurological deficit.

Conclusion. Halo reposition is a technique eliminating, completely or partially, ventral compression in certain traumatic and non-traumatic dislocations. The choice of a surgical corridor should be performed after preliminary Halo correction. If the nasopalatine line runs in the odontoid neck projection, the submandibular approach may be used in the case of a Halo-intractable dislocation, and the endonasal approach may be used in the case of a Halo-tractable dislocation.

Keywords: odontoid fracture, C1 fracture, C2 fracture, C1 transligamentous dislocation, C1—C2 rheumatoid lesion, C1—C2 nonspecific spondylitis, atlanto-axial dislocation, C1—C2 ventral decompression, transoral decompression, transnasal decompression, odontoidectomy, Halo reposition, Kassam line.

Odontoid process, cruciate ligament and secondary ligamentous apparatus (pterygoid ligaments, articular capsule) are the main elements ensuring C1—C2 vertebrae stability [1, 2]. Their injury due to trauma (odontoid fractures, disruption of atlas transverse ligament) or disease (rheumatoid arthritis, spondylitis, tumor) may be followed by C1—C2 instability. Further displacement of atlas is called atlantoaxial dislocation (AAD). There are 5 kinds of dislocation depending on its vector: anterior, posterior, lateral, rotational and axial [3—5]. Combination of these types is possible, for example lateral and rotational or front and axial [6, 7].

Compression of ventral spinal cord and/or caudal medulla oblongata is the most dangerous complication of AAD. Advanced neurological deficit along with high risk of vital disorders require prompt elimination of vertebro-medullary conflict with subsequent reliable spine stabilization.

The purpose of the work is to improve surgical treatment of patients with ventral spinal cord compression due to various AAD.

Material and methods

There were 250 patients including 165 men and 85 women aged 15—92 years (mean 40.2) with injuries and diseases of C1—C2 vertebrae for the period from 2002 to 2016. All patients were operated at the Sklifosovsky Institute for Emergency Care. Odontoid fractures were diagnosed in 108 patients, Jefferson fractures — in 34, traumatic spondylolisthesis — in 61, multiple C1—C2 fractures — in 34 patients. Injury of atlas transverse ligament alone was observed in 1 patient, rheumatoid polyarthritis — in 8, granulomas after previous nonspecific spondylitis — in 2, craniovertebral junction abnormality — in 2 patients.

At admission permanent ventral compression of spinal cord and/or medulla oblongata due to AAD was detected in 34 (13.6%) patients. Dislocation due to transcendental luxation was present in 21 of them (Fig. 1a), C1 vertebral fractures — in 6. In one case old transligamentous luxation of atlas was diagnosed. Twenty patients were hospitalized with acute and subacute trauma, 8 — in intermediate and late period after injury.

Dislocation due to rheumatoid arthritis was verified in 4 patients (Fig. 1b), ventral compression with granu-
loma after previous nonspecific spondylitis and AAD — in 2 cases (Fig. 1c).

Anterior or posterior dislocation was diagnosed in 21 patients, axial in 7, combined (front and axial) in 6 ones.

Pain syndrome and neurological deficit were predominantly noted. There was pain syndrome Downie score 3 in 14 patients, score 2 in 19, and score 1 in 1 patient. Among patients with traumatic injuries neurologic symptoms ASIA grade B was observed in 3 patients, C in 6, D in 4 patients. Despite cerebral compression in MRI data there was no neurological deficit. In 6 patients with non-traumatic ventral compression neurologic disorders consisted of progressive spastic tetraparesis and sensory disturbances from C2-level. So, they were urgently hospitalized to Sklifosovsky Institute for Emergency Care.

Results

Firstly, we have assessed rather dislocation would be eliminated by using of Halo-apparatus. In this regard all dislocations were divided into Halo-corrected and Halo-uncorrectable [8]. After anesthesia administration Halo-system was deployed. Further, attempts of partial or com-
plete reposition of vertebrae dislocated were applied under two-plane X-ray control. One of the methods of anterior or posterior spondylodesis was performed if craniovertebral junction was successfully restored (Halo-corrected dislocation). If complete reposition was not achieved (Halo-uncorrectable dislocation) or compression was caused by tumor then anterior spinal cord decompression was applied via transoral, transnasal or submaxillary approach.

Halo-corrected dislocation without anterior spinal cord decompression was observed in 24 patients with traumatic injuries and in 1 case of rheumatoid arthritis followed by odontoid basilar invagination.

Submandibular approach was used in 4 patients: mobilization of dislocated vertebrae followed by Halo-correction was performed in 3 cases of old odontoid fractures, 1 patient with rheumatoid polyarthritis required ventral decompression.

Transoral access was used in 5 patients: odontoid impression due to rheumatoid polyarthritis (2), ventral compression with granulomas after previous nonspecific spondylitis (2) and chronic odontoid fracture (1).

Fig. 2. Halo-correction for AAD.
a — patient P, 53 years old. Odontoid fracture followed by anterior AAD up to 2 cm is observed on lateral X-ray image of cervical spine (arrows); b — postoperative X-ray images: dislocation is completely eliminated, dorsal combined spondylodesis with cannulated screws by F. Magerl and using a hooked plate; c — patient Ya., 55 years old, rheumatoid polyarthritis. Preoperative sagittal CT-scan, odontoid apex is in large occipital orifice, posterior atlantodental interval (PADI) is less than 14 mm that indicates spinal cord compression; d — postoperative sagittal CT-scans: C2 is completely repaired, ventral compression is eliminated, C1 laminectomy and posterior occipitospondylodesis are carried out for dorsal decompression.
Tranasal repair was used in 1 patient with transligamentous luxation of atlas.

Odontoid resection was intraoperatively complicated by liquorrhea within apical ligament in 2 patients that required dura mater repair and sealing with bioglue. There were no postoperative Halo-associated complications. One patient developed upper respiratory tract edema followed by tracheostomy. One elderly patient died due to decompensation of chronic diseases and multiple organ failure. Regression of neurological deficit followed by complete or partial social and labor adaptation was observed in other patients.

**Discussion**

Decompression and craniovertebral junction repair are preferred for traumatic neural compression of upper cervical spine. This may be achieved by Halo-correction, skeletal traction, manual or instrumental intraoperative repair of vertebrae, etc. As a rule, reposition is possible in acute traumatic dislocations and sometimes in rheumatoid polyarthritis. In case of correctable dislocation, we preferred Halo-correction for the first stage followed by ventral or dorsal spondyloodesis (Fig. 2).

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Fig. 3. Transoral decompression in patient with AAD after nonspecific spondylitis.

a — Preoperative sagittal CT-scan: odontoid sclerosis, contours are unclear, basion-dens interval (BDI) is reduced to 4 mm; b — preoperative T2-weighted MRI-scan: C2 granuloma causes spinal cord compression (arrow); c — postoperative sagittal CT-scan: odontoid process, C1 anterior arch and 1/2 of C2 body are removed, occipitospondyloodesis of craniovertebral junction; d — postoperative T1-weighted MRI-scan: spinal cord without compression.
Halo-correction is usually ineffective in chronic injuries or rheumatoid pannus due to rigid chronic vertebral displacement. Closed correction is also inappropriate in case of ventral compression. In these situations, decompression is achieved by compressing substrate resection via ventral surgical approach.

The main criterion determining decompression technique was placement of C2 vertebra relative to nasopalatine line (Kassam line) [9, 10]. Transnasal odontoidectomy is preferred if axis is located above this line (type A). Both transnasal and transoral approaches may be used for decompression if the line passes through odontoid base plane (type B). If Kassam line is projected onto odontoid apex (type C) then transoral decompression is optimal.

In our study transoral access was used in 5 patients. 2 patients had axial AAD (types B and C) due to nonspecific inflammatory process and granuloma followed by atlantodental joints destruction (Fig. 3). Halo-uncorrectable impression and Kassam line corresponding to odontoid apex (type C) were observed in 1 case of rheumatoid arthritis. In another one there was impression type B but accurate Halo-traction was followed by partial recovery of axial displacement. So, odontoid process was more accessible for transoral resection. This approach
was also used in 1 patient with chronic odontoid fracture and compressing substrate below nasopalatine line.

The main disadvantages of transoral surgery are postoperative edema of upper respiratory tract and velopharyngeal insufficiency due to dissection or trauma of soft palate [9]. In our sample edema followed by tracheostomy occurred in one patient after granuloma resection (Kassam line type B).

Endonasal approach has some advantages compared with transoral access [10, 11]: absence of no soft palate injury, postoperative edema of tongue and pharynx, less incidence of infectious complications due to wound contamination by less aggressive flora of nasal cavity. In our work, endonasal access was used in 1 patient with chronic transligamentous cleavage of atlas. Dislocation was rigid (Halo-uncorrected), and Kassam line corresponded to odontoid neck (type B). Transnasal decompression was applied due to some patient’s features (severe cicatrical deformation of anterior cervical surface and face with impaired mouth opening). The first stage included posterior decompression via C1 laminectomy and large occipital orifice edge resection followed by subsequent occipitoplasty. After that endonasal odontoid resection was carried out. It should be noted that odontoidectomy without C1 anterior laminectomy was performed due to sufficient distance between clivus and atlas arch for endoscope and instruments placement (Fig. 4).

Submandibular access is not widely used for ventral decompression. C2 — vertebra and C1 anterior arch are visualized under acute angle via this approach if endoscopy is additionally used [11]. This procedure was made in 1 patient with rheumatoid arthritis in our work. There was Kassam line type B, but impression was corrected up to type C by using of Halo-system. Long thin neck and highly placed lower jaw allowed to visualize C1—C2 vertebrae via transcervical approach by using of microscope.

Submandibular access may be also used to mobilize bone fragments in chronic transdental atlas dislocations with subsequent Halo-reposition [8]. In our work it was done in 3 patients.

Conclusion

Halo-reposition is followed by complete or partial repair of ventral compression in certain traumatic and non-traumatic dislocations. It is advisable to define surgical approach after preliminary attempt of Halo-reposition. In case of Halo-corrected dislocation and Kassam line within odontoid neck (type B) submandibular access may be used. At the same time, endonasal approach is preferable for Halo-uncorrectable dislocations.

Authors declare no conflict of interest.

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This article is devoted to one of the most important and urgent problems of current neurosurgery and orthopedics — atlantoaxial dislocation followed by spinal cord compression. There is no universal treatment strategy for this pathology despite modern technical achievements. Therefore, the question of preoperative correction to restore normal anatomical relationship between neural and bone structures is extremely relevant.

The authors present a great material consisting of their own experience of AAD treatment. Halo-correction prior to surgery has definitely entered routine surgical practice. There are 34 patients with permanent spinal cord compression in the article. As a result, 24 (70%) out of 34 patients underwent successful Halo-correction with repair of craniovertebral junction and C1—C2 segment. The authors emphasize absent Halo-associated complications.

It was noted that complete correction was achieved only in patients with traumatic AAD. Unfortunately, authors do not indicate terms of injury in Halo-corrected group, grade of correction and type of fixation, time of spondylodesis in long-term period. Was the injury isolated? Of course, all these facts would enrich this study.

Halo-correction can improve treatment of AAD. It would be interesting in the future to compare intraoperative Tongtraction of parietal knolls and Halo-correction in order to confirm the advantage of the last technique.

Absence of general surgical complications in all cases is admirable. At the same time, meta-analysis of Elliott et al. (69 articles for 2002—2011, 31,46 patients, outcomes of C1—C2 stabilization by Harms/Magerl) reported vertebral artery injury in 6%, screws displacement in 9.5%.

Considering volume of material and novel view on the problem the article is certainly complete research and can be extremely valuable for readers of our magazine.

N.A. Konovalov, V.A. Korolishin (Moscow, Russia)
Rheumatoid Atlantoaxial Dislocations

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Pathological processes in the craniovertebral region (CVR) are usually accompanied by dislocation complications leading to gross neurological disorders. One of the diseases that affect the CVR and lead to atlantoaxial dislocation (AAD) is rheumatoid arthritis. Errors in the diagnosis of rheumatoid disease and in the choice of a treatment approach may cause adverse outcomes.

**Objective** — to define the approach for surgical treatment of AAD associated with rheumatoid disease of the CVR, with allowance for the rigidity of deformity.

**Material and methods.** Five patients with rheumatoid AAD, 4 females and 1 male, aged 54 to 73 years underwent surgery. All dislocations were anterior ones. Three patients had mobile pannus-associated dislocation. In 2 cases, AAD was rigid and combined with odontoid invagination into the foramen magnum (FM).

**Results.** In all mobile AAD cases, decompression of the brainstem and restoration of the normal anatomical relationships in the CVR were achieved by dislocation correction and atlantoaxial fusion performed from the posterior approach, avoiding transoral interventions. In this case, spontaneous resorption of the pannus occurred within several months after surgery. In the postoperative period, all patients achieved significant regression of pain and neurological disorders. Complications in the form of wound infection developed in 1 case.

**Conclusion.** A decision algorithm for choosing a surgical treatment option was based on the degree of deformity stability. Mobile AADs serve as an indication for indirect decompression using instrumental correction of dislocation and atlantoaxial fixation from the posterior approach. In the case of fixed AAD, posterior fixation is complemented by anterior decompression via the transoral approach.

**Keywords:** craniovertebral region, atlanto-axial dislocation, transoral approach, atlanto-axial fusion, occipitocervical fusion.

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Atlantoaxial dislocation (AAD) is pathomorphological substrate of various craniovertebral injuries and diseases rather independent pathology. Rheumatoid arthritis is often cause of AAD besides traumatic, inflammatory, tumoral reasons [1—3].

Rheumatoid arthritis is chronic autoimmune systemic connective tissue disease affecting small joints as a rule. Its incidence is 0.8—2% [4]. Rheumatoid arthritis is predominantly observed among women (3 times more often than in men) [1, 4]. Manifestation occurs on the 4th—6th decade of life [5, 6]. According to different authors [5—7], 40—80% of patients with rheumatoid arthritis have clinical symptoms of cervical spine lesion with x-ray signs in most of them. Herewith, in 65% of patients with cervical spine subluxations and deformities rheumatoid arthritis destroys atlantoaxial junction followed by AAD.

Craniovertebral junction (CVJ) is unique anatomical complex aimed at protection of vital cerebral and vascular structures and various motor functions. Complex biomechanics of CVJ is provided by atlantooccipital and atlantoaxial joints and their ligaments. While paired atlantooccipital joint is quite stable, atlantoaxial junction consisting of paired lateral atlantoaxial and median atlantoaxial joints (Cravelhier’s joint) is more mobile complex providing 60% of head movements [8]. However, the last is followed by certain vulnerability and dislocation due to CVJ trauma and diseases including rheumatoid process. AAD pathogenesis in rheumatoid arthritis is associated with destruction of capsular-ligament and bone structures of atlantoaxial junction and its instability. Neurological complications are caused by brainstem compression due to odontoid dislocation or rheumatoid granuloma (pannus) [9].

There are several types of dislocations in CVJ rheumatoid lesions: anterior (49%), lateral (20%), posterior (7%) and rotational (extremely rare). They may be non-fixed or rigid. Rigidity of dislocation is determined by stage of arthritis. Late stage is followed by anchylosis and rigid AAD. In 38% of cases AAD is combined with basilar invagination because of destruction of lateral atlantoaxial joints [10].

Clinical symptoms of rheumatoid cervical spine lesion are not always observed. Some authors [11, 12] reported pain syndrome alone in 40—88% of patients with x-ray signs of rheumatoid lesion of cervical spine and neurological disorders in only 7—34% of them. Clinical picture of AAD is accompanied by various neurological disorders due to brainstem and superior spinal cord compression and impaired vertebrobasilar circulation.

**Material and methods**

In 2015—2016 we have operated 5 patients with rheumatoid AAD including 4 women and 1 man aged 54—73 years. Rheumatoid arthritis with anamnesis over 20 years was diagnosed in all patients. There were anterior AAD in all of them. Three patients had pannus dislo-
cation. In 2 cases AAD was rigid and combined with odontoid invagination into large occipital orifice. AAD severity was determined by anterior atlantodental interval and varied from 6 to 10 mm.

All patients with rheumatoid disease underwent functional spondylography besides conventional preoperative survey in order to assess grade of AAD rigidity. It was necessary to define treatment strategy.

In some cases, ataxia, neurogenic dysfunction of pelvic organs, bulbar disorders, transient vertebrobasilar ischemic circulatory disorders were observed besides pain syndrome, spastic tetraparesis and conductive sensitivity disorders. Advanced neurological deficit rather than pain syndrome was a cause for recourse of medical care as a rule.

Severity of neurological disorders was directly related to AAD grade. Indication for surgery was anterior atlantodental interval over 6 mm.

Surgical approach was determined by stability of deformation. Mobile AAD was an indication for indirect decompression via instrumental repair of dislocation and atlantoaxial fixation through posterior access. Anterior

<table>
<thead>
<tr>
<th>Grade</th>
<th>Sign</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>Pain, no neurological deficit</td>
</tr>
<tr>
<td>Grade II</td>
<td>Moderate myelopathy with weakness, hyperreflexia, dysesthesia</td>
</tr>
<tr>
<td>Grade IIIA</td>
<td>Severe conductive disorders, patient moves with difficulties, ambulatory</td>
</tr>
<tr>
<td>Grade IIIB</td>
<td>Extremely severe neurological deficit, patient cannot move by himself or move with external support, non-ambulatory</td>
</tr>
</tbody>
</table>

Table 2. Ranawat pain scale

<table>
<thead>
<tr>
<th>Pain</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pain</td>
<td>0</td>
</tr>
<tr>
<td>Mild</td>
<td>1 (responsive to analgesics)</td>
</tr>
<tr>
<td>Moderate</td>
<td>2 (responsive to immobilization)</td>
</tr>
<tr>
<td>Severe</td>
<td>3 (unresponsive to both analgesics and immobilization)</td>
</tr>
</tbody>
</table>

Fig. 1. Case report №1. Preoperative survey.

a, b — functional spondylograms: non-fixed AAD (arrows); c, d — MRI-scan: severe brainstem compression by dislocated odontoid process followed by focal myelomalacia at this level and pannus (arrows); e, f – CT-scan: anterior AAD and basilar impression (arrows).
decompression through transoral access in addition to posterior fixation was applied for rigid AAD.

We have used C. Ranawat scales (Tables 1 and 2) for assessment of neurological disorders and pain syndrome severity in case of rheumatoid lesion of CVJ [13].

Three patients with unfixed dislocations underwent instrumental repair of deformation and atlantoaxial fixation with screws-based metal construction. Screws were inserted into C1 lateral masses and transpedicularly into C2 body by J. Harms followed by instrumental correction of dislocation and metal construction deployment. One patient with insufficient AAD correction required arthrolysis of lateral atlantoaxial joints in order to increase mobility. Bilateral exposure of C2 spinal radixes was applied to visualize these joints.

In case of rigid AAD combined with basilar invagination we performed combined simultaneous procedures. There were C0—C2—C3 occipitospondylodesis in one case and posterior fixation of C1—C2 by Harms in another one followed by transoral decompression (resection of atlas anterior arch and odontoid process).

Case report № 1


Patient has suffered from rheumatoid arthritis for 20 years with lesion of hands and feet joints, knee joints followed by their secondary deformation. There were pain syndrome, severe spastic tetraparesis followed by arms and legs weakness up to 3 scores, cerebellar and sensitive ataxia, neurogenic pelvic dysfunction of central type, transient circulatory disorders ("drop-attacks") in sharp change of head position (Ranawat III B, pain 2 scores). Lhermitte’s symptom was observed. Neurological symptoms occurred 2 years before hospitalization with gradual progression.

Functional spondylography revealed non-fixed deformation (Fig. 1a, b). Magnetic resonance imaging (MRI) and computed tomography (CT) confirm AAD followed by severe brainstem compression with dislocated odontoid, focal myelomalacia and rheumatoid granuloma (pannus) at the C1—C2 level (Fig. 1c—f).

Fig. 2. Case report №1. Survey data after instrumental repair of dislocation and atlantoaxial spondylodesis by J. Harms.

a, b — functional spondylograms, c, d — CT-scan: normal anatomical interrelations of CVJ; e, f — MRI-scan: normal anatomical interrelations of CVJ, no inflammation and spontaneous resorption of rheumatoid granuloma.
Surgery: in prone position with head fixation in Mayfield clamp the screws were inserted into C1 lateral masses and transpedicularly into C2 body, dislocation was instrumentally repaired followed by metal construction deployment.

Postoperative period was uneventful. There were arms and legs strength recovery up to 4—5 scores, relief of pain syndrome, regression of sensitive disorders and normalization of extremities’ muscle tone, no vertebrobasilar circulatory disorders (Ranawat I, pain 0 scores).

Control CT and spondylography confirmed restoration of correct anatomical interrelations in CVJ and absent brainstem compression (Fig. 2a—d). MRI in 8 months after surgery revealed complete spontaneous resorption of rheumatoid pannus (Fig. 2e, f).

Case report № 2

Patient A., 68 years old. Diagnosis: rheumatoid lesion of CVJ. Rigid AAD. Spastic tetraparesis.

Anamnestic of rheumatoid arthritis followed by secondary deformation of joints is over 20 years. Neurological disorders included severe spastic tetraparesis with arms and legs weakness up to 3 scores, bulbar disorders (Ranawat III B, pain 0 scores). Neurological disorders have appeared several months before hospitalization.

CT and functional spondylography revealed rigid AAD with odontoid dislocation into large occipital orifice and severe brainstem compression (Fig. 3a—d).

Surgery: patient’s prone position, we have firstly carried out resection of large occipital orifice’s margin and posterior hemiarch of atlas, arthrolysis of lateral atlantoaxial joints, occipitospinolodesis with screw-based metal construction and repair of deformation. Therefore, in supine position patient underwent transoral resection of lower clivus, anterior hemiarch of atlas, odontoid process up to dura mater.

Event-free postoperative period was observed. There was favorable neurological dynamics including augmentation of hands and legs strength up to 4 and 3 scores, respectively, regression of sensitive disorders and normalization of extremities’ muscle tone (Ranawat III A, pain 0 scores).

Fig. 3. Case report №2. Preoperative survey.

a, b — functional spondylograms: rigid AAD; c, d — CT-scan: anterior AAD and basilar impression.

Fig. 4. Case report №2. Survey data after instrumental repair of deformation, occipitospinolodesis and transoral odontoidectomy.
a, b – CT-scan: no medulla oblongata compression and normal anatomical relationships of CVJ.
According to control CT there was no brainstem compression due to both decompression and instrumental repair of CVJ deformation (Fig. 4).

Results

1-year outcomes were followed-up. Significant postoperative regression of pain syndrome and neurological disorders were observed in all patients (Table 3). Postoperative wound infection occurred in 1 patient after surgery through posterior approach. Drainage and irrigation of the wound were effective. Brainstem decompression followed by CVJ repair via correction of dislocation and atlantoaxial spondylodesis through posterior approach were successfully achieved in all cases of non-fixed AAD. Herewith, transoral interventions were not necessary and spontaneous resorption of pannus in few months after surgery occurred. Grade of cervical spine rotation became physiological within follow-up in patients after atlantoaxial spondylodesis. Significantly limited rotation, flexion and extension of cervical spine were observed only in 2 cases after occipitospondylodesis.

Discussion

Early AAD is characteristic for rheumatoid injury of CVJ. Risk of severe neurological complications determine indications for surgery. Correction should be carried out as early as possible in these cases in view of unfavorable prognosis.

The purpose of surgery for rheumatoid AAD is brainstem decompression and reliable fixation of affected area. Decompressive laminectomy and advanced posterior fixation is now necessary to be considered redundant in treatment of rheumatoid injury of CVJ. Instrumental repair of AAD and reliable "short" fixation via posterior approach are followed by brainstem decompression, restoration of normal CVJ anatomy, minimum surgical trauma and significant improvement of functional outcomes. It is possible due to not only current equipment, but also features of AAD including stability of deformation that determines surgical strategy.

AAD rigidity depends on duration of rheumatoid arthritis. Dislocation is non-fixed in manifestation of rheumatoid lesion. Neurological complications are caused by dislocated odontoid process and rheumatoid granuloma. In these cases, repair of deformation is possible via posterior fixation by Harms. This technique avoids prolonged fixation and provides optimal functional outcomes. Moreover, C1—C2 fixation is followed by discontinuance of inflammation and spontaneous resorption of pannus.

Late stage of rheumatoid arthritis is accompanied by rigid AAD due to ankylosis. Indications for surgery in these cases are determined by neurological disorders.

Transoral decompression is not justified if AAD is even minimally mobile. In this situation, arthrolysis of atlantoaxial joints, posterior fixation of C1—C2 by Harms and instrumental correction of AAD are associated with indirect brainstem decompression while transoral approach is avoided.

Transoral decompression is indicated only for rigid AAD after occipitospondylodesis or posterior fixation of C1—C2 by Harms.

Conclusion

All patients with rheumatoid arthritis should be specifically screened for early diagnosis of CVJ damage. Dislocation is an absolute indication for surgery due to risk of neurological disorders.

Whether deformation is stable is key factor to determine surgical approach.

Instrumental correction of deformation and atlantoaxial spondylodesis via posterior approach are indicated for non-fixed AAD even in neurological symptoms.

Rigid AAD followed by neurological disorders is indication for surgery. Occipitospondylodesis or posterior fixation of C1—C2 and transoral decompression are required in these cases.

Our approach for AAD is accompanied by restoration of normal anatomy of CVJ, brainstem decompression and minimal postoperative functional disorders.

Authors declare no conflict of interest.
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Received: 31.05.17

Commentary

Five cases of rheumatism-associated atlantoaxial dislocation are described in the article. The authors use generally accepted tactics depending on type of instability (anterior, posterior) and duration of disease. All variants of surgical approaches (including transoral) as well as various types of local and advanced stabilization are used.

The article is of interest due to rare pathology.

A.O. Gushcha (Moscow, Russia)
Opect Optical System in Neurosurgical Practice

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1Federal Center of Neurosurgery, Nemirovich-Danchenko Str., 132/1, Novosibirsk, Russia, 630087, 2Tokyo Women’s Medical University, Tokyo, Japan

Introduction. Modern neurosurgical practice is impossible without access to various information sources. The use of MRI and MSCT data during surgery is an integral part of the neurosurgeon’s daily practice. Devices capable of managing an image viewer system without direct contact with equipment simplify working in the operating room. Aims and objectives. To test operation of a non-contact MRI and MSCT image viewer system in the operating room and to evaluate the system effectiveness. Material and methods. An Opect non-contact image management system developed at the Tokyo Women’s Medical University was installed in one of the operating rooms of the Novosibirsk Federal Center of Neurosurgery in 2014. In 2015, the Opect system was used by operating surgeons in 73 surgeries performed in the same operating room. The system effectiveness was analyzed based on a survey of surgeons. Results. The non-contact image viewer system occurred to be easy-to-learn for the personnel to operate this system, easy-to-manage it, and easy-to-present visual information during surgery. Conclusions. Application of the Opect system simplifies work with neuroimaging data during surgery. The surgeon can independently view series of relevant MRI and MSCT scans without any assistance.

Keywords: Opect system, non-contact neuroimaging data management.

Currently, surgeon’s intraoperative work is associated with the need for constant access to neuroimaging data (MRI and CT). Availability of computer in operating theatre which is integrated into local hospital network with possible visualization of DICOM-files is integral component of modern surgical units. Thus, on-line intraoperative data about certain patient are available for surgeon. These systems are controlled by additional employee who does not directly participate in surgery. In our opinion, development and introduction of equipment with out-of-touch control is advisable due to some advantages for surgeon and other fellow workers. In this situation surgeon is able to obtain independently necessary intraoperative information while other participants are free from this process. Results of Opect system application are described in the article. The aim of this work is to evaluate system’s effectiveness, learning curve and quality of neuroimaging data.

There were no purposes to calculate cost of this equipment and its comparison with intraoperative work of personnel.

The objective of the work is assessment of contactless control of MRI and CT-scans viewing in neurosurgical theatre.

Material and methods

In December 2014 innovative equipment was deployed in one of operational theatres of Novosibirsk Federal Neurosurgery Center — Opect optical system for intraoperative out-of-touch control of MRI and CT-scans viewing. The last was developed at the Tokyo Women’s Medical University.

There are 3 components in the system (Fig. 1). The main part is a tablet computer (Windows OS) integrated into local computer network and equipped with special software for images viewing. Necessary DICOM (or JPEG) files are previously loaded into the tablet from local network. Screen for displaying of images is located on one of the walls in operating theatre so surgeon standing near operating table is able to see them. Kinect infrared antenna fixing surgeon’s movements is directed toward operating table. Surgeon controls images on the screen by

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these movements. Kinect (Microsoft) is out-of-touch touchscreen game controller introduced for personal computers (Windows OS). It allows the user to interact with computer without contact device (joystick or keyboard). Infrared emitter of antenna creates a beam of rays towards the surgeon which are reflected from him and return to device. Then these rays are perceived by camera and analyzed. System assessed human movements in three planes (left-right, up-down, forward-backward). Optimal distance from antenna to surgeon is 2—3 m (Fig. 1).

System is ready as soon as images are downloaded into tablet computer. Surgeon can intraoperatively assess any files at any time. For this purpose, he must be within coverage area of Kinect infrared antenna. Program is automatically activated, color of image’s frame on the screen changes from red to green. Surgeon’s silhouette appears on the screen and physician is able to control process from this moment by using his hand. The system responds to the hand movements like a pendulum when the palm is uplifted and turned to the antenna. Surgeon’s hand fixed by the antenna is displayed on the screen as green sphere that is analog of cursor. Primary slide of the first MRI or CT scans series downloaded into system is displayed on the monitor. Image is identical to primary DICOM-scan obtained by MRI or CT. Whole information about patient is presented on the image including its number in series and magnification in relation to original file. Images may be changed by using of interface of the right half of screen with corresponding arrows (Fig. 2).

Sphere navigation on one of these icons activates series scrolling forward or backward. 2-, 4- or 8-fold magnification is available. Grade of magnification is displayed in upper right part of monitor. Smaller original image with subsequently enlarged area is located in lower right part of monitor for convenience. Palm’s movement towards the screen is needed to change image magnification. Icon of four arrows appears after that (up, down, left, right) to analyze entire picture in different directions (Fig. 3).

Cursor’s movement towards upper screen is followed by change of series of files. Thus, surgeon can receive all necessary information while he is aseptic and without help of other persons.

At the Novosibirsk Federal Neurosurgical Center Opect system has been used in 73 procedures for the period from January to December 2015. Patients’ characteristics are presented in the Table.

Three surgeons of the oncology department of the Novosibirsk Federal Neurosurgical Center took part in the study. All Opect system-assisted interventions were carried out in the same operating theatre. In each case

<table>
<thead>
<tr>
<th>Disease</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial meningioma</td>
<td>26</td>
</tr>
<tr>
<td>Glioblastoma</td>
<td>19</td>
</tr>
<tr>
<td>Pituitary adenoma</td>
<td>17</td>
</tr>
<tr>
<td>Cranioopharyngioma</td>
<td>6</td>
</tr>
<tr>
<td>Microvascular decompression for trigeminal neuralgia</td>
<td>3</td>
</tr>
<tr>
<td>Vestibular schwannoma</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>73</td>
</tr>
</tbody>
</table>
surgeon decided to view MRI and CT-images in necessary manner by himself. Postoperatively surgeon expressed his opinion about system regarding intraoperative visualization of the images. Herewith, he pointed out the most relevant factors for us:

— learning time required for working with system in the future;
— simplicity or complexity of training;
— quality of data;
— system’s drawbacks.

**Results**

Simple and convenient application of system were noted in all cases. Learning time was 3—5 minutes in all 3 surgeons who have used equipment in following interventions. Re-training or further clarification for work with system were not required during the 2nd and subsequent procedures. Interface is clear and easy for understanding. System is able to view any DICOM or JPEG data including angiographic scans. However, intraoperative 3D-modeling and viewing of 3D-format are impossible. Drawback of this system is need to duplicate imaging data from storage server to tablet by using of special program that takes few minutes. Since system activated it is necessary to exclude foreign moving objects (equipment, personnel) in camera’s coverage field to prevent false triggering. Number of series is limited (<3) that may be unsatisfactorily for surgeon and requires more careful preoperative assessment and selection of the most informative scans.

Despite above-mentioned shortcomings there was no need to use additionally stationary computer for MRI and CT-scans viewing among 73 procedures. In our opinion, the last fact indicates adequate work of system regarding intraoperative neuroimaging.

**Conclusion**

In our opinion, Opect system can greatly simplify intraoperative neuroimaging without additional help. We consider that introduction of intraoperative out-of-touch equipment is followed by great prospects for further improvement of surgical interventions.

**Authors declare no conflict of interest.**

**Commentary**

Report of A.V. Kalinovskiy et al. is dedicated to current technology of out-of-touch control of images viewing in neurosurgical operating theatre. This technology is realized via infrared camera tracking surgeon’s hands movements. The problem of DICOM-files control within aseptic surgical environment is obviously relevant. Routine practice requires additional staff or technical specialists sometimes to use image viewer software during surgery that increases the number of people in operating theatre. Surgeon gives instructions verbally about necessary images that can disrupt work under stressful conditions when rapid decision-making is required and quick response is important.

It is described modern system of out-of-touch interaction with computer («Opect») which was developed at the Tokyo Women’s Medical University (Japan). This product was created on the basis of computer games technologies and is designed to improve safety of medical images viewing within neurosurgical operating theatre. In most cases, only one surgeon is required to work with system, while computer is controlled by gestures without additional input devices. The authors summarize their positive experience of Opect system application. The number of Opect-assisted interventions (n=73) is more than 2 times higher than that in report of K. Yoshimitsu et al. in 2014 (n=30). For the first time ever this report has shown an effectiveness of this system. Russian authors confirmed the results Japanese colleagues.

Advanced computer and information technologies are followed by extended capabilities to work with medical information in neurosurgery. Adequate representations about effectiveness and convenience of such tools are essential for neurosurgical community. Opect system demonstrates the possibility to improve efficiency, safety and comfort of operating team’s work through the use of modern computer solutions.

*S.A. Goryainov (Moscow, Russia)*
Evidence-Based Medicine: Propensity Score Matching (PSM) Approach to Eliminate Systematic Selection Bias in Retrospective Neurosurgical Trials

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To date, a large amount of retrospectively collected data about treatment of neurosurgical pathology have been accumulated. Modern methods of medical statistics are necessary for correct interpretation of the data. The article purpose is to demonstrate application of one of the modern methods, Propensity Score Matching (PSM), in neurosurgery. Results and discussion. The use of PSM avoids misinterpretation of retrospectively collected data and obviates errors in planning further prospective studies. For the past 10 years, the number of published international PSM-based studies has increased more than 10-fold, with the number of articles by Russian authors accounting for less than 0.2%. In line with the tendencies of international studies, application of PSM in analysis of retrospectively collected data will enable testing of a number of hypotheses and correct planning of prospective randomized studies.

Keywords: Propensity Score Matching, neurosurgery, medical statistics, selection bias.

Experience of national neurosurgeons over the last years is a unique basis for retrospective analysis. It is necessary for comparative evaluation of efficacy and safety of various interventions, objectification of results from large heterogeneous samples of patients (including different centers) and planning of subsequent prospective studies. However, considerable heterogeneity of initial data due to systematic sampling error can significantly hinder direct comparison of results and influence conclusions. In this regard correct methodology of retrospective analysis and consequently adequate statistical processing are needed.

The design of most clinical trials is based on comparison of different effects and identifying relationships between approaches and outcomes [1]. Effect can consist of not only different treatment approaches but also influence of environmental parameters, attachment to particular social group or risk group. As a rule, the main purpose of medical researches is assessment of correlation between some factors and observed outcomes. Requirement of comparable groups in analysis is fundamental, so equivalence of groups by key factors should be controlled. It is may be achieved either by randomization (randomized controlled trials, RCTs) or by using of Propensity Score Matching (PSM) and its analogues [2] followed by elimination of systematic selection bias. Usually only two groups (control and main) are considered, so we will use such design for analysis.

RCTs are ”gold standard” to correct systematic selection bias in treatment safety and efficacy assessment. Correct randomization is followed by equivalent distribution of known and unknown factors affecting outcomes. This is the fundamental condition for analysis of outcomes in both groups. In other cases, RCTs are either impossible or extremely time-consuming due to various reasons. These causes are too large sample size, limited budget and/or time, impossible randomization because of ethical considerations or significantly different interventions, etc. [3].

PSM for data analysis

If RCTs are impossible for any reasons, other types of trials are preferred. Usually, it is a retrospective analysis of large sample size for a long time. In this case, systematic selection bias may be followed by significant inaccuracies or incorrect conclusions. That is why editors of authoritative journals try to avoid publishing of retrospective studies with potential systematic selection bias.

PSM is effective to achieve equivalent distribution by certain key characteristics. Key characteristics of the groups include the most significant variables (clinical and demographic). PSM is followed by reduced systematic selection bias and equivalent groups [4]. So, qualitative retrospective analysis and highly evidenced conclusions are obtained.

There are 2 steps in PSM algorithm: correction of selection bias in order to obtain comparable groups and directly comparative analysis of modified data.

PSM foundations were considered in the middle of the last century [1, 5], detailed development has occurred

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**Fig. 1.** Increasing number of articles with PSM in SCOPUS database.

**TABLE 1.** Unmatched and Propensity Matched Measures of Resident Involvement on Surgical Outcomes

<table>
<thead>
<tr>
<th>Measures</th>
<th>Unmatched</th>
<th>Propensity matched</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No resident</td>
<td>Any resident</td>
</tr>
<tr>
<td>Vascular surgery (mean wRVUs = 46.6 ± 19.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients, n</td>
<td>12,848</td>
<td>24,321</td>
</tr>
<tr>
<td>Operative mortality, %</td>
<td>5.4</td>
<td>5.9&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Composite morbidity, %</td>
<td>25.5</td>
<td>32.7&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Failure to rescue, %</td>
<td>15.8</td>
<td>13.9&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Values suggest significantly worse outcomes associated with resident involvement.

<sup>b</sup>Values suggest significantly better outcomes associated with resident involvement (all p < 0.001).

wRVU, work-related relative value unit.

**Fig. 2.** Part of the table from the article "Impact of Residents on Surgical Outcomes in High-Complexity Procedures" [17] showing different results before and after PSM application.

**TABLE 2.** Poor neurological outcome and death at hospital discharge before and after PS matching in the TTM group<sup>*</sup>

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Before PS Matching (n = 687 patients)</th>
<th>After PS Matching (n = 262 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>p Value</td>
</tr>
<tr>
<td>Poor neurological outcome</td>
<td>0.76 (0.63–0.91)</td>
<td>0.003</td>
</tr>
<tr>
<td>Death</td>
<td>0.68 (0.52–0.88)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

<sup>*</sup> Cox proportional-hazards analysis.

**Fig. 3.** Part of the table from the article "Therapeutic modulation in severe or moderate traumatic brain injury: a propensity score analysis of data from the Nationwide Japan Neurotrauma Data Bank" [20] showing different results before and after PSM application.
in 1970—1990 [6—8]. Advanced computer technology at the end of the last century was followed by development of software products to implement this approach. So, PSM has become available for wide range of researchers [9]. Nevertheless, technical features of PSM can cause difficulties in medical researchers. However, specialist for biostatistics can facilitate this problem.

PSM is based on conditional probability of each research object falling into intervention group. Clinically relevant factors must be determined to create propensity scores (PS). Since PS is a probability, its values are in the range from 0 to 1. Multivariate logistic regression model is usually applied for PSM.

Conditional probability may be balanced between intervention and control groups by using of PS values. Various PSM approaches are used for this purpose [10] — stratification/subclassifications, inverse probability of treatment weighting (IPTW) and covariate adjustment. Choice of the most effective method to correct systematic selection bias becomes the object for particular trial. None of available methods is sufficiently universal and applicable in all situations. For example, PSM has some advantages in contrast to regression adjustment: simple analysis of models’ quality, closer to RCTs idea due to separate phases of subgroup selection and analysis and other advantages which are comprehensively presented in P. Austin’s report [11].

PSM is associated with reduced systematic selection bias, so this approach is considered as a kind of randomization for retrospective data. However, there is principal difference between both methods: randomization eliminates systematic selection bias for both considered and unaccounted factors, while PSM corrects selection bias only for factors considered and measured.

To date, the number of publications with PSM for analysis and retrospective data interpretation is steadily growing [12]. There are about 3,000 publications in 2016 according to SCOPUS database (Fig. 1). At the same time, for the period 2007—2017 Russian publications for neurosurgical problems are also few among them [15—30]. We see a steady interest of researchers to use PSM in neurosurgical studies. For example, PSM-assisted trial was published in Spine journal in 2017 [31]. We expect that retrospective analysis will become an integral part of researches [8]. Considering advanced ethical requirements and accumulation of large amount of these data relevance and effectiveness of their analysis will be increased. It is not surprisingly, that development of PSM and its analogs is one of the most important areas of medicine.

PSM is used the report of V. Ferraris et al. [17] where the authors investigated the effect of surgical team on the outcomes of highly difficult general surgery, neurosurgery, vascular surgery, cardiothoracic surgery. Since literature data about the role of trainee surgeon in interventions are extremely controversial, the authors have analyzed treatment of 266 411 patients.

Large database was retrospectively analyzed by using of PSM to minimize systematic sampling bias. Fundamentally different conclusions were obtained with PSM approach despite initial assumption about assistant’s negative impact on the outcomes according to preliminary analysis (Fig. 2).

In particular, analysis of bias-uncorrected data revealed significantly higher trainee-associated intraoperative and overall mortality. There were other data if PSM was applied: participation of trainee surgeon positively affects surgical outcomes (less mortality from postoperative complications) and does not influence intraoperative and overall mortality.

This example demonstrates that bias-corrected approach is followed by other outcomes and conclusions.

The article of K. Miyata et al. (Japan) is an example of systematic selection bias minimization with PSM can radically change results of observational trial [20]. Effect of therapeutic temperature modulation (TTM) on neu-
rological outcomes and mortality rate was assessed in this article (Fig. 3).

There were 687 patients with brain injuries. Preliminary analysis of bias-uncorrected data confirmed that TTM procedure was significantly associated with lower risk of poor neurosurgical outcome and death. However, trivial negative effect of this procedure was observed as soon as groups were equalized by age, severity of injury, terms and conditions of medical care.

A. Seicean et al. [23] analyzed outcomes of surgery for intracranial aneurysms in patients with/without severe anemia requiring transfusion. There were 668 patients who underwent open surgery in 2006—2012. PSM was applied due to preoperative heterogeneity of groups (age, features of aneurysms, comorbidities and risk factors for adverse outcomes and complications).

Different incidence of early major complications before and after PSM application was demonstrative. In groups with/without anemia incidence of complications changed from 20 (25% vs. 45% prior to PSM) to 10% (34% vs. 44% after PSM).

Incidence of complications is often used to determine sample size needed for subsequent randomized controlled trials. If we will accept difference near 20% in above-described example, then predicted sample size will be at least 3 times less than necessary to obtain reliable data (Fig. 4).

As examples, we have considered some publications [20, 23, 24] for 2015—2016 and significance of PSM for analysis has been presented.

**Conclusion**

PSM significantly affects interpretation of retrospective data and design of subsequent studies. Correction of systematic selection bias is followed by more accurate estimation of sample size for further trials and adequate interpretation of results. PSM for analysis of retrospective data of national neurosurgical centers will allow us to test some hypotheses and to schedule further RCTs.

The research is partially supported by grants of the Russian Foundation for Basic Researches 17-01-00683 A, 17-41-540759 p_a.

Authors declare no conflict of interest.

**REFERENCES**

Commentary

One of the most important and nontrivial objectives of clinical neurosurgical researches is adequate selection of patients in order to analyze relationships between surgical outcomes and certain variables. Because of ethical and medical limitations groups analyzed (in observational studies) are not comparable by many factors influencing outcomes as a rule. Main and control groups formation through routine accumulation of clinical data leads to systematic errors including so-called "selection bias". As a result, these groups turn out to be disparate by basic characteristics which affect the outcomes. Therefore, conclusions about some effects and relationships may be incorrect. For example, better results of minimally invasive approaches in neurosurgery may be associated with improved condition of patients who undergo these procedures rather "minimal surgical invasiveness" alone.

Maximally equivalent groups by all apparent and unknown characteristics except that under analysis are necessary to assess adequately the effect of certain factor. In prospective studies it is achieved via randomization. There are certain methods to reduce selection bias in retrospective trials. This article is devoted to one of these methods — Propensity Score Matching (PSM).

The authors have demonstrated an importance of PSM in neurosurgical researches. The article is of interest for certain specialists because mathematical technologies followed by reduced selection bias and substantially increased evidence level are described. These methods are very useful to ensure high quality of researches within evidence-based medicine precisely in neurosurgical studies. This is due to impossible randomization as a rule for medical and ethical reasons.

Retrospective analysis is the most common in neurosurgical researches. It seems the simplest due to routine accumulation of data and no need for special selection protocol. However, retrospective analysis is much more difficult due to insufficient data quality control and systematic selection bias. The authors concluded very important statement about need for correct retrospective analysis with involvement of specialists for biostatistics who understands clearly methodology of clinical researches, control of clinical data and systematic errors. This is one of the cornerstones of ensuring high-quality researches within evidence-based medicine.

G.V. Danilov (Moscow, Russia)
Advisability and Effectiveness of Decompressive Craniectomy in Patients With Subarachnoid Hemorrhage After Microsurgical Repair of Aneurysms

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In recent years, the so-called primary or preventive decompressive craniectomy (DC) has been increasingly used in patients with aneurysmal subarachnoid hemorrhage (SAH). The main goal of the technique is prevention of refractory intracranial hypertension (ICH) and its consequences.

Purpose. The study purpose was to define the CT criteria for reasonability and efficacy of DC as well as clarification of the indications for preventive DC in patients with SAH after microsurgical aneurysm exclusion.

Material and methods. The study included 46 patients who underwent microsurgical clipping of aneurysms and DC in the period between 2010 and 2016. All patients underwent surgery in the period of 1 to 12 days after SAH. Preventive DC (simultaneously with clipping of aneurysms) was performed in 38 patients. Secondary (delayed) DC was performed in 8 patients.

Results. Mortality in a group of all patients with DC was 15.2%. Preventive DC was considered as “reasonable” when the patient had signs of cerebral edema in the postoperative period. The X-ray criteria of reasonable DC included a more than 5 mm brain prolapse into the trephination defect or a lateral dislocation of more than 5 mm. If the patient had no prolapse and dislocation in the postoperative period, DC was considered unreasonable. Among patients with ICH in the postoperative period, including 20 patients with reasonable preventive DC and 8 patients with delayed DC, mortality was 23%. The CT signs of efficient DC were found to be a more than 5 mm brain prolapse into the trephination defect in combination with a decrease in the lateral dislocation less than 5 mm. All seven patients with inefficient DC in our group died. To clarify the indications for preventive DC, we analyzed various preoperative factors in patients with reasonable and unreasonable DC.

Conclusion. In most cases, preventive DC in microsurgical aneurysm exclusion is indicated for patients in an extremely grave condition (Hunt—Hess Grade V), a lateral displacement of the mline structures of more than 5 mm, an intracranial hematoma of over 30 ml., and symptoms of acute cerebral ischemia (pronounced cerebral vasospasm and emerging ischemic foci).

Keywords: decompressive craniectomy, craniectomy, acute period of hemorrhage, cerebral aneurysms, vasospasm.

Some reports demonstrated effectiveness of decompressive craniectomy (DC) in patients with aneurysmal intracranial hemorrhage followed by intracranial hypertension [1—3].

In the previous publication we have discussed indications for DC in aneurysmal subarachnoid hemorrhage by using of current reports [4]. It is generally accepted that main indication for DC is refractory to therapy augmentation of intracranial pressure (ICP) over 20 mm Hg.

According to literature data [4], so-called primary or preventive DC has been often used by many clinicians in recent years to prevent refractory intracranial hypertension (ICH) and its consequences. As a rule, such procedures are performed in patients with high risk of advanced ICH.

At present time some signs have been identified to predict postoperative ICH [5, 6]. Nevertheless, severe cerebral edema is not observed in some patients who undergo preventive DC. So, this procedure may be considered unjustified in these situations. On the other hand, severe ICH followed by death is possible even after DC in some cases, that indicates inefficient surgery.

The aim of the work is to determine CT-criteria of advisability and effectiveness of DC, to clarify the indications for preventive DC in patients with subarachnoid hemorrhage after microsurgical repair of aneurysms.

Material and methods

There were 46 patients who underwent microsurgical clipping of aneurysms and DC in 2010—2016. 23 (50%) patients were operated within 72 hours after subarachnoid hemorrhage, 17 patients — in 4—7 days after hemorrhage, 6 patients — in 7—12 days after hemorrhage. In all cases aneurysms were placed in anterior parts of Willis circle.

DC was performed in standard fashion [4]. Skin incisions are shown in Fig. 1.

Bone borders of DC were: 1) anteriorly — segment between zygomatic bone and middle of supraorbital arch; 2) superiorly — line 2 cm lateral to sagittal suture (midline); 3) posteriorly — line 3—4 cm behind external auditory canal, lambdoid suture in lower parts; 4) inferiorly — line parallel to zygomatic arch (Fig. 2).

Dura mater repair with periostome flap or artificial patch was made in all cases to enlarge subdural cavity.

Preventive DC (simultaneously with aneurysms clipping) was performed in 38 patients.

Indications for preventive DC were:
- severe intraoperative cerebral edema in neurosurgeon’s subjective assessment (n=7);
- Hunt—Hess grade V (n=11);
— several risk factors of ICH (n=20): Hunt-Hess grade III-IV, hemorrhage Fisher grade 3—4, intraoperative complications (blood loss over 1 l, prolonged forced blood flow cessation in major artery due to ruptured aneurysm (over 10 min), ultrasonic signs of preoperative angiospasm (Vsys over 240 cm/s in M1-segment of middle cerebral artery) (Fig. 3).

These factors were chosen as indications for preventive DC in view of results of I.A. Sazonov et al. [7]. Their research was carried out at the Burdenko Research Institute for Neurosurgery in 2006.

Secondary (delayed) DC was performed in 8 patients.

Indications for delayed DC were:
— postoperative hematoma in CT-scans followed by advanced cerebral dislocation syndrome and impaired consciousness (n=3);
— impaired consciousness combined with severe (over 20 mm Hg) ICH resistant to therapy due to CT-confirmed cerebral ischemia (n=5). Preoperative characteristics of patients with preventive and delayed craniec- tomyes are given in Table 1.

Previous reports justified DC by its effectiveness. The last was determined by overall outcomes of aneurysms repair and their comparison with those without craniectomy in similar groups [1—3].

We suggested postoperative CT-criteria to evaluate advisability of DC. CT-data were processed in Inobitec DICOM Viewer program. We used following concepts:
1) lateral dislocation — transverse displacement magnitude of median cerebral structures that was measured at the level of septum pellucidum;
2) prolapse — severity of cerebral protrusion through cranial defect. Prolapse grade was measured along the line between outer cerebral boundaries at the level of nuclei caudate heads perpendicular to midline. Caudate nuclei heads were chosen due to the fact that the line through these anatomical formations usually corresponds to center of cranial defect circumference. The greatest cerebral prolapse is noted here (Fig. 4). Such measurement we used in 42 patients with unilateral DC.

The second, more difficult calculation of prolapse is software fusion of pre- and postoperative scans (Fig. 5). This approach was applied in 4 cases of bilateral craniectomy.

Lateral dislocation and prolapse were estimated by using of CT in 2—6 days after surgery. In cases of redo CT-imaging maximum values within this period were taken into account. Prolapse and lateral dislocation were measured in millimeters. Postoperative 30-day neurological outcomes were estimated according to Glasgow coma scale (GCS).

Results

**Preventive DC**

Cerebral prolapse through cranial defect and lateral dislocation were observed in 25 (65.8%) and 14 (36.8%) patients with preventive DC, respectively.

Outcomes of patients with preventive craniectomy correlated with prolapse and lateral dislocation severity.
1. Patients with prolapse and lateral dislocation less than 5 mm.

Prolapse and lateral dislocation less than 5 mm were observed in 18 patients. In 10 of them prolapse was absent, moreover cerebral compression within cranial defect occurred due to edema and hematomas in soft tissues. 8 patients had prolapse within 1—4 mm (mean 3 mm). In most of patients lateral dislocation (n=13) was absent or did not exceed 5 mm (n=5).

In our opinion, both these factors indicated absent severe cerebral edema in postoperative period. Accordingly, DC was unjustified in these patients since the goal was not realized (empty space filling with edematous
An example of unjustified craniectomy is shown in Fig. 6.

Other instrumental and clinical data have also confirmed no severe cerebral edema in these patients. In particular, ICP was invasively monitored in 8 patients. There were short-term postoperative elevations of ICP over 20 mm Hg in 4 cases followed by successful medication. ICP was normal in other cases.

In 30 days after subarachnoid hemorrhage good or satisfactory outcomes were observed in this group: GCS 5 in 5 cases, 4 in 6 and 3 in 7 patients. Persistent vegetative status and lethal outcomes were absent.

Severe postoperative neurological deficit was associated with ischemic cerebral accidents as a rule. According to postoperative CT, ischemic foci within the same cerebral lobe were revealed in 6 patients.

2. Patients with prolapse over 5 mm and lateral dislocation less than 5 mm.

Cerebral prolapse within 6—22 mm (mean 11.4 mm) was noted in 17 patients. Cerebral edema predicted prior to surgery was confirmed in postoperative period, that indicates advisability of DC in these cases. Lateral dislocation was absent in 11 patients and did not exceed 5 mm in 6 patients.

Invasive postoperative monitoring of ICP was performed in 13 out of 17 patients of this subgroup. ICP within 20 mm Hg has been observed in 9 patients for 7 days after DC. There were single short-term elevations of ICP above this threshold value in 4 patients.

Among 17 patients, neurological outcomes GCS score 5 were in 1 case, score 4 in 4 cases, score 3 in 8 cases, score 2 in 2 cases and score 1 in 2 cases. In 1 woman vegetative state in 30 days after subarachnoid hemorrhage was caused by multiple foci of ischemic circulatory disorders in both hemispheres, in other one — severe cerebral lesion due to 5 recurrent hemorrhages with parenchymal component prior to surgery. Two patients died from infectious complications: purulent meningoencephalitis in one patient and pneumonia followed by sepsis in another one.

Thus, DC was effective in this subgroup in order to prevent ICH and dislocation syndromes. An example of advisable and effective craniectomy is presented in Fig. 7.

3. Patients with prolapse and lateral dislocation over 5 mm.

Severe postoperative cerebral edema was observed in 3 patients that justified preventive DC. In 1 case of advanced hemispheric ischemia contralateral to cranietomy cerebral protrusion was 19 mm, in another patient with ipsilateral hemispheric ischemia — 13.5 mm. Prolapse near 16 mm was noted in patient with edema due to postoperative hematomas.

Despite DC persistent lateral dislocation 7—19 mm (mean 12.7 mm) was observed in these patients, and ambient cistern was compressed. In 2 patients with advanced brain). An example of unjustified craniectomy is shown in Fig. 6.

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### Table 1. Preoperative patients' characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Preventive DC</th>
<th>Delayed DC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>38</td>
<td>8</td>
</tr>
<tr>
<td>Mean age, years</td>
<td>46.9 (20—69)</td>
<td>45.7 (25—72)</td>
</tr>
<tr>
<td>Male/Female</td>
<td>17:21</td>
<td>4:4</td>
</tr>
<tr>
<td>Hunt—Hess grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II, n (%)</td>
<td>5 (13.2)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>III, n (%)</td>
<td>12 (31.6)</td>
<td>2 (25)</td>
</tr>
<tr>
<td>IV, n (%)</td>
<td>10 (26.3)</td>
<td>5 (62.5)</td>
</tr>
<tr>
<td>V, n (%)</td>
<td>11 (28.9)</td>
<td>—</td>
</tr>
<tr>
<td>SAH Fisher grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2, n (%)</td>
<td>1 (2.6)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>3, n (%)</td>
<td>14 (36.8)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>4, n (%)</td>
<td>23 (60.5)</td>
<td>6 (75)</td>
</tr>
<tr>
<td>Severity of preoperative vasospasm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Vsyst M1 segment of MCA) [8]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild + moderate (120—230 cm/s), n (%)</td>
<td>28 (73.7)</td>
<td>7 (87.5)</td>
</tr>
<tr>
<td>Severe (240—290 cm/s), n (%)</td>
<td>9 (23.7)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>Critical (over 300 cm/s), n (%)</td>
<td>1 (2.6)</td>
<td>0</td>
</tr>
<tr>
<td>Localization of ruptured aneurysms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACA, n (%)</td>
<td>13 (45.4)</td>
<td>5 (62.5)</td>
</tr>
<tr>
<td>MCA, n (%)</td>
<td>16 (39.3)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>ICA, n (%)</td>
<td>9 (15.1)</td>
<td>2 (25)</td>
</tr>
<tr>
<td>Time from SAH to craniectomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0—3 days, n (%)</td>
<td>23 (60.5)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>4—7 days, n (%)</td>
<td>11 (28.9)</td>
<td>5 (62.5)</td>
</tr>
<tr>
<td>8—14 days, n (%)</td>
<td>4 (10.5)</td>
<td>2 (25)</td>
</tr>
</tbody>
</table>

Footnote: ICA — internal carotid artery.
ischemia persistent elevations of ICP up to 45 and 70 mm Hg were observed. There was no direct measurement of ICP in patient with intracerebral hematomas. All 3 patients died due to severe ICH and dislocation syndrome that indicates ineffectiveness of DC. An example of justified but inefficient craniectomy is shown in Fig. 8. Thus, there were 3 types of craniectomy in this group: 1) unjustified; 2) justified and effective; 3) justified, but ineffective. Criteria of advisability and effectiveness of DC are presented in Table 2.
Preoperative factors associated with justified DC

Various preoperative factors in groups of justified and unjustifiable craniectomy were analyzed to clarify indications for preventive DC (Table 3). Differences were statistically assessed with non-parametric criteria: Mann-Whitney U-test, Fisher’s exact test.

Following reliable factors of justified DC were established: Hunt-Hess grade V, increased blood flow velocity over 240 cm/s, dislocation over 5 mm and intracerebral hematoma over 30 mL.

Thus, advisability of preventive DC was confirmed in 10 (90.1%) out of 11 patients with Hunt-Hess grade V (Table 3), that is maximum compared with less severe conditions (Fisher’s exact test, \(p=0.003\)). At the same time, procedure was effective in 9 patients who had no clinical signs of brain strangulation intraoperatively. It is noteworthy that all patients with Hunt-Hess grade V underwent surgery within 1 day after aneurysm rupture.

There were 80% of patients with blood flow velocity over 240 cm/s and justifiable DC (Table 3) compared with 42.9% of justified procedures at velocity \(\leq 240\) cm/s (Fisher’s exact test; \(p=0.007\)). It should be also noted that 2 patients underwent surgery on background of progressing ischemic disorders. Preventive craniectomy was justified in both cases.

Intracerebral hematoma was preoperatively diagnosed in 19 patients with preventive craniectomy. Therefore, DC was advisable in 73.7% of cases (Fisher’s exact test; \(p=0.02\)). At the same time, number of justifiable craniectomies became maximum (86%) if the volume of hematoma was over 30 mL (Table 3). Hematoma less than 30 mL was associated with advisable craniectomy in 33% of cases (Fisher’s exact test, \(p=0.002\)). Localization of intracerebral hematoma and advisability of craniectomy were not significantly correlated (Table 3).

Lateral dislocation was able to be preoperatively assessed by CT-imaging in 32 patients (Table 3). DC was justified in all patients with dislocation over 5 mm (\(n=7\)). The same procedure was advisable only in 36% of cases among 25 patients with no dislocation or its value less than 5 mm (Fisher’s exact test; \(p=0.00003\)).

Delayed DC

Delayed craniectomy was performed in 8 patients. Delayed craniectomy is not necessary to be discussed since it was performed for severe ICH and dislocation in all cases. Therefore, we can only determine its effectiveness.

In 3 cases postoperative intracerebral hematomas (30—35 mL) occurred. They were diagnosed and repaired in early postoperative period after aneurysms clipping. Delayed craniectomy was effective in this case (cerebral protrusion 6—16 mm, mean 11 mm). Lateral dislocation was absent in one of these patients and did not exceed 5 mm in 2 of them. Satisfactory 30-day outcome after subarachnoid hemorrhage was noted in 2 patients (GCS score 4—5), one had disabling symptoms (GCS score 3).

Five patients with ischemic disturbances underwent craniectomy within 1—6 days (mean 3 days) after primary surgery with following results: 2 patients — GCS 3, 1 patient — GCS 2, 2 patients — GCS 1. In 1 patient vegetative state was caused multiple ischemic foci in both brain hemispheres. 2 patients died from advanced ischemic le-
sion contralateral to primary trepanation. Delayed craniectomies were ineffective.

It should be noted that effective delayed DC for ischemia ($n=3$) was associated with cerebral protrusion 6—9 mm (mean 7 mm) and dislocation ≤4 mm. In 2 patients with prolapse 12 and 10 mm and dislocation 6 and 8 mm respectively delayed procedure was ineffective.

**Effectiveness of craniectomy depending on cause of ICH**

There was no severe cerebral edema in patients who underwent unreasonable preventive DC. Therefore, causes of ICH were analyzed only in group of justified preventive ($n=20$) and delayed procedure ($n=8$).

Edema was associated with intracerebral hematoma in 15 patients, cerebral ischemia in 11 and other disorders (liquorodynamic) in 2 patients (Table 4).

DC was more effective (in 14 out of 15 patients) in case of intracerebral hematoma (Table 4). One woman with hematoma and effective preventive DC died due to infectious complications. In one dead patient with ineffective preventive craniectomy ICH was caused by 2 hematomas. One of them was removed simultaneously with clipping of aneurysm, the other (imbibition, volume of about 30 mL) occurred in temporal lobe near posterior margin of trepanation. DC with anteroposterior dimension 9.5 cm did not ensure elimination of advanced dislocation syndrome (Fig. 9). There was acute aggravation of patient’s state in 2 days after primary surgery (up to GCS 3—4). Redo surgery consisted of excision of edematous cerebral tissue and enlargement of craniectomy. However, intervention was ineffective.

Effective craniectomy was noted in 7 (63.6%) out of 11 patients with ICH and cerebral ischemia. Four patients died from progressive ischemic cerebral edema despite craniectomy. There were preventive decompressive craniectomies 9.4 and 12 cm respectively in 2 of them. 2 patients had bilateral delayed craniectomies (11 and 10.5 cm in one patient and 10.8 and 9.7 cm in the other one). In 3 out of 4 cases of ineffective craniectomy advanced ischemia occurred in hemisphere contralateral to primary trepanation (Fig. 10).

Efficacy of DC was separately assessed in patients with cerebral ischemia and ICH depending on terms of surgery.

Six patients with ischemia underwent simultaneous clipping of aneurysm and DC (Table 4). Two patients died, vegetative status was observed after 30 days in 1 patient. Severe disability (GCS 2—3) and death were caused by ischemia of several lobes of the brain. Ischemic disorders of 1 lobe were diagnosed in 2 patients with relatively favorable outcomes (GCS 4 and 5).

Five patients with ischemia of several lobes of the brain had delayed craniectomies. There were similar outcomes in this subgroup: 2 patients died, vegetative state was in 1 patient.

Impaired liquor flow due to blood tamponade of arachnoid cisterns and cerebral ventricles can also cause ICH besides ischemia and intracerebral hematomas. It is difficult to analyze effectiveness of DC for this type of ICH in our study, since only 2 patients with preventive craniectomy were referred to this group. In both cases X-ray criteria confirmed advisability and efficacy of craniectomy. One of these patients died from infectious complications.

Postoperative mortality rate among 28 ICH patients was 25% ($n=7$). Mortality among all patients with DC was 15.2% (7 out of 46 cases).

**Discussion**

In order to determine X-ray criteria of advisability of DC we used previous data [9] and our own ideas that cerebral edema is followed by brain protrusion through trephination defect. At the same time, in our opinion ef-

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**Table 2. Criteria of advisability and effectiveness of decompressive craniectomy**

<table>
<thead>
<tr>
<th>Postoperative type of DC</th>
<th>Prolapse (&gt;5 mm)</th>
<th>Lateral dislocation (&gt;5 mm)</th>
<th>Refractory ICH (&gt;20 mm Hg)</th>
<th>Impaired consciousness up to coma (GCS&lt;9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unjustified</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Justified, effective</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No/Yes</td>
</tr>
<tr>
<td>Justified, ineffective</td>
<td>No/Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

---

**Fig. 8. Justified ineffective craniectomy.**

Large ischemic focus in right hemisphere followed by brain prolapse through defect on the right for about 15.7 mm and left-sided dislocation by 7.1 mm.
Effective craniectomy means increased brain prolapse proportional to decreased dislocation that is followed by reduced ICH and risk of severe neurological complications. Craniectomy should be considered ineffective in severe dislocation followed by strangulation-associated death. Absent dislocation and prolapse may be considered as signs of unjustified procedure since there was no cerebral edema or it was mild.

Data confirmed that DC is advisable and effective within the first days after subarachnoid hemorrhage when signs of ICH are intraoperatively identified.

Our study also showed that preoperative risk factors of advanced postoperative cerebral edema are patient’s condition Hunt-Hess grade V (early after hemorrhage), intracerebral hematoma over 30 mL and dislocation over 5 mm. Validity of these factors as indications for preventive DC is also confirmed by literature data [3, 7, 9].

It is difficult to predict refractory ICH associated with cerebral ischemia and to determine indications for preventive DC in such patients.

According to our data, indication for preventive craniectomy in patients with aneurysmal subarachnoid hemorrhage may be severe vasospasm (over 240 cm/s) or signs of acute cerebral ischemia.

Obviously, DC is indicated in patients with clinical and/or X-ray signs of brainstem strangulation (unilateral mydriasis, severe compression of ambient cistern in CT-data). However, surgery is ineffective in these patients as a rule with unfavorable outcome in most of them [10, 11].

According to the literature [12], ineffective craniectomy may be caused by insufficient dimension of defect and absence or small size of dura mater repair. In our opinion, cerebral protrusion may be also discouraged by hematomas between dura mater and skin-aponeurotic flap. It is also clear that DC cannot always prevent brainstem compression in severe ischemic lesion, large hematomas and cerebral ventricles tamponade with blood.

Some reports [9, 13] consider preventive craniectomy more appropriate over delayed procedure since outcomes in these patients are retrospectively better. At the same time, we did not find any literature data about inexpediency of this procedure in patients with aneurysmal subarachnoid hemorrhage. Perhaps, it is partly related to incorrect analysis of the outcomes. For example, in our data overall mortality in patients with DC was 15.2%, in patients with reliable ICH (preventive justified and delayed procedures) — 25%.

It is reasonably to ask what is the cause of unjustified preventive craniectomies in our group? It is more likely that our own indications developed in our center were not sensitive enough to determine the risk of advanced ICH. However, it is worth to note that previous trial [7] devoted to DC for aneurysmal subarachnoid hemorrhage was based on the analysis of patients for the period 1995—2005. At the same time, ICP sensors were not routinely used and CT within intensive care unit was unavailable. Accordingly, decision about emergency proce-

### Table 3. Preoperative factors of justified and unjustified preventive craniectomy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unjustified craniectomy</th>
<th>Justified craniectomy</th>
<th>Between-group differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>40—70</td>
<td>40—80</td>
<td>NS</td>
</tr>
<tr>
<td>Time from SAH, days</td>
<td>4—7</td>
<td>4—7</td>
<td>NS</td>
</tr>
<tr>
<td>Recurrent SAH, %</td>
<td>12—14</td>
<td>6—14</td>
<td>NS</td>
</tr>
<tr>
<td>Hunt—Hess grade</td>
<td>V—II</td>
<td>II—I</td>
<td>NS</td>
</tr>
<tr>
<td>Velocity over 240 cm/s</td>
<td>15—16</td>
<td>15—16</td>
<td>NS</td>
</tr>
<tr>
<td>Localization of aneurysm</td>
<td>ACA—MCA</td>
<td>ACA—MCA</td>
<td>NS</td>
</tr>
<tr>
<td>Intracerebral hematoma, ml</td>
<td>30—&gt;30</td>
<td>&gt;30</td>
<td>NS</td>
</tr>
<tr>
<td>Localization of IH (lobe)</td>
<td>Frontal—Temporal</td>
<td>Frontal—Temporal</td>
<td>NS</td>
</tr>
<tr>
<td>Lateral dislocation, mm</td>
<td>2—7</td>
<td>2—7</td>
<td>NS</td>
</tr>
</tbody>
</table>
| Data confirmed that DC is advisable and effective within the first days after subarachnoid hemorrhage when signs of ICH are intraoperatively identified.

Our study also showed that preoperative risk factors of advanced postoperative cerebral edema are patient’s condition Hunt-Hess grade V (early after hemorrhage), intracerebral hematoma over 30 mL and dislocation over 5 mm. Validity of these factors as indications for preventive DC is also confirmed by literature data [3, 7, 9].

It is difficult to predict refractory ICH associated with cerebral ischemia and to determine indications for preventive DC in such patients.

According to our data, indication for preventive craniectomy in patients with aneurysmal subarachnoid hemorrhage may be severe vasospasm (over 240 cm/s) or signs of acute cerebral ischemia.

Obviously, DC is indicated in patients with clinical and/or X-ray signs of brainstem strangulation (unilateral mydriasis, severe compression of ambient cistern in CT-data). However, surgery is ineffective in these patients as a rule with unfavorable outcome in most of them [10, 11].

According to the literature [12], ineffective craniectomy may be caused by insufficient dimension of defect and absence or small size of dura mater repair. In our opinion, cerebral protrusion may be also discouraged by hematomas between dura mater and skin-aponeurotic flap. It is also clear that DC cannot always prevent brainstem compression in severe ischemic lesion, large hematomas and cerebral ventricles tamponade with blood.

Some reports [9, 13] consider preventive craniectomy more appropriate over delayed procedure since outcomes in these patients are retrospectively better. At the same time, we did not find any literature data about inexpediency of this procedure in patients with aneurysmal subarachnoid hemorrhage. Perhaps, it is partly related to incorrect analysis of the outcomes. For example, in our data overall mortality in patients with DC was 15.2%, in patients with reliable ICH (preventive justified and delayed procedures) — 25%.

It is reasonably to ask what is the cause of unjustified preventive craniectomies in our group? It is more likely that our own indications developed in our center were not sensitive enough to determine the risk of advanced ICH. However, it is worth to note that previous trial [7] devoted to DC for aneurysmal subarachnoid hemorrhage was based on the analysis of patients for the period 1995—2005. At the same time, ICP sensors were not routinely used and CT within intensive care unit was unavailable. Accordingly, decision about emergency proce-
dure has been accepted later. Thus, indications for DC were extended in order to prevent mortality from advanced ICH.

It is difficult to determine indications for preventive craniectomy because even preoperative ICH is not obligatory followed by postoperative hypertension. This is due to the fact that removal of hematoma, elimination of blood clots from basal cisterns, external ventricular drainage may be effective for ICH management. We also admit that in patients with advisable preventive craniectomy according to our criteria ICH may be prevented and/or stopped by other measures (elevated head position, osmotherapy, deep sedation, hypothermia, etc.).

Following data are not in favor of preventive DC in patients without ICH and acute cerebral ischemia:
— advanced ischemic areas in hemisphere contralateral to craniectomy that makes this procedure ineffective;
— similar outcomes in patients with advanced ischemic cerebral disorders who underwent preventive and delayed decompressive craniectomies.

There are following assumptions besides above-mentioned ones:
— advanced surgery consisting of craniotomy enlargement is inevitably followed by more severe blood loss, while anemia with vasospasm aggravate ischemic cerebral disorders [14];

— if cranial defect will be not filled with swollen brain within the first few days after craniectomy then it is likely to be that in future blood and liquor between dura mater and skin-aponeurotic tissues will prevent protrusion of swollen brain.

Potential complications of craniectomy including infections, hemorrhagic events, etc. should be considered for DC. Moreover, this procedure is followed by increased cost of treatment due to prolonged surgery, need for additional materials for dura mater repair and subsequent cranioplasty in most of survivors.

Thus, we consider preventive DC unjustified in patients with aneurysmal subarachnoid hemorrhage without severe vasospasm, acute ischemic disturbances and signs of hematoma followed by ICH during clipping of aneurysm. Patients with high risk of vasospasm and ischemia (massive basal hemorrhage, recurrent hemorrhages, advanced age, etc.) should be followed-up at ICU after microsurgical repair of aneurysm. Invasive measurement of ICP is required in case of impaired consciousness or elective sedation. Prevention of severe course of vasospasm is the main goal of treatment in these patients (correction of hypercoagulation, transfusion, hemodynamic therapy regarding central perfusion pressure, systemic and selective endovascular administration of calcium channel blockers, etc.). Urgent delayed craniectomy is indicated for the first signs of unresponsive to

### Table 4. Efficacy of DC and postoperative outcomes in patients with ICH

<table>
<thead>
<tr>
<th>Cause of ICH</th>
<th>DC type</th>
<th>Number of patients</th>
<th>DC efficacy</th>
<th>GCS in 30 days after SAH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>VI—V</td>
<td>III—II</td>
</tr>
<tr>
<td>IH</td>
<td>Preventive DC</td>
<td>12</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Delayed DC</td>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Ischemia</td>
<td>Preventive DC</td>
<td>6</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Delayed DC</td>
<td>5</td>
<td>3</td>
<td>–</td>
</tr>
<tr>
<td>Other disturbances</td>
<td>Preventive DC</td>
<td>2</td>
<td>2</td>
<td>–</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>28</td>
<td>23</td>
<td>7</td>
</tr>
</tbody>
</table>

Fig. 9. Ineffective preventive DC in patient with two IHs.

CT-scan in 1 day after clipping of left middle cerebral artery aneurysm, left-sided brain prolapse through DC by 4.3 mm and dislocation to the right by 9.4 mm. Explanations in the text.
therapy ICH. Hemisphere with more severe edema or bilateral approach for lesion of both hemispheres should be preferred.

It is worth to note that intraoperative factors also affect probability of postoperative ICH.

It is impossible to determine objective intraoperative risk factors of ICH due to their variability. Therefore, need for simultaneous craniectomy during aneurysm clipping will depend on subjective assessment of situation by neurosurgeon: brain trauma severity, coagulation of small arteries and veins within surgical approach, features of hematoma removal and others.

In our opinion, analysis of correlation between duration of cerebral vessels clipping and hemorrhage severity on the one hand and postoperative ICH on the other hand is perspective.

Concepts of advisability and effectiveness of DC for aneurysmal subarachnoid hemorrhage may be used for further study of ICH and its correction in prospective samples. The main purposes of our further research are to reduce the incidence of unjustified craniectomies, to increase effectiveness of advisable procedures and to improve overall outcomes in patients with aneurysmal subarachnoid hemorrhage.

Conclusion

Sign of effective craniectomy is brain protrusion into trephination defect over 5 mm followed by decreased location less than 5 mm and no unresponsive to therapy ICH.

In most of cases preventive DC in aneurysms clipping is indicated in extremely ill patient (Hunt-Hess grade V), lateral dislocation over 5 mm, intracerebral hematoma over 30 mL and signs of acute cerebral ischemia (severe cerebral vasospasm and ischemic foci formation). In other cases, it is advisable to apply intensive therapy aimed at prevention and treatment of vasospasm and delayed craniectomy for the first signs of refractory ICH.

Authors declare no conflict of interest.
Indications for DC in patients with aneurysmal SAH is still unclear problem. Despite this fact there are only few publications in world literature. Outcomes in decompenated patients are still unfavorable. The main pathophysiological features encountered by neurosurgeon regarding DC are consequences of primary hemorrhage, secondary ischemia due to cerebral vascular spasm, cerebral edema and ICH.

In this report authors retrospectively analyzed sufficient number of patients \( n = 46 \) in order to develop criteria of advisability and effectiveness of DC, to clarify indications for preventive DC in patients with SAH after microsurgical clipping of aneurysms.

Most of patients \( n = 38 \) underwent preventive DC that indicates their severity and risk of advanced postoperative ICH.

The authors formulated the main criteria for preventive DC in certain cases. In our practice we also adhere to similar recommendations. It is important that besides ICH control, DC eliminates the need for total sanation of distal Sylvian fissure on background of ruptured aneurysms of middle cerebral artery. The last is followed by reduced trauma of cerebral tissue.

We prefer bifrontal decompression instead of bilateral DC for axial dislocation.

This work is undoubtedly relevant and concretizes concepts for further researches.

\[ R.S. \text{ Dzhindzhikhadze (Moscow, Russia)} \]
Authors’ main objective was to clarify indications for preventive DC in patients with SAH after microsurgical clipping of aneurysms and to decrease incidence of unjustified procedures. Criteria of "justified" and "unjustified" preventive DC have been developed.

In authors’ opinion, unjustified DC is considered in postoperative brain dislocation less than 5 mm. Choice of this variable as criterion of unjustified DC is not entirely clear, since dislocation may be absent in edema and/or ischemia unilateral to trephination defect. This situation arose in the 2nd group where advanced brain protrusion without dislocation were observed in 17 patients. In our opinion, deployment of ICP sensor at preoperative level would be able to assess more objectively ICH and to determine "justified" and "unjustified" DC (only 21 out of 38 patients underwent invasive ICP monitoring in this trial).

Due to some limitations (retrospective analysis, small sample size) authors were unable to significantly establish the role of some important prognostic factors of unfavorable outcomes including age, terms of surgery, redo ruptured aneurysm, SAH severity [6]. Nevertheless, the question of advisability and efficacy of craniectomy is very important. Obviously, surgeon determines type of craniectomy in view of both preoperative data and intraoperative subjective considerations in some patients. Objective verification of these subjective factors and prevention of craniectomies without proper causes is the main goal of this work. Undoubtedly, more frequent invasive ICP monitoring would only strengthen evidence base for the study.

The article is a new step towards further research of preventive DC in patients with high risk of ICH.

V.G. Dashyan (Moscow, Russia)

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Neuroparalytic keratitis (NPK) is caused by dysfunction of trigeminal and facial nerves and includes two clinical components: corneal injury — neurotrophic keratitis and paralytic lagophthalmos.

In our practice, NPK is the most common after surgery for cochlear nerve schwannoma, cerebellum tumors and strokes in some cases. Impaired function of trigeminal nerve is associated with aggravation of corneal sensitivity and tissue metabolism. There is decreased level of trophic factors and neurotransmitters (insulin-like growth factor-1, substance P, nerve growth factor, etc.) which are key to maintain anatomical integrity and function of ocular surface [1]. It is accompanied by neurotrophic keratitis with recurrent inflammation, recurrent or persistent corneal erosions and impaired regeneration [2—4]. Dysfunction of facial nerve additionally leads to lagophthalmos that aggravates the course of neurotrophic keratitis.

NPK is poorly responsive to medication because it is characterized by pronounced tear deficiency, impaired or absent corneal sensitivity. These factors aggravate healing of corneal epithelial defects and lead to “clean” corneal ulcers and melting of corneal stroma. It is especially true in concomitant lagophthalmos.

The situation is complicated by contraindications to medicines stimulating corneal epithelialization (solcoseryl, actovegin, etc.), vitamins and physiotherapeutic procedures in NPK patients after surgery for brain tumors.

All above-mentioned factors increase risk of secondary infection, progressive suppurative corneal ulcers (SCU), perforation, endophthalmitis followed by loss of the eye [5—7]. Keratoplasty is often preferred by ophthalmologists due to inefficient medication and unfavorable prognosis of corneal ulcers [8].

Various methods of lagophthalmos repair are known [9—11]. However, they are insufficient per se for NPK correction. Similarly, corneal repair alone is also ineffective without treatment of lagophthalmos.

We did not find any optimal surgical algorithm for NPK-associated SCUs in available literature.

The aim of our study was to develop surgical treatment of NPK-associated SCUs. Keratitis is a result of intracranial pathological processes in these cases.

Material and methods

There were 12 patients (8 women and 4 men aged 28—65 years, mean 43±5 years, 13 eyes) with NPK-associated SCUs. Mean anamnesis of SCUs was from 2 weeks to 1.5 months prior to admission to Research Institute of Eye Diseases. Outpatient antibiotic therapy was administered in all patients without positive effect.

Mean visual acuity was 0.09±0.05. Schirmer’s test on affected eye revealed moderate and severe impairment of tearing in all patients (1—10 mm), on contralateral eye — mild or moderate grade (5—15 mm, norm 15—20 mm). Corneal sensitivity was assessed by using of Radzikovsky’s algesimeter with a weight of 10 g, it was absent in all quadrants in all patients. Palpebral fissure width was 8.6±0.16 mm, lagophthalmos — 5.86±1.35 mm (Table).

Staphylococcus aureus, epidermal staphylococcus and pseudomonas aeruginosa were revealed in conjunctival cavity in 8, 4 and 1 case, respectively.

Besides lagophthalmos, clinical signs include mild conjunctival hyperemia, copious mucopurulent discharge from conjunctival cavity. Central SCUs with advanced corneal melting were predominant. Patients were divided into 2 groups depending on severity of disease: group 1 with moderate severity of SCUs and group 2 with severe grade. In group 1 (4 patients, 4 eyes) SCUs occupied ½ of corneal stroma depth, ulcers’ diameter was...
5—7 mm. These patients underwent lamellar keratoplasty (LK). There were advanced SCUs in the 2nd group (8 patients, 9 eyes): in 5 eyes deep ulcers 5—8 mm in diameter occupied over 2/3 of corneal depth; in 4 eyes SCUs with diameter of 7—10 mm extended entire corneal layers: descemetocoele was in 2 cases and corneal perforation — in other 2 patients. In this group penetrating keratoplasty (PK) was performed.

In all patients flicker fusion rate was over 25 Hz, lability — 20 uA. There were no signs of endophthalmitis according to beta-scanning.

Two aspects we indications for surgery: 1) advanced suppurative process without positive dynamics despite adequate medication; 2) threat of perforation or perforation of cornea.

In view of severe state of patients with NPK-associated SCUs surgical treatment was aimed at corneal sanation and correction of neurotrophic disorders.

All patients underwent keratoplasty followed by total auto-conjunctival covering of the graft (auto-conjunctiva was fixed to the limbus by interrupted seams) and partial permanent tarsorrhaphy (patent of the Russian Federation “Method of treatment of neurotrophic keratitis with lesion of central corneal optical zone in lagophthalmos” No. 2299048 dated May 20, 2007).

LK and urgent K were applied in groups 1 and 2, respectively. In 5 cases sinus trabeculectomy was performed simultaneously with PK du to decompensated intraocular pressure (IOP). Silicone drainage tube into lower outer quadrant was required in 2 patients with abundant purulent exudation and hypertension (“Method of treatment of complicated purulent corneal ulcer” No. 2309710 dated February 21, 2006). Silicone drainage tube was useful already in the first hours after keratoplasty for permanent outflow of abundant fibrinous exudate from anterior chamber of the eye and IOP normalization. 2 patients with cataract and no profuse purulent exudation required extracapsular cataract extraction followed by intraocular lens deployment simultaneously with PK.

Active postoperative medication was administered in all patients: frequent or forced instillations of antibiotics and antiseptics (fluconazole and chlorhexidine in suspected fungal infection); nonsteroidal anti-inflammatory drugs, preservative-free artificial tears drugs, parabulbar injections of antibiotics, oral intake of antibiotic and antifungal agents. Instillations of antiseptics have been performed for a long time (12—15 months), preservative-free artificial tears drugs — for life.

Follow-up period was 1—8 years. Median of catamnesis — 39.4 months.

Results

In 1 eye conjunctival flap adhered to lower third of cornea. In other cases, partially dislocation downwards with exposure of epithelialized central zone of corneal transplant was observed after 2.7±0.4 weeks.

In the 1st group engraftment was pellucid in all 4 cases without recurrent suppurative keratitis within follow-up (5 years). In the 2nd group PK was followed by pellucid engraftment in 5 eyes and translucent in 4 eyes, mean visual acuity increased from 0.09±0.05 to 0.21±0.13 (in 29% — by 0.55), lagophthalmos decreased from 5.86±1.35 to 3.01±0.75 mm (Table, Figs. 1, 2).

Recurrent SCUs on the transplant (Pseudomonas aeruginosa in 2 cases, staphylococcal infection — 1, in 2 cases causative agent was unknown) occurred in 5 patients (5 eyes) of the 2nd group within 1.5±0.5 years on the average. Therefore, redo keratoplasty was performed. After that muddy engraftment was observed in all patients. In view of severe comorbidities this outcome was considered favorable since eye was preserved as organ. Moreover, there was preserved visual acuity from correct light projection to 0.02.

In 1 patient (1 eye) of the 2nd group “clean” melting of corneal stroma 4×5 mm occurred on penetrating graft. Amnioplasty and biocoverage with sclerocorneal flap was carried out that was followed by stable transplant epithelization within further follow-up (6 years).

Histological examination of excised corneal discs revealed necrosis and incomplete regeneration that is typical for neurodystrophic keratitis as a symptoms of advanced corneal lesion.

Increased tearing in affected eye occurred in 2 patients after 5 years (Schirmer’s test value increased from 0 to 5 mm in one patient and from 0 to 20 mm in the other). In our opinion, it is due to surgical facial nerve repair in 3 years after keratoplasty. In other cases, tearing was permanently impaired even in long-term period.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Visual acuity</th>
<th>Lagophthalmos, mm</th>
<th>Palpebral fissure, mm</th>
<th>Schirmer’s test of affected eye, mm</th>
<th>Schirmer’s test of contralateral eye, mm</th>
<th>Corneal sensitivity, from 0 to 2 scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior to surgery</td>
<td>0.09±0.05 (correct light projection 0.4)</td>
<td>5.86±1.35 (2—10)</td>
<td>8.6±0.16 (8—12)</td>
<td>5.5±2.86 (1—10)</td>
<td>8.75±2.07 (5—15)</td>
<td>0.57±0.28 (0—2)</td>
</tr>
<tr>
<td>1 year after keratoplasty</td>
<td>0.21±0.13 (correct light projection 0.8)</td>
<td>3.01±0.75 (1—5)</td>
<td>5.11±0.84 (3—8)</td>
<td>5.5±2.5 (1—10)</td>
<td>8.94±2.1 (5—15)</td>
<td>0.65±0.3 (0—2)</td>
</tr>
<tr>
<td>5 year after keratoplasty</td>
<td>0.21±0.14 (correct light projection 0.7)</td>
<td>3.3±0.7 (1—6)</td>
<td>5.26±1 (3—8)</td>
<td>6.86±2.43 (1—15)</td>
<td>8.8±1.8 (5—15)</td>
<td>0.71±0.3 (0—2)</td>
</tr>
</tbody>
</table>
Discussion

Keratoplasty, autoconjunctival repair and partial permanent tarsorrhaphy are optimal for unresponsive to treatment NPK-associated SCUs.

Palpebral fissure repair and total autoconjunctival coverage of the graft are followed by complete epithelization of transplant. Trophic support of the graft is achieved through the contact of "denervated" cornea with conjunctival bloodstream, mechanical protection of the graft from damage and drying, and epithelial cells migration from conjunctival flap to corneal surface. This mechanism was experimentally confirmed by V.A. Vasilieva and some foreign authors [11—13]. Autoconjunctival flap as a permanent source of epithelial cells reduces the risk of persistent erosions of the graft. In our opinion, growth of conjunctival vessels and adhesion of autoconjunctival

Fig. 1. Right eye of patient P., 69 years old. State after previous stroke.
a — lagophthalmos, suppurative corneal ulcer; b — 1 month after PK, total autoconjunctival coverage, partial external tarsorrhaphy; c — 12 months postoperatively, complete epithelization, pellucid engraftment.

Fig. 2. Right eye of patient R., 35 years old. State after cochlear schwannoma removal.
a — lagophthalmos, advanced suppurative corneal ulcer with local thinning; b — 2 weeks after PK, total autoconjunctival coverage, partial external tarsorrhaphy; c — 10 months after PK, complete epithelization, pellucid engraftment.
flap to corneal surface are considered favorable factors due to permanent protection and nutrition of the cornea.

Patients with NPK should be carefully followed-up due to high risk of recurrent purulent infection on the eye with impaired innervation: early detection and treatment of corneal erosions and ulcers and prevention of secondary infection. Patients with NPK should be informed by ophthalmologists about high risk of complications, need for regular observation and use of local antiseptics and permanent administration of preservative-free tear eye drops.

Keratoplasty, autoconjunctival repair and tarsorrhaphy helps are able to save eye as an organ and to achieve favorable outcomes in most of cases. Good results after LK are probably associated with less severe preoperative corneal lesion. We managed to keep the eye as an organ in all 13 cases, eyesight in 6 patients and improve visual acuity in 4 patients.

Conclusions

1. Optimal treatment of NPK-associated advanced supplicative corneal ulcer is corneal transplantation with simultaneous autoconjunctival covering and partial permanent tarsorrhaphy.

2. There is high risk of recurrent corneal erosion in patients with neuroparalytic keratitis and supplicative corneal ulcers due to permanent decrease of tearing and impaired innervation. Preservative-free tear eye drops are indicated in all patients with neuroparalytic keratitis.

3. Regular lifelong follow-up is required after keratoplasty and autoconjunctival repair for neurotrophic ulcerative keratitis and paralytic lagophthalmos followed by corneal ulcers because of high risk of recurrent infection.

Authors declare no conflict of interest.

REFERENCES


Received: 07.06.17

Commentary

Problem of NPK-associated supplicative corneal ulcers is of interest for neurosurgeons and neurologists despite its predominant ophthalmological field.

It is known that in neurosurgical practice neurotrophic keratopathy complicated by lagophthalmos is caused by tumors (brain tumor, meningioma), traumatic brain injury, brainstem stroke, etc.

Current approaches to treatment, intraoperative monitoring, advanced medication, development of various methods for prevention and treatment of keratopathy significantly reduced incidence of severe neurotrophic keratopathy and especially corneal ulcers. Nevertheless, this serious complication can occur in some circumstances (medical, social). Thus, review of this issue in neurosurgical literature is actual.

Treatment of 12 patients with supplicative corneal ulcers is presented in the article. Surgery included elimination of unresponsive to therapy focal inflammation. Authors proposed combination of corneal repair (lamellar or penetrating depending on grade of corneal lesion), autoconjunctival coverage of the graft and partial blepharorrhaphy. There are favorable outcomes due to effective management of inflammation, improved visual acuity in some cases and preserved eye as an organ in all cases. It is important that it was done in patients with impaired corneal regeneration and high risk of graft rejection. The last is confirmed by redo keratoplasty almost in half of cases after previous penetrating keratoplasty.

N. K. Serova (Moscow, Russia)
Tumors of subcortical nuclei are rare pathology accounting for about 1—5% of all intracerebral tumors in children and adults. Incidence of correct diagnosis of subcortical tumors was low (about 10%) and postoperative mortality was 50—70% before introduction of current neuroimaging methods [1—3]. CT and MRI are useful to correctly determine intracerebral tumors topography while neurosurgeons are able to define the most optimal surgical approach with lower risk of postoperative complications [4—10]. Nevertheless, precise topical diagnosis of subcortical nuclei tumors may be still difficult, while surgical procedure may be followed by high risk of injury of deep cerebral structures and accordingly severe disability of patient.

MR-tractography makes it possible to determine normal course of motor conductive pathways within inner capsule and brainstem and their dislocation in tumors of subcortical nuclei [11—13]. This method gives more accurate information about tumor topography and optimal approach without involvement of functionally important zones may be determined.

The objective of the study was to demonstrate the choice of surgical approach and surgery for deep local tumors by using preoperative MR-tractography, MRI and neurological status in two cases.

Normal MR-anatomy of the main subcortical structures and inner capsule is presented in Fig. 1.

**Clinical case №1**

Patient A., 8 years old, awkwardness in right hand has been occurred 3 months before admission to the Burdenko Neurosurgery Center. Therefore, advanced weakness in the arm followed by weakness in the right leg was noted. In contrast-enhanced MRI left-sided cystic tumor of lenticular nuclei and lateral thalamus was observed (Fig. 2a, b). Tumor with clear borders deformed adjacent thalamic parts, inner capsule and bottom of lateral ventricle. Contrast agent accumulation was noted within solid node.

There was severe right-sided hemiparesis with impaired muscular strength up to 2 and 3 scores in arm and leg, respectively. Extrapyramidal muscular disorders were diagnosed. Visual fields were intact.

MR-tractography was used to determine tumor topography and optimal surgical approach (Fig. 2c—e). Reconstruction of motor pathways of inner capsule revealed their deformation and dorsal and medial displacement on the left. So, tumor of lenticular nucleus was supposed. There was predominant dorsomedial displacement of inner capsule and thalamus and lateral dislocation of insular cortex.

Transinsular approach seemed to be optimal in view of dorsomedial and medial displacement of motor pathways of inner capsule.

**Surgery.** Osteoplastic frontotemporal craniotomy followed by dissection of posterior lateral fissure was made. Deformed insular cortex was found. Cortex was dissected within the most severe deformation and swelling. Cystic tumor lied 5 mm deep to the cortex, large volume of xanthochromic output was drained. Dense gray tumor node was visualized. Tumor was excised by using of bipolar coagulation, suction, ultrasonic suction. There were clear borders of tumor as a rule. Direct stimulation of motor pathways has been simultaneously performed. Response from inner capsule fibers was obtained. We completely excised tumor up to visually intact brain tissue. Tumor removal was followed by formation of large cavity.

Histological diagnosis: pilocytic astrocytoma (WHO I).

Early postoperative improvement of right-sided hemiparesis was noted.
Control MRI: picture of total tumor removal, no deformation of subcortical structures. There is left-sided postoperative defect in posterior lenticular nucleus (Fig. 2f, g). Thalamus and inner capsule are intact. No deformation of left corticospinal tract in MR-tractography (Fig. 2h, i).

Further rehabilitation was followed by complete recovery of right limbs’ function.

Clinical case № 2

Patient S., 15 years old with periodic headaches and transient numbness and weakness in right limbs for 1.5 years before hospitalization. Therefore, advanced weakness and impaired walking were observed.

MRI-imaging revealed left-sided anterobasal thalamic tumor (Fig. 3a, b). Trivial deformation of lateral ventricle’s bottom and dorsal thalamus was noted.

MR-tractography was used to determine tumor topography and optimal surgical approach (Fig. 3c, d). Reconstruction of corticospinal tracts confirmed posterolateral dislocation of inner capsule’s pathways on the left.

Right-sided hemiparesis with impaired muscular strength (4 scores) was diagnosed. Hemianopsia was absent.

In view of MRI and MR-tractography data transcortical approach was preferred despite no hydrocephalus, minimal deformation of lateral ventricle and need to dissect anterior thalamus. It seemed to be the least traumatic due to posterior displacement of corticospinal tract.

Surgery. It was performed linear incision of soft tissues in frontal area. Right-sided osteoplastic frontal craniotomy was followed by exposure of sagittal sinus margin. Dura mater was dissected arcutately with base turned to sagittal sinus. Right hemisphere was withdrawn laterally to visualize corpus callosum, pericallosal cistern has been opened, anterior cerebral arteries were diverged to the sides. Corpus callosum was dissected for 1.5 cm in order to enter left lateral ventricle. Its bottom was somewhat deformed. There were vascular plexus, interventricular orifice and thalamo-striate vein in ventricular lumen. Ependyma was dissected within the most severe deformation of lateral ventricle’s bottom between vascular plexus and thalamo-striate vein at the level of Monro foramen. Gray-yellow tumor lied at the depth of 5 mm. Specimen was excised for histological examination. Tumor removal was carried out by using of conventional and ultrasound suction, bipolar coagulation, dissector and fenestrated forceps. Resection of central tumor followed by subsequent excision of peripheral parts were applied. Basal penetrating vessels were partially coagulated and intersected. It should be noted that borders were unclear in some zones. Entire tumor was gradually excised up to intact cerebral tissue. Regression of lateral ventricle deformation was observed after tumor removal. Hemostasis was achieved with bipolar coagulation and gauze.

Histological diagnosis: pilocytic astrocytoma (WHO I).

Hemiparesis remained the same in postoperative period.

After 1 year MRI-data of postoperative left-sided defect of anterior thalamus without residual tumor were obtained (Fig. 3e, f). MR-tractography did not show de-
Fig. 2. Case report №1.
a, b — MRI prior to surgery. Contrast-enhanced T1-mode in axial (a) and frontal (b) planes. Explanations in the text; c—e — MR-tractography prior to surgery. Thinning, dorsal and medial displacement of corticospinal tract on the left (arrows); f, g — contrast-enhanced MRI after surgery in axial (f) and frontal (g) planes.

See continue of the Figure on the next page
formation and displacement of inner capsule on the left (Fig. 3g—i).

Complete muscular recovery of right arm and leg was noted.

Discussion

It is often difficult to define optimal surgical access for subcortical surgery due unclear data about tumor placement. There are similar problems in surgery for thalamic tumors. The most advisable approach is determined depending on localization of the tumor within these structures, its dimensions, dislocation of adjacent structures (inner capsule, rostral midbrain, fornix, lateral and third ventricles), presence or absence of hydrocephalus. Surgical access should be able to avoid injury of functional structures and disability of the patient.

Until now, surgeons have adhered to medication for subcortical tumors due to high incidence of postoperative complications and mortality [6, 14]. High-field MRI, comprehensive awareness for neurosurgical anatomy, accumulation of microsurgical experience and development of minimally invasive procedures are followed by advanced indications for subcortical surgery. At the same time, postoperative mortality and morbidity are significantly improved. There are more and more publications highlighting outcomes of surgery for subcortical nuclei tumors in not only single cases but also in series of patients [4, 9, 15]. Authors [6, 9, 11, 16] classify deep tumors depending on their topography, describe neurosurgical approaches to subcortical tumors depending on localization, highlight their advantages and disadvantages.

In current neurosurgery the main objectives of intracerebral tumors management are their radical removal and minimization of postoperative disability. At the present time it is undoubtedly to excise subcortical focal tumor (pilocytic astrocytoma) because radical surgery may be followed by improved neurologic symptoms, prolonged disease-free period or recovery. Neurosurgical treatment of subcortical tumors is particularly important due to high incidence of pilocytic astrocytoma in children. Infiltrative tumors with compact part (in MRI) may be also successfully resected with improvement of patient’s state. It is a factor of better recurrence-free and overall survival.

Standard MRI-scans including high anatomical quality don’t assess conductive pathways, their deformation and dislocation or destruction in focal and infiltrative brain tumors. In this regard MR-tractography is very important for deep tumors located near corticospinal and visual tracts.

Diffusion-tensor MR-tractography is based on measurement of water molecules movement along nerve fibers. It is followed by reconstruction of normal conductive pathways and those in different pathologies of central nervous system such as metabolic cerebral lesions, disseminated sclerosis, vascular encephalopathy, severe craniocerebral trauma, brain and spinal cord tumors [12, 13].

Burdenko Neurosurgery Center accumulates an experience of tractography for deep tumors. This report describes two cases of subcortical tumors with certain topographic features. Surgical approach was determined via analysis of MR-tractography data. It was confirmed that subcortical tumors depending on dimensions and location can deform and displace corticospinal tract within inner capsule and brainstem. This information is valuable to choose optimal approach. Thus, transcallosal access is advisable for posterolateral displacement of motor pathways (case report №2). Transinsular or temporal transchoroidal approaches are less traumatic for anterome-
Fig. 3. Case report №2.

a, b — MRI prior to surgery. Contrast-enhanced T1-mode in axial (a) and frontal (b) planes. Explanations in the text; c, d — MR-tractography prior to surgery. Posterolateral displacement of corticospinal tract on the left (arrows); e, f — MRI in 1 year after surgery. Contrast-enhanced T1-mode in axial (e) and frontal (f) planes. Explanations in the text. Trajectory of contralateral transcalsal approach is determined in frontal projection.

See continue of the Figure on the next page
dial and medial dislocation of inner capsule (case report №1). Complete excision was performed in both cases that was followed by improved neurological symptoms and quality of life.

Conclusions

MR-tractography is useful to determine features of dislocation or destruction of corticospinal tract within inner capsule and brainstem and to detail tumor location within subcortical nuclei. Therefore, it is followed by choice of optimal approach, radical resection of focal tumor with regression of neurological symptoms and improved quality of life.

Authors declare no conflict of interest.

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Besides brainstem deep cerebral structures are also somewhat difficult for surgery. Choice of approach is the key for outcomes after these procedures. Complications due to trauma of functionally important adjacent deep structures such as inner capsule, midbrain can lead to severe disability of patient. Constant desire to reduce invasiveness in both medical and diagnostic medicine has been reflected in this work. It is natural that clinicians strive to obtain as much information as possible about both anatomical and functional individual characteristics of particular patient.

Radiological diagnosis has come out beyond X-ray procedures alone. Advanced development of MRI (new applications, contrast agents, quantitative and visual post-processing) influenced quality of neurosurgery. One of these applications (tractography) is analyzed in the article. MR-tractography is able to give information about normal course of motor pathways within inner capsule and brainstem and their dislocation in case of subcortical tumors. Method is not absolutely new, however advanced quality significantly improves diagnostic assessment of cerebral and spinal conductive pathways, their relationship with affected zones and vessels.

Technique is actual because dislocation and destruction of conductive pathways may be estimated by using of diagnostic data. There is an opportunity to choose the most optimal surgical approach besides accurate information about tumor’s boundaries and invasion into nerve fibers.

There are various reports in foreign literature about this issue in contrast to national databases. Relatively low prevalence of this technique is due to difficult post-processing of data although methodology is not technically complex in general.

The authors rightly note that until now surgeons preferred medication for subcortical tumors due to high incidence of postoperative complications.

M.B. Dolgushin (Moscow, Russia)
Nasal liquorrhea is one of the serious problems in skull base tumors surgery and associated with high risk of suppurative-septic complications. Liquoric fistula repair after endoscopic and microsurgical surgery for basal tumors usually results closure of the defect with various autologous materials (fat, fascia, pedicled periosteal-aponeurotic or mucoperiosteal flap) and occlusion with fibrin-thrombin glue [1, 2].

Endoscopic transnasal approaches to ACF base become more and more popular because minimally invasive technique is able to avoid traction of brain and cranial nerves [3]. However, only small tumors located along midline are suitable for such procedures. Disadvantage of endoscopic procedures is high incidence of nasal liquorrhea (5—31.6%) [4, 5].

Intracranial microsurgical accesses (subfrontal/supraorbital) are indicated for large meningiomas of ACF base, as well as in patients with intact smelling in order to prevent postoperative anosmia [6].

Platelet gel (thrombogel) is a two-component glue consisting of concentrated fibrinogen solution with platelet growth factor and thrombin solution. Both components are obtained from autologous PRP that is followed by completely autologous gel and prevents risk of infections [14].

J. Thorn et al. [14] used thrombogel combined with bone crumb for reconstructive maxillofacial surgery.

We present successful closure of frontal sinus fistula after removal of large ACF meningioma via right-sided subfrontal approach by transcutaneous platelet gel injection into the sinus.
Case report

Patient G., 60 years old, with large basal ACF meningioma (Fig. 1) followed by emotional (reduced criticism, memory for current events) and visual impairment (visual acuity: OD=1.0; OS=0.4. Visual field: OD — normal, OS — impaired central vision, narrowed in temporal half).

Tumor was excised via right-sided subfrontal approach without any peculiarities and technical difficulties. Intraoperative dissection of frontal sinus was followed by its repair with pedicled periosteal-aponeurotic flap and fixation to dura mater (Fig. 2). Tumor was completely removed. There were no postoperative neurologic disorders and nasal liquorrhea.

Severe stunning and hiccough appeared after 3 days. There were CT-signs of advanced diffuse edema of frontal lobes which was prior to surgery, diencephalic edema and narrowing of ambient cistern (Fig. 3).

Patient underwent bilateral decompressive trepanation next day (primary bone flap and external parts of sphenoid wing resection on the right; frontotemporal trepanation on the left). Right-sided frontal subcutaneous and epidural accumulation of pus was intraoperative-ly observed (Enterobacter asburiae). Frontal sinus repair with aponeurosis was visually intact — frontal defect was covered by periosteal-aponeurotic flap all over and sutured to DM.

Normal consciousness and no hiccough were revealed after surgery. Meningitis was excluded after lumbar puncture. Antibacterial therapy was administered due to pyoinflammatory changes of the wound (subcutaneous and epidural).

After 2 days nasal liquorrhea occurred. Pneumocephalus progression was revealed on CT (Fig. 4). There were complaints of severe headache, consciousness aggravated up to moderate stunning.

In view of subcutaneous growth of Enterobacter asburiae in right frontal area it was considered that redo repair of frontal sinus was associated with high risk of intracranial infection. External lumbar drainage under advanced cerebral edema could lead to dislocation syndrome.

Therefore, frontal sinus obliteration with autologous platelet gel was preferred. Surgery was performed under sedation with propofol 4 mg/kg/h and respiratory protection with laryngeal mask, SIMV ventilation followed by saturation 98—100%. Patient’s venous blood was conventionally withdrawn into container (CPDA1 stabilizer 63 mL, “Macopharma”, France). Autologous blood 450 mL (+ 63 mL of stabilizer) was separated into red cells 233 mL, PPP 240 mL and PRP 40 mL in Xtra autotransfusion system (“Sorin group”, Germany) according to standard protocol for PRP. Red cells and PPP were intravenously reinfused immediately after separation (36 ml/min). 6 out of 40 mL of PRP were used to prepare thrombin. PRP was mixed with PPP 8 mL and calcium chloride 10% 1 mL. Therefore, mixture was divided into

4 Petri dishes until formation of clot (40 min). 8 mL of thrombin rich liquid were obtained from this mixture after clot retraction (Fig. 5a). In vitro control was performed before thrombogel injection into frontal sinus. Thrombin 1 mL and PRP 4 mL were mixed in a syringe 10 mL followed by stopwatch switching-on. Thrombogel was formed after 15 s (Fig. 5b).

Aseptic percutaneous puncture of frontal sinus was performed within anterior margin of the defect by using of needle 14G. Sinus was irrigated with saline. PRP mixed with thrombin was injected by 5 mL step-by-step (PRP 4 mL + thrombin 1 mL) into frontal sinus where final platelet gel was formed. Entire procedure was per...
formed within 15 min; 30 mL of platelet gel were injected (Fig. 6).

There was no recurrent postoperative liquorrhea. CT confirmed significant regression of pneumocephalus (Fig. 7).

Antibacterial therapy was very effective for suppurative inflammation of postoperative wound. Patient was discharged without severe neurologic disorders and nasal liquorrhea.

Two-month follow-up did not reveal nasal liquorrhea and paranasal sinuses inflammation.

**Discussion**

Frontal sinus repair by temporal muscle or fat from anterior abdominal wall may be associated with risk of infection. In this situation pedicled periosteal flap should be preferred for sinus reconstruction [16].

External lumbar drainage for 5—7 days is usually deployed for nasal liquorrhea after skull base repair. Redo repair of sinus is applied if drainage is ineffective [13].

Lumbar drainage was refused in our clinical case due to risk of dislocation followed by brainstem strangulation.
in conditions of severe edema of frontal lobes. Moreover, redo reconstruction of frontal sinus could be accompanied by intracranial infection, meningitis, cerebral abscesses and epidural empyema due to epidural infection (*Enterobacter asburiae*).

In our opinion, nasal liquorrea was due to cerebrospinal fluid outflow through sutures fixing aponeurosis to the edge of DM. Conventional adhesive compositions (fibrin-thrombin glue) is not advisable for frontal sinus filling and DM sealing because frontal sinus volume is too large for standard amount of fibrin-thrombin glue used for skull base repair. In this situation the use of autologous blood is advisable to prepare enough volume of autologous platelet gel for filling of entire frontal sinus

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*Fig. 5. Type of glue.*

a — mixture of PRP with PPP 8 mL and calcium chloride 10% 1 mL as a thin layer in Petri dish; b — thrombogel appearance.

*Fig. 6. Percutaneous filling of right frontal sinus by thrombogel.*

*Fig. 7. CT in 9 days after the 3rd surgery.*

Improvement of pneumocephalus.
cavity. Fibrin filaments are able to firmly fix entire thrombogel to bone defect followed by hermetic closure of DM.

Viscosity of platelet gel is similar to that of packed red cells, so injection should be done through the needle 16—14G. Gel formation time in particular patient should be assessed in vitro prior to injection. The last is necessary to determine optimal delivery rate and ensure further reliable fixation of platelet gel within the sinus. PRP obtained in Xtra centrifuge (“Sorin group”, Germany) additionally consists of macrophages and granulocytes which stimulate local immunity besides proliferation and reduce risk of infectious complications.

Normal level of red blood cells and platelets is necessary for successful preparation of platelet gel (platelets near upper rather lower limit is desirable).

Aseptic meningitis as complication of platelet glue injection was described by M. Patel et al. [17]. There were no any complications in our practice.

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5. https://doi.org/10.1227/01.NEU.0000335069.30319.1E


https://doi.org/10.1016/j.otc.2015.08.002


Conclusion

Percutaneous obliteration of frontal sinus by thrombogel proved to be effective and minimally invasive procedure for liquoric fistula repair. In our example we have demonstrated efficacy and safety of platelet gel for skull base repair in case of infectious wound complications. We consider thrombogel is only effective sealant with local disinfectant effect rather main material for repair. Main disadvantages of this technique for transphenoidal surgery are dense consistency of the gel that requires large needle and uncontrolled rate of polymerization.

Authors declare no conflict of interest.
The authors presented treatment of liquoric fistula of frontal sinus after transcranial removal of anterior cranial fossa meningioma.

Prolonged liquorhea after transsphenoidal surgery or craniotomy followed by frontal sinus dissection often requires additional treatment or redo surgery. Liquorrhea may be followed by inflammation and need for long antibacterial therapy in 5—10% of cases. So, adequate closure of the defect is prerequisite for successful treatment.

Focal traumatic fistula is usually closed spontaneously and does not require surgery in acute period while iatrogenic fistula often needs for additional intervention. Obviously, prevention of postoperative fistula is the most optimal. The use of temporal muscle and adipose tissue combined with pedicled periosteal flap is standard for fistula repair. In our clinic fibrin glue (TISSEEL, Baxter, Deerfield, IL, USA) is standard method besides above-mentioned approach. Adhesive is used for filling of epidural space and sinus defect.

One of the first reports about fibrin glue for fistula repair belongs to Fujii et al. (Simple management of CSF rhinorrhea after pituitary surgery, Surg Neurol, 1986; 26: 345—348).

However, there is risk of adverse reactions if these products are applied. These reactions are described in the literature despite their small incidence due to use of autologous plasma. High cost of commercial products is another limitation.

Authors applied autologous blood for fibrin glue. This technique almost eliminates the risk of adverse reactions associated with commercial products. Procedure may be recommended if access to such products is limited or undesirable or large volume of fibrin glue is required. The authors used percutaneous administration of the glue. It should be noted that localization of the clot after injection is unclear despite complete closure of the fistula. Either navigation or transsphenoidal endoscopy-assisted administration seem to be more appropriate in this situation. However, these comments do not derogate interest to the article.

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Awake Neurosurgery: Forward to the Past
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We present an analytical review of various neurosurgical interventions in conscious patients. An analysis of the literature indicates growing interest in this problem. Craniotomy in conscious patients has been extensively used in resection of space-occupying cerebral lesions in the eloquent hemispheric areas and in epilepsy surgery. In recent years, there have been a number of reports on interventions in conscious patients with other neurosurgical pathologies, which may be regarded as a new emerging tendency in neurosurgery and neuroanesthesiology. Neurosurgery in conscious patients provides a special advantage because it enables highly functional neuromonitoring without use of complex devices.

Keywords: neurosurgery, craniotomy in conscious patients, neuromonitoring.

Abbreviations:
ICA — internal carotid artery
EP — evoked potentials
DNM — dynamic neurological monitoring
AC — awake craniotomy
CSR — chiasmatic-sellar region
CCT — craniocerebral trauma
EEG — electroencephalography
ECoG — electrocorticography
DBS — deep brain stimulation
AC in surgery for cerebral aneurysms, extracranial–intra-
cranial bypass, transphenoidal surgery for chiasmatic-
sellar tumors, carotid endarterectomy, endovascular and 
functional neurosurgery, spinal neurosurgery and even in 
surgery for cochlear neuroma. This work is an attempt to 
understand this trend. Why do neurosurgeons around the 
world prefer general anesthesia despite certain difficulties 
evitably associated with awake neurosurgery?

Hemispheric tumors surgery

This is perhaps the most known field for AC in mod-
ern neurosurgery. We are talking about tumors or less of-
ten arteriovenous malformations of posterolateral, pari-
etal and temporal lobes in dominant hemisphere which 
may be associated with risk of postoperative aphasis. The 
most impressive results of AC are obtained in these cases. 
There are a lot of reports about this issue including our 
works devoted to various aspects of the technique: neuro-
surgical and anesthesiological features, unfavorable 
events and personal patient’s feelings [19—36]. So, we 
suggest to consider those publications rather detailed de-
scription here. I note only the most representative in my 
conference report. It is a meta-analysis published in the 
Journal of Clinical Oncology in 2012 and devoted to out-
comes of neurosurgery for hemispheric tumors [18]. 
Analysis included 90 publications enrolling 8091 pa-
tients. Two important aspects were considered: postop-
erative neurological deficit and type of resection. Results 
of neurological deficit were generally expected: 3.4% 
(2.3—4.8%) in group of intraoperative mapping vs. 8.2% 
(5.7—11.4%) without mapping (significant difference). 
Interestingly, incidence of radical surgery was also differ-
ent between groups: 75% (66—82%) in intraoperative 
mapping vs. 58% (48—69%) in control group. The au-
thors logically explain these data: mapping is followed by 
more active neurosurgeon’s actions without fear of unfa-
vorable functional outcomes.

Surgery for drug-resistant epilepsy

This is a classic direction for AC without any changes 
since its introduction. In fact, it is a special variant of 
functional neurosurgery where functional outcome is 
one of the main purposes [37—39]. Large literature data 
are devoted to this procedures including articles and 
handbooks [40]. AC technology in epilepsy surgery is 
similar to that in neurooncology, but the main surgical 
goal is area of epileptic signals generation.

Functional neurosurgical procedures

Some functional neurosurgical interventions are prin-
cipally impossible in deeply anesthetized patient. 
Firstly, it is deployment of deep electrodes for DBS in 
Parkinson’s disease, essential tremor, dystonia, chronic 
pain and epilepsy [11, 41—45]. Correct placement of 
electrode and selection of effective stimulation mode re-
quire interaction with patient during test loads. Intraop-
erative DBS testing in 34-year-old professional pianist 
with severe dystonia in right hand is presented in figure 
(photo is given by Dr. E.M. Salova). Intraoperative play-
ing on synthesizer was applied to evaluate effect of DBS 
and select stimulation parameters. Undoubtedly, such 
procedure is absolutely impossible under general anes-
thesia.

Carotid arteries repair

It is one of the most interesting and at the same time 
controversial field for AC. Background is understandable 
here: ICA cross-clamping and complete blood flow ces-
sation (15—30 min on the average) are followed by the 
risk of ipsilateral hemispheric ischemia due to inadequate 
collateral circulation. In case of general anesthesia these 
disorders may be diagnosed only by various modes of 
neuromonitoring including transcranial sonography, ce-
rebral oximetry, scalp EEG and EP, pressure in distal 
carotid stump [46—49]. This approach is associated with 
serious cost (equipment, specialists), but more important 
— certain percentage of false-positive and, that is espe-
cially unpleasant, false-negative results [47—49]. Rea-
sonable clinical alternative to complex and not always 
reliable hardware neuromonitoring is simple DNM 
which may be easily applied in awake neurosurg-
y [50—52]. Acute hemiparesis contralateral to proce-
dure’s side or aphasia in right-handed people during left-
sided surgery after ICA cross-clamping clearly demon-
strates inadequate collateral circulation and need for ur-
gent correction (temporary bypass and/or increase of 
blood pressure). Both approaches (general or locoregion-
al anesthesia) have their supporters and opponents, and 
debate is still continuing now [53—61]. Certain expecta-
tions were for GALA European trial comparing immedi-
ate and long-term results of carotid endarterectomy un-
der general or local anesthesia. First of all, cardiac (myo-
cardial infarction) and cerebral (stroke) events and mor-
tality were assessed. This study involved 95 centers from 
24 countries and 3526 patients. Results were published in 
November 2008 and confirmed similar outcomes and 
morbidity [62]. And this is despite various reports have 
earlier demonstrated advantages of local anesthe-
sia [63—65]. In fact, these studies justified GALA trial. 
You can talk a lot about the reasons for such results. 
Probably, someday we will understand the reasons of 
negative outcomes in not only this but also other large 
trials. However, simplicity of neuromonitoring during 
carotid endarterectomy under DNM and local anesthesia 
is absolutely obvious and does not require other special 
evidence despite GALA trial data.

Endovascular neurosurgery

The majority of endovascular neurosurgical proce-
dures are not associated with severe pain and do not re-
quire deep anesthesia. Therefore, anesthesiologist can 
use only consciousness-sparing sedation that is followed 
by certain advantages [66—69]. Obviously, DNM may be 
easily realized in such situation, as it was rightfully writ-
ten in the above-mentioned guideline for neuromonito-
It is obvious that endovascular neurosurgical interventions under consciousness-sparing sedation may be followed by intraoperative DNM as the most effective neuromonitoring mode [70].

**Extracranial-intracranial bypass**

Case report of extracranial-intracranial bypass under local anesthesia for ICA occlusion has been recently published in Burdenko Journal of Neurosurgery. Surgery was performed in advanced age patient with severe comorbidities according to clinical indications [71]. Procedure was successful, intraoperative DNM was useful to control patient’s state. It should be noted that it is not the first report. Japanese authors were first [72], but whoever was first it is obviously another field for AC.

**Miscellaneous**

Here I gathered information about various AC-associated neurosurgical interventions described within single case reports.

**Transsphenoidal surgery for chiasmatic-sellar tumors.**

Unlike multitudinous ACs in neurooncology or ICAs repair transsphenoidal surgery of chiasmatic-sellar tumors under local anesthesia is an undeniable casuistry. The first of the known case reports of surgery for CSR tumor is quite old and mysterious. It is supposedly excision of Turkish saddle tubercle meningioma under local anesthesia in famous Hungarian pianist C. Haskil [73] by French neurosurgeon M. David. There are no reliable detailed data about this procedure since it was performed in Marseille in 1942 and all materials are still in private archives and not available. However, successful surgery for CSR tumor under local anesthesia is fact. Patient continued her concert activity after surgery and was recognized as an unsurpassed performer of Mozart’s compositions. She died 18 years later from domestic craniocerebral trauma.

About 10 years ago I reviewed article of Japanese authors describing another interesting clinical observation [74]. Chiasmatic symptoms (rapid bilateral impairment of visual acuity) occurred in 88-year-old patient with severe cardiac comorbidities. MRI confirmed large pituitary adenoma that was followed by transsphenoidal surgery under local anesthesia. Partial resection was scheduled and accompanied by visual tracts decompression. Vision was rescued.

**Emergency surgery of brain abscess.**

This is a very recent publication of Swiss colleagues describing rare clinical case: 39-year-old patient with complex cyanotic congenital heart disease and brain abscess underwent successful surgery in AC fashion. This approach was preferred due to advanced perioperative morbidity and mortality in patients with cyanotic congenital heart disease undergoing surgery under general anesthesia [75].

**Intracranial aneurysms repair**

The first two reports were published in 2005. There were 2 short reports in the appendix to Neurosurgery journal. In the first one P. Chen et al. [76] described intraoperative awakening to control visual functions after ophthalmic artery aneurysm clipping. In the second publication J. Luders et al. [77] reported 3 successful AC procedures for mycotic aneurysms. Clinical observation of 46-year-old patient with headache and left MCA aneurysm was published in Surgical Neurology International in 2013. Aneurysm was found to be unsuitable for endovascular occlusion and AC followed by DNM was preferred due to high risk of ischemic complications. Neurological status was intact during temporary MCA occlusion and subsequent trapping [78].

And here is one of the latest publications analyzing 30 patients. Article was published at the end of 2016 in the Journal of Neurosurgery and worthy for discussion [79]. AC approach was used in 30 patients with intracranial aneurysms for transcranial clipping. Four patients were excluded: 2 patients refused themselves, 2 of them had anesthetic risks (sleep apnea in one and difficult previous tracheal intubation in another patient). Besides conventional control (blood pressure, heart rate, ECG, body temperature, capnography and pulse oximetry) intraoperative monitoring included following neuromonitoring modalities: scalp EEG, motor and sensory EP, DNM. Intraoperative monitoring of visual function was applied in another 4 patients with carotid-ophthalmic aneurysms. Neurological deficit after temporary clip deployment occurred in 3 patients and disappeared after its removal. Another patient had neurophysiological symptoms of ischemia and neurological deficits after permanent clip deployment. Clip reposition was not followed by regression of neurological deficit and neurophysiological signs. This patient was discharged with ischemic focus. But what is interesting that in 3 other patients DNM revealed neurological deficit after temporary clipping but neurophysiological monitoring was uneventful! Therefore, authors believe that cerebral aneurysms repair in AC mode.
and dynamic neurological monitoring have certain advantages. Neurological deficit was revealed in 3 patients despite normal data of intraoperative neuromonitoring (false-negative result). And this is 10%! Obviously, these data need to be thought over despite there were patients with unruptured aneurysms in the sample.

**Spinal neurosurgery**

Wake-up test in scoliosis surgery is a classic example of intraoperative consciousness recovery in spinal cord surgery. It is still "gold standard" of intraoperative neurological injury diagnosing along with neurophysiological techniques [80—83]. However, I have recently met editor’s very interesting commentary (M. Lund-Johansen) to one of the articles of Acta Neurochirurgica journal. This Norwegian neurosurgeon witnessed old and experienced neurosurgeons sought to perform spinal interventions under local anesthesia for DNM when he trained for spinal neurosurgery [84].

I can add from my experience that we often used intravenous infusion of propofol for superficial sedation when local (epidural) anesthesia has been introduced into lumbar spine surgery. Patient immediately woke up and informed about his sensations and neurosurgeon’s dangerous actions in case of any traumatic manipulations (spinal compression as a rule). It was followed by significantly lower postoperative morbidity in epidural anesthesia group [85]. Interestingly, recent analysis of local and general anesthesia in lumbar spine surgery confirmed advantages of local anesthesia in these patients [86].

**Cochlear neuroma surgery**

Japanese neurosurgeons’ report has been recently published in Acta Neurochirurgica journal where outcomes of cochlear neuroma surgery under local anesthesia were analyzed [87]. Sample size was only 8 patients who underwent less radical tumor excision. However, functional results were better including hearing preservation. Perhaps, it is only the first sign in this field.

**Outpatient awake craniotomy (OAC)**

This part of modern neurosurgery is still quite problematic because of its unusual nature. We are talking about AC for hemispheric tumors within "one-day surgery"! Canadian neurosurgeon M. Bernstein is the main adherent of this direction [88], therefore we will discuss his works first of all. He had mastered AC approach before he made it clinically routine in surgery for supratentorial tumors even in cases of minimal risk of verbal disturbances. Further analysis of patients’ state after AC, their sensations and postoperative rehabilitation confirmed a simple conclusion: there is no need for postoperative hospital-stay after uneventful surgery in stable patients. So, they may be discharged to indisputably more comfortable home conditions that was confirmed in subsequent work of Bernstein and el. [89—94]. In authors’ opinion, natural and quite actual question about possible postoperative complications seems to be completely solvable in this approach. There were following statistical data in one of the largest sample size: 228 (36%) out of 1,003 prospectively selected patients underwent OAC. 92.8% of patients were discharged in the evening after successful procedure, 5.2% stayed in the clinic for various reasons, but 2% of discharge followed by repeated admission are the most interesting. Severe headache, nausea and vomiting were the main causes of hospitalization. One patient with intracerebral hemorrhage was hospitalized in 12 hours after surgery, medication was effective [95]. Well, everything looks quite reasonable at first sight. However, this apparently does not correspond to realities of our country and risk of even one severe complication at home can easily cross out entire economic attractiveness of this approach considering possible legal consequences. Nevertheless, authors [35] insist on expediency of this approach if financial capacity of health care is limited in the country.

**Functional disorders after neurosurgical procedures and the role of intraoperative neuromonitoring in prevention of neurological deficit de novo**

Probably this is the most important problem and real explanation of advanced interest to AC at present time. Postoperative aggravation of previous neurological deficit or disorders de novo is one of the key problems of neurosurgery. This is a real problem followed by emotional stress and financial risks. Intraoperative neuromonitoring is one of the reasonable approaches for this serious problem. Numerous publications and even guidelines are devoted to this issue. In my opinion, "Intraoperative Neuromonitoring" by C. Loftus, J. Biler and E. Baron is one of the most successful one [96]. This and other manuals describe various intraoperative neuromonitoring modalities aimed at early diagnosis of neuronal injury and prevention of permanent neurological deficit via changing of surgical tactics. These postoperative neurological disorders may be only revealed as soon as patient woke up after general anesthesia. There are motor, sensory and visual evoked potentials, myography in various modes, facial nerve’s function, scalp EEG and ECoG, cerebral and jugular oximetry, transcranial sonography and pressure in vascular stump, retractive pressure and others. Currently, large number of intraoperative neuromonitoring modalities have been developed, but let’s try to understand the essence of this process. First, let’s try to formulate our wishes regarding ideal method of intraoperative neuromonitoring. So, this method should: 1) reflect neurons’ functional state in high risk area; 2) be simple, cheap, reliable and preferably non-invasive; 3) be resistant to effect of anesthetics, temperature changes and electrical interferences. It is easy to understand that there is no such method at present time and it is unlikely to be that it will appear in foreseeable future.

Let’s try other approach. We rank intraoperative neuromonitoring modalities according to informative value. Undoubtedly, monitoring of neurons’ functional state in
area of the greatest risk of injury should be the highest in this hierarchy. There is surrogate assessment of neuronal activity (EEG or ECoG and EP) on the 2nd place followed by secondary modalities including blood flow, oxygenation, metabolism, etc. It is interesting that only dynamic neurological monitoring may be placed on top of this pyramid. There are no any other modalities comparably by their informative value and simplicity at the same time. However, DNM should be followed by AC approach. According to above-mentioned data, this approach is possible for various neurosurgical pathology and may be accompanied by favorable outcomes.

Conclusion

Direction of modern neurosurgery progress is understandable — maximally reduced risk of postoperative ag-gravation of previous neurological deficit or disorders de novo. Different modes of intraoperative neuromonitoring are apparently able to solve this problem. However, advanced costs are necessary while absolute guarantee is absent. AC approach followed by DNM seems to be reasonable alternative. Certainly, this requires changed anesthetic concept and it is currently difficult problem due to technical and pharmacological causes. Modern anesthesiology is able to provide comfortable intraoperative state of patient (controlled superficial sedation followed by easy awakening at the right time, no pain and other unpleasant sensations). Perhaps, it is prospect of our development in near future.

Authors declare no conflict of interest.

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There is no need to look at the title of the article to understand who is author of this distinctive and recognizable report. Reading the article you understand that only specialist with great experience and encyclopaedic knowledge about certain issue is able to recognize awake craniotomy as anesthesiological top in neurosurgery. So, we have an article in scientific essay genre here with the elements of literature analysis and emotions if we consider that even high-quality anesthetics are associated by the author. Advantage of AC approach is also evident, since other words, bottom-up proprioception blockade in neurosurgical zone of interest may be accurately determined by the counter-arguments?


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2. Multimodal neuromonitoring allows to control any disorders on-line and to predict certain delayed violations. So, it is mandatory component of intraoperative management if consciousness is undesirable intraoperatively, for example in intracerebral aneurysms repair.

3. I would refer AC to the highest anesthetic level in neurosurgery, in other words we can hardly talk about wide introduction of this approach among anaesthesiologists of general practice.

A.Yu. Lubnin’s article as polemical and very interesting report completely corresponds to journal’s profile and status.

A.A. Belkin (Yekaterinburg, Russia)
The article presents the literature data on the structural variability and age-related features of the midline anatomical structures of the anterior skull base. Frontal sinus, ethmoid bone, anterior parasellar region, and medial orbital wall. This is the area of surgical interests of neurosurgeons and rhinosurgeons. The study objective is to analyze the literature data on the individual variability and age-related anatomy of these structures. The work is illustrated with original images from the authors’ personal archive. The individual anatomical features of eloquent structures in the surgical area (structures within the surgical corridor, key anatomical landmarks, optic tract, internal carotid and ethmoidal arteries, etc.) should be considered in planning surgery in patients of all age groups because they can limit the view and the amount of safe manipulations or increase the risk of complications. The presented data may be useful for neurosurgeons and otolaryngologists whose surgical interests are focused on the midline structures of the anterior skull base.

**Variability and Age-Related Features of Midline Structures of Anterior Skull Base**

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There is anatomical complex related to internal and external skull base. It is under surgical interest of neurosurgery and rhinosurgery and may be designated as “midline structures of anterior skull base”. Anterior cranial fossa (ACF) base, anterior parasellar area, ethmoid, paranasal sinuses and optic canal should be mentioned among them.

Surgery for anterior skull base disease is based on CT and MRI data (relationship of tumor with bones, dura mater, brain tissue, orbit, great vessels, cranial nerves, etc.), as well as evaluation of individual anatomical features of patient including structural variability and age-related anatomical differences of skull base. This is necessary to determine optimal surgical access, staging and type of resection and to predict possible skull base injuries and their repair.

The purpose of this work is literature data analysis about individual variability and age-related anatomical features of midline structures of anterior skull base (original images from the authors’ personal archive were used for illustrations).

**Variability of Anterior Skull Base Anatomy**

Craniobasal surgery requires good knowledge of intra- and extracranial skull base anatomy [1]. Variability is anatomic peculiarity of middle structures of anterior and middle skull base. It is predominantly actual for ethmoid since ethmoid labyrinths are characterized by difference cellular structure while asymmetry is norm [2]. We are also talking about variable anatomy of key structures such as olfactory fossa, ethmoid arteries, etc. Variable anatomy of midline skull base structures throughout frontal to sphenoid sinus is discussed in the article.

**Frontal Sinus.** Frontal sinus growth begins at the 13th month of life and lasts up to 12 years. After that horizontal enlargement occurs in girls and vertical in boys [3]. Moreover, length and width of left frontal sinus usually exceed those of right one due to unexplained causes [4].

Frontal sinuses are finally formed by 18 years [5]. Left frontal sinus is more developed compared with right one in 57.4% of women and in 54.05% of men. Anteroposterior dimension is 12.019±3.07 and 10.16±2.12 mm in men and women, respectively; height is 31.72±6.47 mm in men and 28.57±7.36 mm in women; mean width 56.33±13.43 mm in men and 51.05±17.74 mm in women; mean volume is 129.96±82.06 mL in men and 80.28±60.81 mL in women [3]. Transfrontal approach followed by intracranial and extracranial structures exposure is advisable in well-developed sinuses (height over 3 cm) [6] (Fig. 1).

**Ethmoid Bone.** Ethmoid bone is sagittally formed by ethmoid lamina, crista galli above and perpendicular lamina below it. Ethmoid labyrinths are placed from each side lateral to ethmoid lamina. External wall of the labyrinth is involved into structure of posterior two-thirds of medial orbital wall [2].

**Crista Galli** is ethmoid bone’s structure with the largest thickness and pyramidal shape. It is necessary for processus falciformis major attachment, there is dura mater invagination between two folds bilateral to crista galli. Mean vertical dimension of size of crista galli is 12.7±2.4 mm (range 8.8—16.8), craniocaudal dimension — 12.9±2.5 mm (range 9.1—16.3) [1]. Crista galli pneumatization occurs in 13% of cases [7]. Foramen cecum consisting of dura mater processus is in front to crista galli, it is open in 1.4% of cases [8].

**Olfactory Fossa** is formed by ethmoid lamina and its lateral lamella as extension of basal lamina of middle nasal concha and its height determines olfactory fossa’s depth [9]. In embryogenesis lateral lamella arises as inde-
pendent part of ethmoid bone and begins to be ossified after birth followed by final development by 10 years [10]. This structure is the thinnest in ACF [11]. In 1962 P. Kerros analyzed 450 observations and identified 3 main types of olfactory fossa depending on lateral lamella’s height: type I — 1–3 mm, type II — 4–7 mm and type III — 8–16 mm [12] (Fig. 2). Their incidence in population is 30%, 49% and 21%, respectively [8].

Ethmoidal labyrinth roof separates ethmoid cells from ACF. It is part of frontal bone with slant posteriorly under 15 ° on the average [13]. Convexity of ethmoidal labyrinth roof is more pronounced at the level of anterior ethmoidal cells; dehiscences are often here (areas without bone tissue) [2].

Anterior and posterior ethmoidal arteries are one of the key anatomical landmarks within ACF base from the side of both ethmoidal labyrinth and orbits. Both ethmoidal arteries originate from ophthalmic artery within orbit and pass between superior oblique and internal rectus muscles along with self-titled nerves. Anterior ethmoidal artery (AEA) is larger than posterior artery (PEA). Arteries enter anterior and posterior ethmoidal orifices and ethmoidal labyrinth therefore. AEA is almost horizontal here and passes close to crista galli at the level of anterior margin of ethmoidal lamina. There are two variants of AEA course through the labyrinth: outside the labyrinth roof in 43% of cases on the right and in 49% on the left, passage through skull base in 57% and 51%, respectively [9] (Fig. 3). PEA reaches lateral margin of ethmoidal lamina and passes through bone channel, then it is behind ethmoidal lamina and anterior to optic nerve before entering cranial cavity. Mean distance from nasal septum to left AEA is 64.81±3.83 mm in both genders (range 60.37—71.86), 63.45±2.27 mm (range 60.37—66.06) in women and 66.17±2.81 mm (range 60.94—71.86) in men. The same values on the right are 72.27±3.97 mm (range 66.39—77.79), 69.15±2.24 mm (range 66.39—72.58) and 75.39±2.47 mm (range 72.05—77.79), respectively [13].

Anterior and posterior ethmoidal orifices in orbit’s medial wall are also characterized by variable topography. Intraorbital ligation of ethmoidal arteries has been successfully applied in practice [14]. There are anterior and posterior ethmoidal orifices as a rule, but additional ones are also found. Frontoethmoidal suture is important anatomical landmark to determine ethmoidal orifices. Anterior ethmoidal orifice is placed within suture in 77.7% of cases, outside — in 23.3% (mean distance 0.5±2.1 mm); posterior ethmoidal orifice is located within suture in 77.25% of observations, outside — in 4.25%. Additional orifices are revealed in 25.5% of cases and placed outside the suture in all cases. Ethmoidal orifices are the weakest points of orbit’s medial wall with the least mechanical resistance [15]. Anterior lacrimal crest is permanent anatomical reference point in transorbital approach to ethmoidal arteries. Distance from anterior lacrimal crest to anterior ethmoidal orifice is 27.6±2.8 mm (range 21.6—25.1), to posterior ethmoidal orifice — 36.6±4 mm (range 24.1—46.1). Mean distance between anterior and posterior ethmoidal orifices is 10.6±3.3 mm (range 4.3—19.3). Posterior ethmoidal orifice close to optic canal should be taken into account: distance between them is 7.4±2.9 mm (range 2.4—17.6). Finally, distance from anterior lacrimal crest to optic canal is 41.4±3.8 mm (range 32.9—60.8) [16].

Anterior parasellar area. These are some key anatomical intracranial structures (Fig. 4a).

Sphenoid bone area is located between small wings. Its anterior margin reaches ethmoidal lamina and frontoethmoidal suture. Mean anteroposterior dimension of sphenoid area is 17.5 mm (range 15.2—21.3) [17]. Posterior margin borders with prechiasmatic sulcus and ante-

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Fig. 1. Hypertrophic frontal sinus.
There is a pronounced pneumatization of orbits’ upper walls and frontal bone.
rior clinoid process on both sides. These two structures form superior wall of optic canal [13].

Optic canal is located lateral to sphenoid bone, below to small wing and medial to optic strut [18]. Optic nerves and ophthalmic arteries pass through the canal. Mean distance between both canals at the level of inlets is 15.13±1.69 mm (range 11.62—17.82), 13.82±1.28 mm (range 11.62—16.37) in women and 16.44±0.79 mm (range 15.20—17.82) in men. Distance between intracranial orifices of optic canals is 15.13±1.69 mm (range 12.37—17.82) [13]. Optic strut pneumatization during endoscopic transsphenoidal surgery is followed by lateral opticocarotid recess exposure as a key reference point to detect projection of optic nerve and internal carotid artery (Fig. 5). K. Abhinav et al. [19] studied relationship between these two structures: distance from posteromedial edge of lateral opticocarotid recess to intracranial orifice of optic canal is 0.65±0.75 mm, distance between anterolateral edge of lateral opticocarotid recess and intraocular orifice of the canal — 0.40±0.50 mm. Length of optic canal is up to 6.05±0.72 mm, distance between ophthalmic artery ostium and proximal optic canal — 2.50±1.24 mm, length of falciform ligament — 1.70±0.47 mm. Optic nerve and internal carotid artery have no bone wall from the side of sphenoid sinus in some persons [20]. Ophthalmic artery is located inferior and medial to optic nerve at the entrance to optic canal, then nerve is circumflexed laterally. This artery occupies inferolateral position in 81% of cases or placed under the nerve in 19% of cases [21]. It must be taken into account in transsphenoidal approach to optic nerve.

Prechiasmatic sulcus separates sphenoid bone from sella turcica. Its width is the distance between postero-medial edges of optic strut on both sides (mean 19.3 mm, range 14—25); length — distance from the limb to sella turcica tubercle (7.45 mm, range 5—10), mean angle between sphenoid bone plane and the line between limb and sella turcica tubercle is 31° (range 5—64°) [22] (Fig. 4b).

Optic chiasm also has variable structure. In 70% of cases it is located above sellar diaphragm, anterior and posterior placement is found in 15% and 15% of cases, respectively [23].

Sphenoid sinus. Sphenoid sinus pneumatization visible at the 6th month of life begins within apertures and spreads in inferior, posterior and lateral directions [24, 25]. Complete pneumatization of recesses continues after puberty period. There are 3 types of pneumatization by Hamberger classification: sellar (86%), presellar (11%) and conchal (3%) [26]. A. Rahmati et al. [27] report postellar type additionally (Fig. 6).

Superior wall of sphenoid sinus is formed by sphenoid bone area anteriorly and sella turcica posteriorly. Sellar type of sinus is characterized by pneumatization anteriorly under sphenoid bone area. The thinnest sinus
wall is within anterior sella turcica and sphenoid bone area [24].

Pneumatization of left-sided anterior clinoid process is observed in 10.7% of cases, right-sided — 7.8%, bilateral pneumatization — in 14.6% [27] (Fig. 7). If small sphenoid wing is medially pneumatized, optic nerve is surrounded by sphenoid sinus. However, optic nerve position does not depend on sphenoid sinus pneumatization grade [17]. There was a single report of optic nerve course through inferior wall of sphenoid sinus [28]. Mean distance between optic canals at the level of anterior edge of sphenoid bone area is 15.6 mm (range 14.7—16.2), at the level of medial edge of canals’ intracranial apertures — 13.7 mm (range 12.9—14.2) [17].

Special variant of sphenoid sinus structure is observed in presence of Onodi cells (sphenoethmoidal cells) which occupy upper position. In this situation approach to optic canals is through Onodi cell rather sphenoid sinus [20, 29, 30]. Sphenoethmoidal air cells are found in 8% of cases [31] (Fig. 8).

General feature of midline structures of anterior and middle skull base is maximum contact of intracranial elements with pneumatic cavities (frontal sinus, nasal cavity, ethmoidal cells, sphenoid sinus). "Pneumosinus dilatans“ phenomenon should be considered. It is abnormally enlarged paranasal sinuses without local bone destruction, hyperostosis or mucosal thickening. "Pneumosinus dilatans“ is characteristic of ACF meningiomas including small ones [32] (Fig. 9).

**Age-related features**

Smaller anatomical structures, incomplete pneumatization of paranasal sinuses, incomplete development of dental system and other aspects should be considered for skull base surgery in children and adolescents [33]. Normal craniofacial development includes growth, configuration changes, ossification and pneumatization of bone structures.

**Ossification.** Interpretation of skull base imaging data may be difficult in children since most of bone structures are in cartilage model stage and ossification occurs in numerous points. Ossification is poorly expressed at birth, but it quickly develops within the first 6 months. Anterior skull base ossification rate is greatly variable, but this process is completed in 100% by 3 years 10 months.

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**Fig. 4. Anterior parts of internal skull base.**

- **a** — anatomical marks of anterior internal skull base (GW — great wing of sphenoid bone, STT — sella turcica tubercle, SOF — superior orbital fissure, OP — orbital process of frontal bone, OC — optic canal, SBA — sphenoid bone area, ELR — ethmoidal labyrinth roof, L — limb, SW — small wing of sphenoid bone, OF — olfactory fossa, PG — prechiasmatic groove, CG — crista galli, ACP — anterior clinoid process, FC — foramen cecum, * — optic strut; b — α angle between sphenoid bone area plane and line drawn through the limb (1) and sella turcica tubercle (2). Explanations in the text.

**Fig. 5. Anatomical marks of sella turcica cavity, left side (anatomical specimen, endoscope 0°).**

ICA — internal carotid artery, ON — optic nerve, SBA — sphenoid bone area, LR — lateral recess of sphenoid sinus, OCR — optic-carotid recess, C — clivus, ST — sella turcica. Optic-carotid recess corresponds to optic strut.
Impaired bone tissue metabolism or dysplasia should be suspected if definitive ossification is absent in children older than 4 years. Some children have persistent cecum orifice (remainder of dural diverticulum extending from anterior margin of crista galli to nasal subcutaneous area). It may be confused with bone defect, but it differs by clear edges formed by cortical bone [34].

**Pneumatization.** J. Spaeth et al. [35] analyzed pneumatization of paranasal sinuses after birth till 25 years and received valuable data. According to CT-data there is equable paranasal sinuses grow almost in all directions in children of different age. Dimensions of left and right sinuses are similar excepting frontal sinuses which are almost always asymmetrical in favor of left one.

**Frontal sinuses** are detected in CT-scans in 1.4—1.5% of newborns of both genders and are distinguishable in only 10.7% of 4-year-old and 50% of 8-year-old children. They are found in 90% of people over 15 years old. Further development of frontal sinuses is absent after 18 years in boys and 15 years in girls. Advanced growth in pubertal period is absent. Frontal sinuses aplasia was more common in girls (18.2%, mean incidence after complete development — 9.4%) compared with boys (10 and 4.9%, respectively). According to M. Gulisano et al. [36], frontal sinus is absent in 5% of people, hypoplasia is noted in 4.8% (Fig. 10). J. Pondé et al. [3] reported aplasia in 6.86% of persons (9.75% of men and 5.26% of women). Septum between both frontal sinuses was not found in 5% of cases.

**Ethmoidal cells** are observed in 94.4% of newborn boys and in 93.9% of newborn girls. Advanced growth of ethmoidal labyrinths in length rather width is observed in 4—5-year-old boys. Labyrinths reach their final dimensions after 13 years. There is no further enlargement up to 25 years. Final width and length of ethmoidal labyrinths in girls are observed after 10 and 13 years, respectively. Complete development of ethmoidal sinuses is noted after 12—13 years in both genders, but it may be near 2 years earlier in girls.

**Sphenoid sinus** is found in 6.3% of boys and 6.7% of girls within the first year of life, in 2-year children — in 51.1 and 57.7%, respectively. CT-scans visualize sphenoid sinus after 8 years, craniograms — after 6 years. Sphenoid sinus is seen in more than 90% of children older than 8 years. Sphenoid sinuses are characterized by stable development. Rapid development is completed before

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**Fig. 6. Variants of sphenoid sinus pneumatization.**

- a — conchoidal type (sphenoid bone body is almost completely formed by spongy tissue; sinus is reduced);
- b — pre-sellar type (posterior wall of sinus corresponds to the level of anterior wall of pituitary fossa);
- c — sellar type (sinus cavity is also projected onto pituitary fossa);
- d — retro-sellar type (sinus cavity extends to sella turcica; * — retro-sellar pneumatization).

**Fig. 7. Bilateral pneumatization of anterior clinoid processes (arrows).**
5 years old. It is obviously that sphenoid sinuses growth is stopped after 16 years in boys and 14—15 years in girls [35].

**Anatomical features of ethmoid bone.** C. Güldner et al. [37] compared courses of AEA and incidence of various types of olfactory fossa in persons younger and older than 18 years. There were 3 AEA courses: 1) through skull base directly; 2) through ethmoidal labyrinth within 3 mm from skull base; 3) through ethmoidal labyrinth at a distance over 3 mm from skull base. AEA was predominantly located in skull base in younger patients (48.1% vs. 44.1%, p<0.05), AEA type II was more typical for older group (11.2% vs. 18.5%, p<0.05), type III was more common in young people (40.1% vs. 37.4%, p<0.05). Olfactory fossa Keros type I was significantly more frequent in "young" group (27.6% vs. 15.7%, p<0.001), while types II and III were more common in persons older 18 years (50.9% vs 59.8%, p<0.001 and 21.5% vs. 24.5%, p<0.001, respectively). It is noteworthy that other researchers revealed similar structure of central ACF regardless age.

**Influence of anterior approaches on facial skeleton and dental system development in children**

Facial skull growth and development is one of the factors limiting extracranial approaches in pediatric patients with intra- and extracranial skull base tumors [38].

In children younger 6 years ACF is smaller and frontal sinuses are not completely formed. Therefore, transcranial accesses in children are technically simpler compared with adults [39]. Moreover, small cerebral skull and thin cranial vault require special surgical techniques of craniotomy [40]. There are no conventional anatomical reference points in children younger 8 years such as supraorbital orifice or incisura [41, 42]. Frontonasal suture as active growth point of facial skeleton up to 16 years old should be kept in mind in choosing transcranial approach. Nevertheless, some effect of subcranial approach (<10%) on vertical and horizontal growth of facial skeleton in middle zone was reported [43]. Another feature of transcranial surgery in children is possible difficult brain relaxation; ventricular puncture and liquor evacuation from basal cisterns are less effective than in adults [44].

Sublabial approaches are followed by wide exposure but dangerous for permanent teeth development in children younger 6—10 years [39, 45]. Endoscopy-assisted "midfacial degloving" approach was used in children of various ages [46]. Complications of sublabial approaches included teeth denervation and anesthesia of infraorbital nerve’s innervation zone [45], oro-antral fistulae and epiphora [47].

Endoscopic endonasal approaches including transphenoidal access are widely used in children [48, 49]; unlike traditional transfacial approaches they do not affect dental system development and facial skeleton growth. However, advanced excision of bone and cartilaginous tissue from nasal cavity walls can lead to impaired growth later [49]. It should be also taken into account that sphe-
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20. Berhouma M, Jacquesson T, Abouaf L, Vighetto A, Jouanneau E. Endoscopic endonasal optic nerve and orbital apex decompression for nontraumatic sinus pneumatization is rare in children younger 3 years [33]. There is a point of view that endoscopic approaches are limited in children due to small nasal cavity and need for very thin endoscopes and instruments [50]. Nevertheless, according to literature endoscopy is possible in children of any age (even 1.5 months) despite small nasal cavity. So, F. Di Rocco et al. [49] reported no correlation between age and outcomes of endoscopic endonasal repair of anterior skull base defects.

Conclusion

Individual characteristics, variability of structures and age-related features of ACF should be considered if surgery for anterior skull base tumors is planned. It is true for both children and adults. Bones growth and ossification, pneumatization of sinuses, dental system development determine choice of optimal and safe surgical approach in young patients with incomplete development of craniofacial area. Individual anatomic features of critical structures within surgical field (surgical course, key anatomical marks, optic tracts, internal carotid and ethmoidal arteries, etc.) should be taken into account in any patients. These aspects can impair exposition, safe manipulations, or increase risk of, for example, vascular injury or impaired skull base impermeability (in transnasal accesses), etc. Age-related and individual variability of midline structures of anterior skull base is summarized in this article. These data may be useful for neurosurgeons and otorhinolaryngologists with interests in this anatomical area.

The authors are grateful to K.E. Klimenko, M.Z. Dzhafarova and G.B. Bebchuk for help in illustrations selection.

Authors declare no conflict of interest.

BURDENKO’S JOURNAL OF NEUROSURGERY 1, 2018
The report is devoted to the actual issue of topographic anatomy variability of anatomically complex area per se. Interdisciplinary approach to anterior skull base is of additional interest: internal base is historically a field of neurosurgery, while transnasal approaches are being studied together with otolaryngologists. Thus, the article is integration of both specialties. Moreover, age-related topographic features determining optimal access are discussed. The last forces the reader to think about advanced surgical approaches and to step back from accepted stereotypes in favor of the most anatomically advisable procedure in certain patient. The authors rightly point at the need for CT- and MRI-data for preoperative planning of both optimal surgical approach and skull base repair. For example, it is known that transcranial approach is preferred over transnasal transcribriform access in pediatric practice due to small area of nasoseptal flap.

The authors rightly emphasize considerable anatomic variability of ethmoidal bone, that has been recently studied in numerous publications along with endoscopic rhinosurgery development. However, it is necessary to unify some terms to generally accepted concepts according to European Position Paper on the Anatomical Terminology of the Internal Nose and Paranasal Sinuses (Rhinology Journal Supplement 24, European Society of Rhinologists) and their official Russian translation.

In total, the most important “points of variability” are considered which must be assessed to determine endoscopic approach to median structures of anterior skull base: olfactory fossa’s depth by Keros, variable placement of ethmoidal arteries within skull base, presence of Onodi cells, which should be taken into account in advanced transthyroidal sphenotomy and optic channels decompression, sphenoid sinus and clinoid processes pneumatization which are the key in sellar and parasellar exposure.

Age is an important factor emphasized by the authors (paranasal sinuses pneumatization, presence of teeth rudiments, advanced indications for endoscopic transnasal approach in children if it is surgically justified). In early 2000s we got acquainted publications about dangerous endoscopic surgery of paranasal sinuses in children due to injury of growth zones of facial skeleton. This paradigm has been completely changed over the last decade, when large trials have shown that endoscopic procedures do not affect growth rate of facial skull. It should be noted that endoscopic rhinosurgery in pediatric practice is being rapidly developed as independent direction — PESS (Pediatric Endoscopic Sinus Surgery). Thus, relevance of this issue is confirmed once again.

G.A. Polev (Moscow, Russia)
Neurosurgery Followed by Facial Nerve Injury: Rehabilitation Potential of Botulinum Therapy

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Surgical treatment of posterior cranial fossa and cerebellopontine angle tumors is associated with a risk of facial nerve dysfunction. The causes for facial muscle paresis include nerve compression by the tumor, destruction of the nerve structure by the tumor growing from nerve fibers, nerve injury during surgical removal of the tumor, etc. The first 3 months after facial nerve injury are a potential therapeutic window for the use of botulinum toxin type A (BTA). During this period, the drug is introduced both in the healthy side to improve the facial symmetry at rest and during mimetic movements and in the affected side to induce drug-induced ptosis. Post-paralytic syndrome develops 4—6 months after facial nerve injury. At this stage, administration of BTA is also an effective procedure; in this case, drug injections are performed on the affected side at small doses and symmetrically on the healthy side at doses doubling those for the affected side. BTA injections are mandatory in complex treatment of facial muscle paralysis.

Keywords: posterior cranial fossa tumors, cerebellopontine angle tumors, skull base tumors, facial nerve injury, drug-induced ptosis, synkinesis, botulinum toxin type A.

Preservation of facial nerve function is important problem in treatment of tumors of posterior cranial fossa and cerebellopontine angle first of all (cochlear and facial nerves neuromas, meningioma of posterior cranial fossa base, trigeminal nerve neuroma). This pathology is often associated with involvement of intracranial or intracanal segments of facial nerve (Figs. 1, 2) [1—4]. Facial nerve injury leads to severe functional disturbances and psychological trauma in view of important aesthetic component in face lesion. So, treatment of cerebellopontine angle tumors requires coordinated actions of multidisciplinary team including neurosurgeons, neurophysiologists and anaesthesiologists in order to reduce likelihood of facial nerve injury and paralysis of facial muscles.

At present time there is low incidence of facial nerve injury followed by postoperative dysfunction in various medical centers [5, 6]. Nevertheless, this unfavorable event (dysfunction House-Brackmann grade III—IV) occurs in 6—20% of cases after surgery especially in large tumors (over 3 cm) [7—9]. Anatomically intact facial nerve is not always accompanied by good long-term functional recovery.

Paresis or paralysis of facial muscles occur due to facial nerve compression, its destruction by tumor (facial nerve neuroma) and surgical injury. Tumor dissection may be followed by postoperative paresis or paralysis of facial muscles even in anatomically intact facial nerve. In case of large tumors of cerebellopontine angle facial nerve may be adherent to tumor capsule as thin membrane under operating microscope. In these cases, radical excision of tumor is inevitably associated with nerve trauma and advanced probability of postoperative facial muscles dysfunction. In this regard, most authors suggest subtotal resection and subsequent follow-up [10] or combined treatment (resection + radiosurgery) of large cochlear neuroma [11].

Postoperative function of facial nerve depends on various factors. Thus, large tumors are associated with less favorable outcomes compared with small and middle neoplasms [12—14]. Relationships of facial nerve and tumor also affect the outcome. Usually, nerve is located within anteroinferior pole of tumor. Rarely (about 1%) nerve may be placed on posterior or inferior fragments of capsule (Fig. 3) [15]. Advanced intraoperative manipulations and dislocations of facial nerve are also associated with less favorable outcomes [16].

Morphological features of tumor can affect surgical outcome especially in its tuberous structure (cerebellopontine angle neurofibroma in neurofibromatosis type II) or if nerve passes through the tumor (meningio-ma overgrowing cochlear-facial nerves, cystic cochlear neuroma). There are literature data [17, 18] confirming correlation between cystic tumor and adverse outcomes, while other reports revealed similar postoperative function of facial nerve regardless cystic or solid tumors.

Surgeon’s experience and arachnoid membrane dissection are significant favorable factors for postoperative function of facial nerve [19]. In case of cochlear neuroma, the greatest adhesion of tumor and facial nerve is usually observed within internal acoustic canal. Therefore, trepanation of its wall followed by subsequent excision of intracanal neuroma is necessary after intracapsular tumor extraction. Intraoperative neurophysiological monitoring of facial nerve function is useful to locate facial nerve intraoperatively and to minimize its trauma [20, 21].
Acute injury of facial nerve is manifested by unilateral paralysis or paresis of facial muscles due to impaired anatomic integrity or function of nerve. Facial muscles dysfunction aggravates eyelids closure, eating, articulation, and subsequently quality of life [22—24].

House-Brackmann (Table 1) and Yanagihara (Table 2) scales are the most famous and widely used classification of facial nerve lesion [25].

House-Brackmann 6-score scale is used to assess motor dysfunction of facial muscles. It includes eyebrow and mouth angle movements and their comparison with those on the opposite side. Special scale with divisions of 0.25 cm is used to estimate facial asymmetry. Maximum possible value is 8 (4 or 1 cm for mouth and 4 or 1 cm for eyebrow). Yanagihara scale evaluates 10 motor reactions of facial muscles from 0 (severe palsy) to 4 scores (no disorders) for each movement. Both these scales are sufficiently demonstrative and choice should be made by specialist [26, 27].

The first weeks and months of postoperative rehabilitation are the most difficult for patients [28]. Corneal protection is one of the most important measures at this stage. Ineffective conventional methods including ointments and protective dressings to prevent corneal changes should be emphasized. It is true even if treatment was started from the 1st postoperative day [29]. Currently, temporary blepharoptosis by botulinum toxin injection followed by corneal protection is possible for postoperative paresis of orbicular muscle of the eye. Thus, conventional invasive approaches such as blepharoplasty are not so actual at present time. Early period after facial nerve injury (within 3 months) is considered as potential therapeutic window for botulinum toxin type A (BTA) administration to achieve unilateral blepharoptosis [2] and to improve facial symmetry at rest and in mimic movements on contralateral side [1, 30, 31].

BTA injection into contralateral facial muscles early after facial nerve lesion is performed to reduce muscular hypertonicity [32]. Hyperactivity of these muscles is associated with advanced facial asymmetry. It is followed by paretic muscles affection and their impaired recovery [32, 33].

BTA injection into m. levator palpebrae superiors is followed by blepharoptosis is adequate care for acute trophic keratopathy, corneal erosions or ulcers. This procedure prevents severe corneal disorders and allows to avoid unjustifiably aggressive correction of lagophthalmos [1].

BTA-induced ptosis is achieved by injection of toxin 10—25 units into m. levator palpebrae superiors through superior orbital-palpebral fissure (Lantox, Botox, Xeomin). Initial effect is observed after 2 days. Complete BTA-induced ptosis occurs in 3 days (length of effect — 25—35 days). This period is followed by residual ptosis until the end of BTA effect (30—40 days after toxin injection) (Figs. 4, 5) [25].
Ptosis is useful for mechanical corneal protection until facial nerve function will be restored. Surgical repair is considered if this approach is ineffective.

Indications for BTA-induced ptosis:
— lagophthalmos and/or unresponsive to therapy early postoperative severe trophic keratopathy;
— aggravation of trophic keratopathy in long-term postoperative period despite adequate protective therapy;
— delayed repair of lagophthalmos in facial nerve dysfunction.

Some reports confirmed BTA effectiveness for postoperative paresis of orbicular muscle of the eye. J. Prell et al. [4] reported percutaneous and transconjunctival BTA injections (25 units) for postoperative paresis of facial muscles House-Brackmann grade IV and over, keratopathy, corneal erosions or ulcers. Temporary eyelids closure for 2—6 months followed by sufficient recovery of facial nerve function was achieved in all cases. The authors concluded that BTA-induced ptosis is adequate low risk alternative to other invasive approaches for severe postoperative lagophthalmos and anatomically intact nerve.

Post-paralytic syndrome including contractures and synkinesis of facial muscles, fasciculations, lacrimation and salivation besides mimic insufficiency develops in 4—6 months after facial nerve injury [34]. Synkinesis is involuntary movement accompanying voluntary movement (eye screwing up in orbicularis oris muscle movements) or contraction of entire unilateral mimic muscles during voluntary work of certain group of muscles. Sun-

nybrook Facial Grading Scale is used for assessing synkinesis (Table 3) [35].

This scale is useful for monitoring of postoperative rehabilitation in long-term period after facial nerve injury and consists of 3 points (resting symmetry, voluntary movements symmetry and synkinesis).

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**Table 1. House-Brackmann scale**

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<th>Grade</th>
<th>Dysfunction</th>
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<td>No dysfunction</td>
<td>8/8</td>
</tr>
<tr>
<td>II</td>
<td>Mild dysfunction</td>
<td>7/8</td>
</tr>
<tr>
<td>III</td>
<td>Moderate dysfunction</td>
<td>5/8—6/8</td>
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<td>IV</td>
<td>Moderate-to-severe dysfunction</td>
<td>3/8—4/8</td>
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<tr>
<td>V</td>
<td>Severe dysfunction</td>
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**Table 2. Yanagihara scale**

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<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>At rest</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Wrinkle forehead</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Blink</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Slight closure of both eyes</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Closure of one eye</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Depress lower lip</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Swell cheeks</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Whistle</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Grin</td>
<td>0</td>
<td>1</td>
<td>2</td>
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</table>
BTA injection is effective for synkinesis. Small doses of toxin are used on affected side and 2 times higher doses on the contralateral side symmetrically [36—38].

Rehabilitologists of Burdenko Neurosurgery Center revealed that BTA administration reduces severity of post-paralytic syndrome after facial nerve injury [1, 28, 33]. Six-month and 1-year incidence of synkinesis after facial nerve injury was significantly lower in patients after BTA injections compared with conventional approaches. Facial Disability Index and SFGS scores were also significantly better [1].

Other trials have also shown effectiveness of BTA for synkinesis management. Thus, E. Toffola et al. [39] reported 55 injections of BTA (2.5 units per each area) in 30 patients with facial muscles palsy followed by synkinesis. Orbicular muscle of the eye, temporal muscle, depressor labii inferioris muscle, platysma, frontal muscle and corrugator supercili muscle were target. Improved synkinesis was subsecuently observed in all patients. The authors concluded that BTA injections effectively reduce facial synkinesis severity and improve resting and voluntary movements symmetry.

K. Choi et al. [40] analyzed 42 patients with partial recovery after facial nerve injury. There were 1.5—2.5 units of BTA per each unilateral area and total dose near 10—26 units. Dose injected into contralateral hypertonic muscles was 2.5—5 units. Reduced synkinesis and improved facial symmetry were noted in all patients after bilateral BTA injections. SFGS score before and after injection was 38.8±10.68 and 58.4±12.46, respectively. The authors concluded that BTA administration is associated with significantly reduced synkinesis and improved facial symmetry. Therefore, improved quality of life, social interactions, appearance and eating may be observed.

**Conclusion**

Adequate administration of botulinum toxin improves rehabilitation in patients with postoperative dysfunction of facial nerve. BTA therapy should be per-
formed both in early (for BTA-induced ptosis on affected side and to improve contralateral facial symmetry) and long-term (post-paralytic syndrome correction) period after facial nerve damage. This approach is followed by improved rehabilitation and reduced incidence of long-term complications. Facial muscles palsy due to complete intraoperative intersection of the nerve requires consultation of maxillofacial surgeons to define terms of repair. BTA injection is advisable for facial asymmetry correction in these cases.

Authors declare no conflict of interest.
This research is actual due to high incidence of intraoperative facial nerve injury especially in tumors of posterior cranial fossa. Problem of postoperative facial nerve dysfunction is caused by anatomical proximity of tumor and cochlear-facial nerves followed by increased risk of prosoplegia and impaired rehabilitation. This lesion requires longer and more intensive recovery compared with idiopathic paresis of facial nerve.

Botulinum toxin injection is one of the most current and effective approach for facial neuropathy. Advantages of this method are local prolonged effect and no systemic undesirable reactions. Main effect of BTA is inhibition of presynaptic release of acetylcholine.

Authors reviewed literature data about botulinum toxin administration in early and long-term period after facial nerve damage. Botulinum toxin is used for different purposes. Its administration on intact side is useful to improve facial symmetry. According to our experience and other researchers it is followed by significantly improved rehabilitation and reduced long-term morbidity including contractures and synkinesis. Botulinum toxin is widely used for induced unilateral ptosis preventing such formidable complication of facial nerve dysfunction as lagophthalmos. This unfavorable event leads to advanced corneal disorders while medication alone is often ineffective. It seems to be that botulinum toxin is also effective for synkinesis in long-term period. This problem has always been considered difficult for rehabilitators and extremely undesirable for patients.

There are numerous references in the review, it is easy and interesting to read this report. Description of anatomical features of cochlear-facial nerves and tumor is supplemented by images that makes it possible to present this pathology in more details.

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Received: 27.06.17