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The choice of method of electroneuromyography in remote consequences of gunshot and mine-blast injuries of limb nerves

Oleksandr S. Solonovych 1, Albina I. Tretyakova 1, Ihor B. Tretyak 2, Lidiya L. Chebotaryova 1, Oleksandr O. Gatskyi 2, Oksana I. Mytsak 1

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Objective. Clarification of the nature of damage and degree of functional disorders in the remote consequences of gunshot and mine-blast injuries of limb nerves using neurophysiological techniques (NP) of functional diagnostics (stimulation and needle electromyography), correlation of these data with the nerve damage characteristics determined during surgical interventions (operative findings).

Materials and methods. 480 military personnel and civilians, men aged 18-64 years (average age 33.5 years), with gunshot and mine-blast injuries of limb nerves (LNI) within 1 to 11 months after injury were examined. A total of 1400 EMG studies were conducted. Clinical-neurological methods were used to determine the level, degree, and nature of LNI.

Results. Among the examined 480 patients, complete nerve damage was detected in 299, and partial in 181. Causes of nerve damage included: shrapnel, gunshot, mine-blast injuries, nerve rupture due to bone fractures, injuries by sharp objects, iatrogenic damage. In 62.3% of cases of complete LNI surgical interventions were performed using the technique of neurotization using branches of donor nerves. Provided anatomical integrity of nerve structures and presence of conductivity during EMG testing, external or internal neurolysis was performed. Surgical intervention timing: up to 6 months post-injury - 68.1% of cases; up to 3 months - 31.9%. Based on the results of comprehensive clinical-NP research, adapted schemes for assessing NP data corresponding to each pathohistological type of LNI were developed, and NP criteria for classifying consequences of LNI into three degrees of severity of functional deficit - mild, moderate, and severe were proposed.

Conclusions. Criteria for choosing the optimal NP diagnostic methodology for the remote consequences of gunshot and mine-blast injuries of limb nerves have been determined. Comprehensive clinical-instrumental diagnostics allows to objectify the level and degree of limb nerve damage, signs of neuromuscular apparatus recovery, provides information for planning of the surgical tactics and subsequent rehabilitation therapy.

Keywords: trauma; gunshot nerve injuries; mine-blast injuries; pain syndrome; diagnosis; electromyography; surgical treatment

Introduction

According to contemporary data, peripheral nerve (PN) injuries occur in 9-25% of cases of mine-blast trauma. Damage to brachial plexus structures accounts for 12 to 25% of all combat injuries [1, 2]. The severity of a patient's injury is determined by the caliber and type of projectile, the presence of associated injuries to blood vessels, nerves, limb bones, and soft tissues, which are detected in approximately 80% of cases.

The results of surgical treatment of combat trauma of PN, even with the availability of modern diagnostic equipment and a high level of surgical technique, are often unsatisfactory. This is due to the widespread damage to nerve trunk, the combined action of different types of energy, its direction, and the complex effects of blast waves on the body, as well as the features of the consequences of combat trauma of PN such as intrastem scars, purulent-inflammatory complications frequently accompanying combat trauma, disruption of microcirculation due to frequent injuries to major vessels, and significant damage to surrounding soft tissues.

Data of S.S. Strafun (2018) [3] indicate that even without disruption of the anatomical integrity of nerves in gunshot and mine-blast injuries, pathological changes occur in the injury zone, potentially causing direct muscle trauma or ischemia in muscles innervated by the damaged nerve. Therefore, there is a need to...
determine the nature and severity of nerve damage and, most importantly, to predict future recovery [3,4]. For optimal restoration of lost nerve functions in the limbs, modern neurophysiological (NP) diagnostics is crucial. It allows for the objectification of the level, type of injury, and nature of the pathological process, selection of the surgical treatment option, determination of the features of rehabilitation therapy, as well as monitoring of recovery dynamics.

Thus, the study of the clinical-NP features of the course of remote consequences of combat injury and the use of a complex of modern electroneuromyographic (ENMG) and electromyographic (EMG) diagnostic methods as pathognomonic for objectifying the condition of nerves and muscles after trauma is actual.

**Objective:** to specify the nature of damage and the degree of functional disorders in the remote period of gunshot and mine-blast injuries to the nerves of the limbs using NP diagnostic methods (stimulation and needle EMG), to study the correlation of these data with the features of nerve injuries detected during surgical interventions.

**Materials and methods**

**Study participants**

During the period from March 2022 to November 2023, ENMG-diagnostics of nerves function and limb muscle was performed in 480 servicemen and civilians aged 18 to 64 years old (mean age - 33.5 years) with gunshot and mine-blast injuries of the PN at the department of Functional Diagnostics of the State Institution of Rodmanov Neurosurgery Institute of the National Academy of Medical Sciences of Ukraine. All patients were male. A total of 1400 ENMG and EMG studies were performed. The patients were admitted for specialised treatment within 1 to 11 months after the injury. Upper limb nerve damage was recorded in 53.9% of cases, lower limb nerve damage - in 46.1%.

Informed and voluntary written consent for participation in the study and publication of data was obtained from all patients. The study was approved by the Ethics Committee of the SI "Rodmanov Neurosurgery Institute of the National Academy of Sciences of Ukraine" (Minutes No. 2 dated April 14, 2021).

The following research methods were used: 1) general clinical - to establish the diagnosis of "combat injuries of PN" (gunshot, mine-blast); 2) clinical and neurological - to assess the degree of traumatic injury of PN using modern generally accepted scales (assessment of the initial neurological status of patients, determination of the topical level of nerve injury, detailed assessment of existing neurological deficit motor (MRC Scale from M0 to MS) and sensory (Seddon від S0 до S5) functions, determination of lost and preserved muscle functions, sensitivity, etc. The degree of expressiveness of the pain syndrome was determined by the visual analogue scale of pain assessment (VAS), neuropathic pain - by the DN4 questionnaire (Bouhassira et al., 2005) [5]). The degree of recovery of movements and sensitivity was assessed using the specified scales and questionnaires; 3) neuroimaging, radiological - as indicated; 4) NP-complex diagnostic methods (preoperative, intraoperative and postoperative electrodiagnostics). The following techniques were used: examination of M-responses to direct nerve stimulation, predominantly innervating this muscle; segmental and step-by-step (short-segmental, as indicated) determination of the excitation conduction velocity (ECV) by motor and sensory fibres of the nerve to identify the site of conduction blockage; intramuscular needle EMG of muscles involved in the pathological process and intact muscles with evaluation of denervation spontaneous activity of muscle fibres and motor units parameters, determination of the severity of damage to structures and signs of recovery. The methods are described in the works [6-10] and are given in national and industry standards.

The studies were performed using the "Neuro-MVP" apparatus ("NeuroSoft", RF). Stimulation was carried out from the cathode with pulses of 0.1, 0.2, 0.5 and 1.0 ms duration, at a of frequency 1-4/s, the stimulation intensity was selected individually, mostly - 20-35 mV (10-30 mA), considering the level at which the maximum amplitude of action potentials (AP) of the nerve and M-response of the muscle was achieved. In some cases, they were recorded simultaneously on two output channels. Skin impedance under the electrodes was 5-10 kOhm. Deployment frequency - 10 ms/division, amplifier sensitivity was 50-100 μV for nerve AP, 100-10000 μV - for muscle AP. The frequency bandwidth was 10-10000 Hz. The mean value of 4 responses was calculated to determine the AP.

At needle EMG with immersion of a standard electrode in the motor point of the muscle, spontaneous activity of muscle fibres, as well as motor unit potentials (MUPS) during voluntary muscle contraction, interference and pattern of MUPS recruitment were investigated (Table 1). Additionally, a modified technique of M-response study during needle electrode withdrawal from the denervated muscle was used.

**Statistical analysis**

The research results were analyzed using the EZR package v. 1.35 (R statistical software version 3.4.3, R Foundation for Statistical Computing, Vienna, Austria). For qualitative data presentation, the frequency of occurrence (%), the risk of not achieving high treatment efficiency (%), and their 95% confidence interval (CI) were calculated. For rank variables - indicators of PN, the frequency (%) for each score rating was indicated. When comparing rank variables before and after treatment, the Wilcoxon T-test for paired samples was used, when comparing results between groups - the Kruskal-Wallis test, and for pairwise post hoc comparisons - the Dunn index multiple comparison test. Two-tailed critical regions were used in the analysis, and the critical significance level was set at 0.05.

**Inclusion criteria**

Military personnel and civilians aged over 18 with nerve damage due to gunshot and mine blast injuries, confirmed by accompanying medical documentation, referred for ENMG/EMG diagnostics and specialized treatment within 1 to 11 months after injury. All

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This article contains some figures that are displayed in color online but in black and white in the print edition
participants provided informed consent to participate in the study.

**Group characteristics**
Participants were divided into two groups based on the severity of PN and muscles damage and the decrease/absence of motor function. The study group comprised 299 (62.3%) cases of complete motor dysfunction and severe nerve damage, while the comparator group included 181 (37.7%) cases of partial nerve damage.

The causes of nerve damage (types of trauma mechanisms) were as follows: mine blast shrapnel wounds - 53.65%, gunshot wounds - 29.87%, nerve damage due to fractures and dislocations of limb bones - 10.36%, nerve injuries during medical evacuation stages (limb damage by tourniquets, iatrogenic injuries during primary surgical treatment) - 6.09%.

Among the examined individuals, 42.5% (204) sustained injuries to the upper limbs, 57.5% (276) to the lower limbs, and 28.0% (134) to both upper and lower limbs. The radial, gluteal, and tibial nerves were most frequently affected (Fig. 1).

**Study Design**
The study is retrospective cohort (Fig. 2).

### Table 1. Investigated nerves and indicators of "key" muscles

<table>
<thead>
<tr>
<th>Nerves</th>
<th>Muscles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>Thenar, radial flexor of the wrist</td>
</tr>
<tr>
<td>Ulnar</td>
<td>Hypotenar, ulnar wrist flexor.</td>
</tr>
<tr>
<td>Brachial plexus</td>
<td>Shoulder girdle: infraspinous, supraspinatus deltoid, biceps brachii, triceps brachii, wrist extensors, wrist flexors, thenar and hypothenar muscles.</td>
</tr>
<tr>
<td>Musculocutaneous</td>
<td>Biceps brachii</td>
</tr>
<tr>
<td>Radial</td>
<td>Wrist and finger extensors, triceps brachii</td>
</tr>
<tr>
<td>Axillary</td>
<td>Deltoid</td>
</tr>
</tbody>
</table>

Normative parameters for the nerves of the upper extremity include ECV >50 m/s, residual latency <3 ms, M-response amplitude not less than 50% compared to the intact side.

<table>
<thead>
<tr>
<th>Nerves</th>
<th>Muscles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gluteal</td>
<td>Anterior tibial, gastrocnemius, short extensor of toes, abductor hallucis</td>
</tr>
<tr>
<td>Tibial</td>
<td>Gastrocnemius, abductor hallucus muscle</td>
</tr>
<tr>
<td>Peroneus</td>
<td>Anterior tibial, short extensor of toes</td>
</tr>
<tr>
<td>Femoral</td>
<td>Quadriceps femoris</td>
</tr>
</tbody>
</table>

Normative parameters for the nerves of the upper extremity include ECV >50 m/s, residual latency <3 ms, M-response amplitude not less than 50% compared to the intact side.

*Note. In cases of significantly reduced conduction velocity (CV) and significantly increased distal latency (70% relative to the lower limit of normal), the possibility of tunnel syndrome or polyneuropathy should be excluded.*

**Figure 1.** Frequency of combat injuries to limb nerves
The aim of the ENMG diagnosis was to: 1) determine objective signs of limb nerve damage; 2) assess the degree of nerve function preservation; 3) evaluate the extent of nerve and muscle function loss (compared to the intact limb); 4) identify signs of nerve regeneration and reinnervation. 5) objectively assess changes in nerve and muscle function parameters compared to preoperative ENMG data. The obtained data allowed for the establishment of criteria for selecting ENMG diagnostic methods within specific time frames, i.e., developing a neurophysiological diagnostic algorithm.

The timing scheme was adhered to, as performing baseline electrophysiological studies at the 6th week post-injury is crucial. Subsequent examinations can be conducted at 3-4 months intervals to monitor nerve function recovery or its absence. It should be noted that in the absence of muscle reinnervation within 12 to 18 months, muscle changes become irreversible, hence excessive delay in surgery should be avoided.

The first assessment of the outcomes of reconstructive interventions was conducted at least 2 months earlier than the predicted regeneration period. The timing of the next (second) follow-up examination was within the predicted regeneration period. Subsequent evaluations were performed at the patient’s repeat visits (on demand) and until there was no significant progress in the recovery of lost neurological functions.

For interpreting the data from the first neurophysiological diagnosis, the following factors were important: 1) the cause of injury and the time elapsed since it (and primary surgical treatment); nerve function recovery.

When choosing the type of surgical intervention for gunshot injuries to the peripheral nerves, the level of nerve damage, the number of damaged structures, the nature of the injury, the extent of diastasis, and the type of intraneural nerve structure were taken into account. Surgical interventions for the consequences of gunshot injuries to the peripheral nerves and brachial plexus included neurolysis, autoneuroplasty, selective neurotization, chronic electrical stimulation, tendon and muscle transposition.

External and internal neurolysis

Neurolysis of peripheral nerve structures was considered the release of anatomically preserved nerve structures from surrounding scar tissue both circumferentially and in the distal/proximal direction relative to the level of injury (external neurolysis). Internal neurolysis involved performing longitudinal epineurotomy above the most affected segment of Figure 2. Study Design
the nerve structure until a typical fibrous structure appeared.

Nerve suturing
In cases of gunshot injuries, nerve suturing most commonly involved techniques of epineurial and perineurial sutures. In some cases, fascicular nerve suturing was performed. Whenever possible, attempts were made to perform direct suturing of the damaged nerve ends. For this purpose, such methods of overcoming the diastasis between nerve ends included mobilization within acceptable limits, transposition of the nerve to a new bed to provide a shorter pathway, optimizing limb position, etc. In cases of direct nerve suturing, a differentiated microsurgical nerve suturing was applied depending on the nerve’s structural type [11].

Autologous nerve grafting
The technique of autologous nerve grafting, involving the placement of segments of appropriate length between the proximal and distal segments of the injured nerve, predominantly sensory nerves, has been described in numerous literature sources [12] and did not differ significantly when performed in the patients involved in the study. Cutaneous nerves (most commonly sural nerve, superficial branch of the radial nerve, medial cutaneous nerves of the upper arm and forearm) were usually used as donor nerves. In cases of significant nerve defects, ulnar, median, or peroneal nerves were used in 14 cases.

Selective reinnervation - neurorization, anatomical, physiological, and technical principles
Nerve transfer (or neurorization) is a reconstructive surgical method aimed at restoring the functional capacity of only the distal part of the damaged peripheral nerve by involving the proximal part of another peripheral nerve with preserved functional capacity, i.e., neurons and their axonal processes serve as donors for reinnervation of the distal effector organ, for example, muscle or muscle groups [13]. The concept of this reconstructive surgical method involves sacrificing the function of less important donor nerves and donor muscles to restore more functionally significant recipient nerves and recipient muscles [14].

The anatomical and physiological principles underlying neurorization are quite simple: a) for restoring sensory function, a sensory donor nerve is used; for restoring effective motor function, a donor nerve with an appropriate number of motor fibers is used; b) loss of function of the donor nerve or donor muscle due to denervation (donor harvesting) should not result in the loss of important or critical function.

Technical principles aimed at achieving maximum functional outcome (effective function): a) harvesting the donor nerve as close as possible to the terminal effector organ; b) performing a direct anastomosis between the donor and recipient nerve without using an autologous graft between them, c) using donor nerves whose primary function closely resembles the desired function of the recipient nerve (agonistic functions) to facilitate cortical re-adaptation, d) performing neurorization at earlier stages for maximal effective recovery.

ENMG diagnostics was used for an objective assessment of nerve function recovery, corresponding muscle functions, and movements of the injured limb to obtain potential criteria for justifying further patient management tactics.

Results and Discussion
Analyzing the peculiarities of clinical manifestations and ENMG diagnostics data of the consequences of gunshot and mine blast injuries to the nerves of the upper and lower extremities at different levels, we proceeded from existing concepts of two possible mechanisms of restoring neuromuscular function: reinnervation of muscle fibers by collateral sprouting of axons of motor fibers or axon regeneration. If "foreign" axons "pick up" denervated muscle fibers (collateral sprouting), this manifests as high-amplitude polyphasic motor unit action potentials (MUAPs). Low-amplitude and polyphasic potentials are manifestations of axon regeneration.

In assessing the ENMG diagnostics data functions of traumatized peripheral nerves were relied on the AAEM EFNS/PNS criteria (Criterion of American Association of Electrodiagnostic Medicine and European Federation of Neurological Societies/Peripheral Nervous System). Surviving Schwann cells are capable of remyelination within 6–12 weeks. Axonal regeneration within the Schwann cell sheath occurs at a rate of approximately 1 mm/day in cases of axonal injury. However, its sprouting may occur in the wrong direction, leading to improper innervation, such as fibers of another muscle, tactile receptors in the wrong location, or temperature receptors instead of tactile ones. Regeneration becomes impossible if the cell body dies, and it is unlikely if the axon dies completely.

ENMG criteria for determining the pathohistological type of limb nerve injury

Neurotmesis (complete anatomical transection of the nerve and its sheaths) at 4–6 weeks after injury was characterized electroneuromyographically by the absence of the M-response with distal and proximal nerve stimulation (Fig. 3, A). Taking into account the innervation characteristics of the muscle, the M-response amplitude of <100 μV to supramaximal stimulation can be considered as the absence of the M-response. At needle ENMG of the corresponding key muscle (muscles), there is absence of motor unit potentials (MUPs) on voluntary contraction, with vigorous spontaneous activity manifesting as fibrillation potentials (FPs) and positive sharp waves (PSWs) (Fig. 3, B, Table 2). According to L.F. Kasatkina (1980), in cases of neurotmesis of long nerves, such an ENMG pattern is typical for 11-16 days after injury [8]. Therefore, the ENMG+EMG diagnostic method proved to be sufficiently sensitive in detecting neurotmesis (87%) and specific (89%). The method is informative regarding the presence of ENMG+EMG signs of neurotmesis and their absence (81–92%) in the subacute period of traumatic nerve injury, which is important in the preoperative period.

The study on the use of ENMG+EMG methods in patients with traumatic nerve injuries of the extremities allows determining the presence and severity of the
injury. The advantages of the method lie in its high sensitivity, specificity, and informativeness (prognostic value), reproducibility in repeated examinations, quantitative assessment of changes, which is important in dynamic monitoring.

Axonotmesis – complete axonal intrastem nerve interruption – due to complete disruption of axonal transport leads to axon death and the development of Wallerian degeneration, therefore, the ENMG picture is similar to that described for neurotmesis. Fibrillation potentials (FPs) appear on days 4–16, positive sharp waves (PSW) - approximately 7 days after FP.

If axonotmesis is partial, there is Wallerian degeneration of only a part of axons within the nerve and partial muscle denervation. Unlike cases of neurotmesis, within 2 weeks, along with denervation, reinnervation processes are activated, characterized by ENMG signs:
- significant decrease in M-response amplitude (by ≥50%);
- significant decrease in ECV (from -50% to 0 m/s);
- conduction block (CB) in the affected segment (due to damage to the myelin sheath) may be so pronounced that there is no M-response to nerve stimulation proximal to the lesion zone;
- loss of nerve sensory response.

In needle EMG:
- during the first week, electrical "silence" is possible;
- on days 7–16, vigorous spontaneous activity in the form of FP can be recorded;
- on days 14–30, vigorous PSWs;
- on the 3-4th week, against the background of pronounced denervation activity of FP and PSW during voluntary muscle contraction (tension), MUPS are recorded (Fig. 4).

In the first six months after injury, signs of contraction were noted only in large proximally located muscles of the limb, and later (6 months–1 year) motor function was restored in muscles located more distally. Already 90 days after the injury, some of the affected individuals exhibited the appearance of substitute movements, allowing compensation for motor impairments through gross undifferentiated locomotion.

Demyelinating lesions are considered as nerve contusion due to accompanying compression of the nerve by bony, fibrotic, or other volumetric formations (hematoma, foreign body). In stimulation ENMG of motor conduction along nerve segments and inching (stepwise examination) in the demyelination site, ECV significantly decreases, and the ENMG phenomenon of CB is revealed. Schwann cells, surviving after trauma, are capable of restoring the affected myelin sheath within 6-12 weeks.

![Figure 3. Complete axonal transection of the median nerve, absence of the M-response (A), vigorous spontaneous activity in the form of fibrillation potentials and positive sharp waves (B)](http://theunj.org)
Modern views on the phenomenon of conduction block (CB) as evidence of demyelinating processes have undergone changes. Conduction block is an electrophysiological phenomenon of decreased amplitude and area of motor response upon stimulation at the proximal point compared to the distal response. There is active discussion on the significance of CB in the differential diagnosis of demyelinating and axonal neuropathies, as well as criteria for diagnosing conditions in which this phenomenon is recorded. It has been established that the

Table 2. Sensitivity, specificity, and informativeness of ENMG+EMG parameters for intraoperative diagnosis of neurotmesis

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Based on changes in M-response and motor ECV</th>
<th>Based on changes in M-response, motor ECV, and intramuscular registration of denervation potentials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity = TP: (TP+FN) · 100%</td>
<td>72</td>
<td>87</td>
</tr>
<tr>
<td>Specificity = TN : (TN+FP) · 100%</td>
<td>80</td>
<td>89</td>
</tr>
</tbody>
</table>

Notes: TP - true positive (correct wear); FP - false positive (false wear); FN - false negative (false non-response); TN - true negative (correct non-response)

Figure 4. ENMG in partial axonal injury of the median nerve – significant decrease in M-response amplitude (A) at 4 weeks after injury, motor unit potentials are registered (B)
detection of CB in electrophysiological studies, as well as
the value of its parameters, is not strictly associated with
morphological changes. Regardless of the presence
of proven myelinopathy or axonopathy, CB with NP positions
does not differ. The general and specific pathophysiological
mechanisms of CB formation in compression neuropathies
should be considered within each nosological form [15].

In our opinion, it is expedient to distinguish three
degrees of CB severity: 1st – decrease in M-response
amplitude <50% relative to the contralateral nerve
index of the intact limb, 2nd – decrease in amplitude
by 50–75%, 3rd – decrease in amplitude by >75% [9].

During the period up to 8 months after gunshot
nerve injuries both in neurotmesis and axonotmesis,
among sensory disturbances, symptoms of loss
(hypoesthesia, anesthesia) predominated, with
manifestations of paresthesia in the denervation zone.
Motor disorders were manifested by weakness, and in
cases of neurotmesis, often (in >35% of cases) also by
the absence of movement in the corresponding muscle
groups; almost all cases involved muscle atrophy, and
in some affected individuals (about 9%), contractures
were present.

Performing distal neurotization was effective,
reducing the distance to the target (muscle, muscles).
It is important to know the internal anatomy of the
nerves, especially the branches. This operation is more
useful, especially in the case of the 3rd degree, when it
is unclear whether anything will change for the better;
the operation allows obtaining a more satisfactory
result [14]. Decompression can be performed in the 1st
degree. The third degree is highly variable: there are
no FP and PSW, and the registration of MUPs becomes
crucial. It should be remembered that the optimal
intervention times are 3-6 months after the injury. If
the operation is performed later, the recovery will be
much worse.

**ENMG signs of axon regeneration and muscle
reinnervation in patients with remote consequences
of combat trauma of limb nerves**

Results were interpreted using the classification
of peripheral nerve injuries [16], which is convenient
and detailed (Table 3). During electrodiagnostic
examination of nerve conduction (ENMG) and with
the help of a needle electrode (EMG) in acute lesions, when
FP and PSW are present, the axonal type of injury is
determined; in the absence of FP and with paresis
present, neuropraxia with a favorable prognosis for
recovery, i.e., demyelinating lesion.

If motor unit potentials (MUPs) are registered in the
affected muscles located proximal to the site of injury
after approximately 3 months, the prognosis for recovery
is favorable. Such a neurophysiological pattern may be
characteristic of grade II axonotmesis. In the absence
of MUPs after ≥4 months or the appearance of initial
MUPs, it is difficult to determine the prognosis (recovery
may be partial or incomplete). If there are no MUPs
during this period, the prognosis is unfavorable, and
consideration should be given to surgical intervention.

The developed classification of the consequences of PN
injuries helps determine the severity of functional deficit
(mild, moderate, and severe).

**Analysis of factors influencing the clinical
and neurophysiological features of the course
of remote consequences of gunshot injuries to the
nerves of the extremities**

Analysis of ENMG data and the results of neurosurgical
treatment of patients allowed the development of
schemes that help predict the rate and possibility of
recovery based on ENMG indicators for a specific type
of extremity nerve injury (Fig. 5).

The proposed schemes also provide a rationale
for decision-making in the treatment of patients
with remote consequences of combat-related nerve
injuries of the extremity. Conducted ENMG studies
allow comparing the identified features of the remote
period of combat trauma of the nerves of the limbs and
adopting as axiomatic recommendations of modern
neurophysiology. The most informative ENMG study,
conducted within 2-3 weeks after nerve injury, taking
into account the distance of the injury to the muscle.
Detection of denervation changes in the muscle
depends on the development of Wallerian degeneration
of the damaged axons. A decrease in the number
of motor units recruited during muscle contraction
(recruitment pattern analysis) is an adequate criterion
for determining the topical level of nerve injury in
the early stages after trauma. Needle EMG allows
identifying two types of recovery processes in nerve
injury - reinnervation of muscle fibers through collateral
sprouting and the formation of new MUPs due to axon
regeneration.

Thus, motor and sensory nerve conduction studies
and needle EMG provide objective data useful for
determining the localization of peripheral nerve injuries,
identifying and quantifying the degree of axonal loss,
predicting recovery, and making decisions about further
treatment. The goal of surgical intervention is often to
improve function rather than normalize it. Achieving
optimal treatment outcomes requires comprehensive
diagnostics with a multidisciplinary approach to the
problem and differentiated use of new surgical treatment
methods for patients with combat-related nerve injuries
of the extremities.

ENMG and needle EMG with the detection of MUPs
denervation phenomena objectively determine the
localization of PN damage, the degree of axonal loss
and recovery prognosis, facilitate decision-making about
further treatment, and the specifics of rehabilitation
therapy. Neurophysiological diagnostics not only help
determine the level and type of nerve injury but also
are an important factor in determining the prognosis
for recovery, the need for surgical intervention, and the
optimal timing for its implementation.
Table 3. Neurosurgical aspect of classification of peripheral nerve injuries with ENMG parameters at different time points after trauma depending on the severity of nerve damage, registration in the distal part of the limb

<table>
<thead>
<tr>
<th>Degree of injury</th>
<th>Recovery prognosis</th>
<th>Recovery period</th>
<th>Recovery</th>
<th>Electrodiagnostic examination</th>
<th>Acute PN injury</th>
<th>Chronic PN injury</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>FP/PSW</td>
<td>MUP</td>
<td>Surgical intervention</td>
</tr>
<tr>
<td>I Neuropraxia</td>
<td>Favorable</td>
<td>Fast (&lt;12 weeks)</td>
<td>Complete</td>
<td>–</td>
<td>Normal</td>
<td>+/-</td>
</tr>
<tr>
<td>II Axonotmesis</td>
<td>Favorable</td>
<td>Slow (1 mm/day)</td>
<td>Complete</td>
<td>Present</td>
<td>+/-</td>
<td>–</td>
</tr>
<tr>
<td>III Variable</td>
<td>Slow (1 mm/day)</td>
<td>Partial</td>
<td>Present</td>
<td>+/-</td>
<td>–</td>
<td>++</td>
</tr>
<tr>
<td>IV Neurotmesis without interruption</td>
<td>Unfavourable</td>
<td>Absent</td>
<td>Absent</td>
<td>Present</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>V Neurotmesis</td>
<td>Unfavourable</td>
<td>Absent</td>
<td>Absent</td>
<td>Present</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>VI Mixed injuries (1-Y)</td>
<td>Mixed</td>
<td>Recovery and the type of surgical intervention depend on the injury and combination of nerve injury grades</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Notes: (–) – absent; (+) – collateral sprouting or emerging potentials; (++) – stable motor unit potentials or emerging low-amplitude polyphasic potentials. (Adapted from Interpreting Electrodiagnostic Studies for the Management of Nerve Injury // Stahs Pripotnev, Robert C Bucelli, J Megan M Patterso, Andrew Yee, Mitchell A Pet, Susan Mackinnon // Hand Surg Am. 2022 Sep;47(9):881-889. doi: 10.1016/j.jhsa.2022.04.008 [16])
Conclusions

1. According to the results of a complex clinical and electroneuromyographic study of the state of the neuromuscular apparatus of the extremities and its functional capabilities in individuals with combat-related nerve injury, it has been established that the peculiarities of the course of the recovery period within 4-6 (8) months after gunshot and mine blast injuries to limb nerves depend on the level and severity of axonal damage. The pathohistological variant of the nerve injury has the greatest impact on recovery outcomes (69.2%), while the localisation of the injury affects to a lesser extent (29.8%).

2. The recovery of lost limb functions in the specified terms due to regenerative sprouting exhibited a slow course and was most effective in the proximal parts of the limb. ENMG correlates of this pattern in the majority of patients (69.5%) were two-stage restoration of electrical excitability and conductivity of the damaged nerve trunk and functionally related muscle groups.

3. Without the use of needle EMG, a current objective assessment of axonal and demyelinating processes in the injured nerve and the effectiveness of motor unit recovery is not possible.

4. According to the results of the complex clinical and neurophysiological study of individuals with the consequences of combat-related injuries of the PN, the classification of the consequences of PN injuries was developed, distinguishing three degrees of functional deficit severity – mild, moderate, and severe.

5. Prediction schemes for the recovery of neuromuscular apparatus function on the basis of a set of ENMG-study data have been created.

Disclosure
Conflict of interest
The authors declare no conflict of interest.

Ethical approval
All procedures performed on patients comply with the ethical standards of institutional and national ethics committees, the 1964 Declaration of Helsinki and its amendments or similar ethical standards.

Informed consent

Informed consent was obtained from each of the patients.

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References


A simple CT-scan-assisted craniotomy for small superficial cortical lesions in rural conditions

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Objective: Despite the excellence and modernization in medicine and neurosurgery, many countries, including Greece, still lack neuronavigational techniques, or hospital budget to cover the neuronavigation expenses. Therefore, help in the craniotomy design is needed, not only to safely remove a superficial lesion but also to help cut the expenses of neuronavigation in cases of economic challenges. The current study aims to present a new simple technique for craniotomy design for superficial cortical lesions.

Materials and methods: The technique was applied as an urgent lifesaving method because of lacking frameless neuronavigation to 35 patients (19 males and 16 females) with superficial cortical lesions during a five-year period. This technique requires computer tomography (CT) scan, needle, and methylene blue dye. The patients were operated on at the neurosurgical department of Democritus University Hospital in Alexandroupolis, Greece.

Results: From those 35 individuals, 16 had brain metastases, six patients had meningioma, six patients had glioma tumor, two had an abscess, two patients had arteriovenous malformation (AVM) and three patients had brain hematoma. The lesion was completely resected in all the 35 patients without any complications from the craniotomy or the colorant dye infusion. The accuracy of the technique compared with the frameless neuronavigation of the literature was extremely high.

Conclusion: This is a simple and cheap technique for craniotomy design in case of superficial cortical lesions. It could be used in rural conditions or in hospitals with limited resources, as long as there is a computed tomography scan, craniotomy device and a dye stain.

Keywords: craniotomy; CT scan; rural conditions; design; superficial cortical lesion

Introduction

Incision and craniotomy planning are crucial components in the field of neurosurgery. The primary target of the optimal craniotomy is to protect the underlying structures and anatomy while permitting the most optimal exposure of the lesion [1]. The lesion is the primary navigation to the used approach.

During the last few years, there has been a rapid development of technological aids designed to solve the issues as mentioned above. The following guidance techniques are indicatively referred to as neuronavigation. These techniques, which are currently available and provide very high accuracy, are still too expensive to obtain. Worldwide, numerous hospitals lack the equipment that would enable them to use the advantage gained from the implementation of these techniques.

The current study aims to present a new technique for the design of craniotomy for superficial lesions in rural conditions and the authors’ experience with the utilization of this simple and easily applicable method.

Material and Methods

Surgical Technique

In order to identify cortical lesions, and thus, design a craniotomy, the author (T.B.) has developed the following simple technique. Each patient has a written consent for the performance of the technique, as well as for his personal data usage.

The leading indicator for the utilization of the technique is the detection of a small (<5cm) superficial lesion so that the precise design of the craniotomy could be achieved.

The requirements for employing the technique are simple and inexpensive materials, in a specific methylene blue solution, a needle and an insulin syringe. It is also required that the hospital has a computer tomography (CT) scanner and a craniotomy device.

The patient undergoes a CT scan of the brain initially. While he is lying in the scanner, we choose the image showing the largest diameter of the lesion. Then, the technician/operator opens the laser of the machine, thus pointing it out to the location of the lesion on the skull.
After that, the physician sterilizes the skull area and inserts a small needle of insulin in the theoretical centre of the lesion (or the location that he believes is the centre of the lesion). The needle remains pinned subcutaneously on the skull.

A second CT-scan is obtained with the needle wedged in the skin (theoretically in the centre of the lesion).

The physician repositions the needle if it is not in the centre so that it is located precisely in the centre of the lesion and obtains a repeated CT scan to ensure that it is.

When the surgeon is confident for the location of the needle, he marks its position on the skin (Figure 1).

After that, a tiny amount of methylene blue (0.5–1cc) is injected into the galea aponeurotica.

On the next day, the patient is taken into the operating room. We make the incision according to our mark at the most optimal location for lesion exposure and postoperative restoration process, trying to position it in the centre. After the skin flap has been restored, the surgeon detects the exact point of stained with methylene blue of the galea aponeurotica. This point is where the first keyhole is made. Thereafter, the drilling is made in a circle-wise way, so that the keyhole can remain in the centre (Figure 2).

**Data Collection and Selection**

This method was adopted in the department of neurosurgery at the University Hospital of Alexandroupolis for a period of five years (2005-2010). The patients were operated on as isolated cases in urgent need of navigation but lacking hospital resources. Each patient was informed for the procedure and possible complications and signed a written consent form. For the present study, the authors retrospectively collected the data from those cases.

The inclusion criteria included superficial lesions <5cm.

The technique was applied in 35 brain surgeries, involving 19 males and 16 females with an average age of 56.5 years. From those 35 individuals, 16 had brain metastases, 6 – meningioma, 6 – glioma tumor, 2 – abscesses, 2 – arteriovenous malformation (AVM) and 3 – brain hematoma.

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**Figure 1.** Preoperative craniotomy design. A - needed tools; B - CT scan showing the largest diameter of the lesion; C - CT scan with pinned needle.
Results

Mean number of CT scans obtained during the preoperative navigation was 2.

The lesion of each participant was superficial so that it was identified macroscopically. Among the sample group (N= 35), 80% (28) of the incidents was associated with superficial cortical brain tumors with a diameter of approximately 3 cm. All the lesions were resected successfully with 100% success rate without any inaccurate resection.

In Figure 3 the localization of the lesions is depicted (18 parieto-occipital; 10 frontal; 7 tempo-occipital).

No complications were observed due to the subcutaneous injection of the dye (e.g. infection) or the craniotomy. The patients were lost for follow-up.

Figure 2. Surgical performance of the technique. A - Craniotomy performance; B - resected lesion; C - Postoperative x-ray

Figure 3. Results. A - Preoperative CT showing the lesion; B - Postoperative CT showing its resection.
Discussion

Craniotomy is one of the most ancient procedures dating up to the Mayan [2]. The craniotomy as procedure, however, was structured for the first time by Hippocrates, who succeeded to review and constitute practice recommendations [3]. Despite of the wide use of craniotomy for the variety of skull injuries, it was not long ago when the craniotomy was first used for the removal of cortical lesion [3, 4].

The resection of the lesion was based on preoperative images, surgeon’s imagination and good knowledge of anatomy [5]. Craniotomies and surgical orientations were applied based on the preoperative images and anatomical landmarks. This was changed with the introduction of neuronavigation systems and stereotaxy. The surgical practice thereafter was easier and safer for the patients.

Currently, patient’s positioning and craniotomy design are fundamental for the neurosurgical practice of lesion resection. Patient’s positioning is also the fundamental part of the neuroanesthesiology. The most favorable head position is the one providing maximal exposure of the lesion at the shortest distance; and if possible, positioned in a way that the craniotomy would be parallel to the ground [6].

According to Clatterbuck et al. [7] there are five classical types of craniotomy approaches: frontal, temporal, parietal, occipital and one to the posterior fossa and six, according to the modern neurosurgery: anterior and posterior parasagittal, pterional, subtemporal, midline and lateral suboccipital. As mentioned earlier, the lesion defines the used approach.

The nowadays known methylene blue dye was initiated by Caro et.al. in the XIX century by replacing the p-phenylenediamine with N, N-dimethyl-p-phenylenediamine [8, 9, 10]. Until now, the methylene blue is known with about 222 other names [10].

Its medical application began early with Paul Ehrlich in 1880 year, who discovered the staining properties of the methylene blue [11]. A few years later, Bodoni et.al. [12] found the “calming” opportunities of the dye without sharing very detailed information on the subject.

Currently, methylene blue is used mainly to treat methemoglobinemia, vasoplectic adrenaline-resistant shock, Alzheimer’s disease, pediatric malaria, priapism and to prevent urinary tract infections in advanced-age patients [10]. Moreover, it is widely used to do lymphatic mapping in cancer patients [13]. Long before that, it has been reported that MB injection could be used in attempt to find an arteriovenous malformation (AVM) in the intestines. Such study was reported by Fogler et.al. [14], where methylene blue injection was used as an intraoperative guide for the resection of AVMs in the small intestine. After this discovery, Gifford et.al. [15] used MB for mapping of the enteric hemorrhage. Similarly, Liu et al. [16] used MB to find the exact structure of a brain AVM.

Other applications include experimental works with animals and plants [10].

After the approval of the methylene blue or PROVAYBLUE® by the Food and Drug Administration (FDA), the latter approved other three dyes, based on the methylene blue formula: Evans Blue, Patent Blue and Trypan Blue [17]. Evans Blue was withdrawn for safety reasons, Trypan Blue (VisionBlue®) is used in ophthalmology and Patent Blue appeared to be the same as the methylene blue in lymphatic cancer mapping [18, 19].

Methylene blue is a dye, used for years in neurosurgery. Initially it was utilized to detect cerebrospinal fluid blockage and leakage [20, 21, 22]. Later, because of its indisputable help in cancer detection, it was used for the detection of glioma [23]. Others, such as Phelan and colleagues [24] used the methylene blue intraoperatively to detect the intracranial extent of the dermoid cysts, thus avoiding unnecessary craniotomy.

Watts et al. [25] tested the methylene blue dye in rats with mild traumatic brain injury (TBI). According to his study, the rats injected with the dye had smaller lesions. Moreover, Shen et.al. [26] found that MB had a protective role in vivo and in vitro for the blood-brain barrier and reduced the rate of apoptosis after TBI.

In a triple-blind randomized placebo-controlled study, Farrokh et al. [27] found that methylene blue improves the postoperative low back pain, as well as the quality of life.

Lee et.al. [28] in a novel study found that MB has cytotoxic action in neuroblastoma and astrocytoma cells, thus, inhibiting the action of guanylyl cyclase. The latter is an enzyme that transforms guanosine triphosphate (GTP) to cyclic guanosine monophosphate (cGMP) and pyrophosphate.

Finally, Snuderl et al. [29] presented the use of MB in the field of perioperative neuro-oncology. In his attempt to achieve better intraoperative diagnosis, he took tissue samples from the tumors and “normal tissue” which should be resected and injected them with methylene blue. After a few minutes the samples were image recorded on the microscope. The images were similar to the ones obtained with a typical histopathological staining with eosin and hematoxylin.

However, to our knowledge, no study has reported its use for craniotomy design to date.

Nevertheless, this method cannot be applied to deep lesions, as no visual contact is feasible in this case. Furthermore, the size of lesions should not be smaller than 5 cm, because in that case the accuracy of the method could not be maintained at the desired level, due to the possible displacement of the skin (during the placement of the head in Mayfield).

Neuronavigation

The need of anatomical localization started gaining importance with the progress of understanding of spatial organization [30, 31]. The progress of imaging such as CT and magnetic resonance imaging (MRI) enhanced the knowledge of anatomical localization and the need for neuronavigation. Leksell [32] and Spiegel [33] improved further the precision of neurosurgery with the frame-based navigation, until the frameless neuronavigation system emerged. The latter combines data from variety of modalities (MRI, functional MRI, diffusion tensor imaging (DTI), CT) reorganizing it into 3Dimensional (3D) images, in order to target a lesion located in any area within the nervous system [31].

The frameless navigation systems are believed to be accurate as much as the frame-based navigation systems, targeting accuracy intraoperatively in the
range of two-three mm [34]. The mistakes of the frameless stereotactic navigation system either from the preoperative technique of probe tracking, or from the preoperative images (too old images or low quality) and their registration to the frameless navigation system.

As mentioned previously, the present technique had a quite high accuracy taking into consideration the fact that it was CT-guided infusion of MB. The images were taken a few hours before surgery and the surgeon, as well as the radiologist were present at the moment of their performance.

To our knowledge, this is the first study in the literature to present the use of MB as a cheap tool for neuronavigation. Even though technology and resources for healthcare are improving, many hospitals lack neuronavigation and resources. Therefore, the physicians should be able to still perform at their best despite the present challenges. Despite of its novelty, the study has a few limitations. The patients were enrolled during a long period of time and no follow up was available. The hospital covers a large area of the North – East Greece and many of the patients were lost due to their localization. Finally, the study sample was too heterogenous and insufficient to obtain any comparison for navigation accuracy.

Conclusion
The present technique is effortless and cheap, with sufficiently good precision for specific lesions. Therefore, the authors would like to introduce the above-described technique as it is a safe, easy and affordable method which can be widely used in hospitals that do not have the potential of using neuronavigation.

Disclosure
Conflict of interest
No conflict of interest to declare.

Ethical approval
The method and research were approved by the hospital’s ethical committee.

Informed consent
Each patient provided a written consent for the performance of the technique, as well as for the use of his/her personal data.

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Vestibular Schwannomas: implementation of PANQOL and Mayo VSOQL Index scales in Ukraine and justification of treatment strategy with preservation of quality of life (problem analysis, own experience, discussion points)

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Objective: To evaluate the treatment outcomes of sporadic vestibular schwannomas (VS) to substantiate the choice of optimal treatment strategy considering quality of life indicators using the Penn Acoustic Neuroma Quality of Life Scale (PANQOL) and the Mayo Clinic Vestibular Schwannoma Quality of Life Index (Mayo VSOQL Index) scales in Ukraine.

Materials and Methods: 1100 patients with VS were treated at the Subtentorial Neurooncology Department from 2001 to October 2023 and 373 were primarily considered for dynamic observation ("wait-and-scan") at the Department of Ear Microsurgery and Otoneurosurgery of the Kolomichenko Otolaryngology Institute. Data on 359 patients (some of whom underwent surgery in the mentioned departments) who received radiotherapy (RT) from 2010 to 2023 in the Radioneurosurgery Department are also provided. The PANQOL and Mayo VSOQL Index scales were implemented to assess the quality of life of patients with VS. Scientific publications from the PubMed database related to the study of the quality of life in patients with VS were analyzed.

Results: The analysis was based on patient data from the database for the period 2017 - October 2023, 391 patients with VS were treated, including 359 who underwent surgical treatment (schwannomas resection), 4 – tarsorrhaphy after VS resection, and 28 who received combined treatment (surgery + radiotherapy). A separate group consisted of 359 patients who underwent radiotherapy (RT). Of 177 patients who underwent radiosurgical treatment, 65 (36.7%) had Stage III VS according to the classification of W.T. Koos, and 112 (63.3%) had stage IV VS. Primarily diagnosed tumors were treated in 110 (62.1%) and 67 (37.9%) patients with residual postoperative. Follow-up data were obtained for 159 patients. At the Kolomichenko Otolaryngology Institute, 373 patients were under observation with the primary "wait-and-scan" strategy, of whom 110 (29.5%) had their VS removed due to symptom progression or progressive course, and 24 (6.4%) underwent RT. Of the 27 patients in the Subtentorial Neurooncology Department study group, 7 (25.9%) underwent surgery, and 8 (15.8%) underwent RT.

Conclusions: Global practice in assisting patients with VS indicates a shift towards dynamic follow-up and an increase in the frequency of using radiation treatment methods. Over the past years, strategy have been proposed that do not recommend the "wait-and-scan" mode due to the risk of life-threatening complications associated with tumor growth. However, there is very little data on long-term outcomes (more than 5 years) and quality of life. VS primarily detected by magnetic resonance imaging in Ukraine significantly larger (Koos III-IV) than those reported in the literature. The implementation of specialized scales for assessing the quality of life of VS patients in Ukraine will help improve outcomes by applying personalized criteria for treatment routes, increasing the level of awareness and responsibility of both patients and doctors.

Keywords: vestibular schwannomas; quality of life; surgical treatment; microsurgery; radiosurgery; morphology

Introduction

The problem of managing patients with vestibular schwannomas (VS) in Ukraine is due to late diagnosis. This is explained by several reasons: low level of the population health self-awareness, absence of state social programs and targeted information policies on disease prevention, insufficient level of trust in healthcare workers, low awareness among healthcare professionals...
Quality of Life Scale (PANQOL) and the Mayo Clinic Vestibular Schwannoma Quality of Life Index (Mayo VSQOL Index) scales in Ukraine.

**Study Objectives**

The adaptation, pilot application, and implementation of the Penn Acoustic Neuroma Quality-of-Life Scale (PANQOL) and the Mayo Clinic Vestibular Schwannoma Quality of Life Index (Mayo VSQOL Index) in Ukraine.

**Materials and Methods**

Out of 1100 patients treated at the Subtentorial Neurooncology Department, the data of 391 patients from the database 2017 - October 2023 were used in the study.

**Patient Groups**

Patients were divided into groups depending on the location of treatment. The first group comprised 391 patients who underwent treatment at the Subtentorial Neurooncology Department of Romodanov Neurosurgery Institute from 2017 to October 2023. Surgical treatment was performed in 363 cases, of which 11 were reoperations due to continued tumor growth, managed with combined treatment in 28 cases.

The second group consisted of 359 patients who received treatment through radiation methods at the Department of Neuroradiology and Radioneurosurgery of Romodanov Neurosurgery Institute from 2010 to 2021. Of the 177 patients who underwent radiosurgical treatment, 65 (36.7%) had stage III VS according to the W.T. Koos classification, and 112 (63.3%) had VS stage IV. Follow-up data were obtained from 159 patients, with 110 (62.1%) having primarily diagnosed tumors and 67 (37.9%) patients with residual postoperative.

The third group comprised 400 patients who were under observation with the primary "wait-and-scan" strategy, of whom 373 were observed at the Kolomichenko Otolaryngology Institute. Among them, in 110 (29.5%) patients subsequently underwent the VS removal due to symptom progression, and 24 (6.4%) underwent radiation therapy. According to the Subtentorial Neurooncology Department of Romodanov Neurosurgery Institute, 7 (25.9%) patients from the study group underwent surgery, and 5 (18.5%) received radiation therapy.

All patients provided informed and voluntary written consent to participate in the study and publish data. The study was approved by the Ethics Committee of the SI “Romodanov Neurosurgery Institute of the National Academy of Sciences of Ukraine” (Minutes No. 2 dated April 14, 2021).

**Inclusion Criteria for the Study:**

- Presence of unilateral primary (sporadic) VS;
- Availability of magnetic resonance or computed tomography scans of the brain with paramagnetic/x-ray contrast intravenous contrast for surgery;
- Histological verification of VS diagnosis;
- Patients aged over 18 years;
- Voluntary patient consent to participate in the study.

**Exclusion Criteria from the Study:**

- Neurofibromatosis type II;
- Absence of imaging data confirming the presence of VS;
- Absence of histological verification;
- Age under 18 years.

**Quality of Life Assessment Scales**

To improve treatment outcomes for VS patients based on the assessment of their quality of life, we selected the PANQOL [8] scale and the Mayo VSQOL Index [9] and performed the procedure of their adaptation for Ukraine.

**Statistical Analysis**

Statistical analysis was conducted using the Deducer package (Java GUI extension for the R statistical software, licensed under GNU).

Demographic and clinical characteristics were evaluated using descriptive statistics (arithmetic mean and standard deviation were used for continuous variables, proportion and frequency distribution for categorical variables). The distributions of categorical variables were compared using the Pearson’s chi-square test and Spearman rank correlation test.

Patients were categorized by age at diagnosis (<45 years, ≥45 years), Karnofsky performance status index (<70 points, ≥70 points), House–Brackman (HB) grading scale (<3 points, ≥4 points), extent of tumor resection (partial, subtotal, and total), tumor size (largest diameter <30 mm, ≥30 mm), and Koos grading scale [10] (from 1 to 4 points).

All statistical tests were two-tailed. A p-value of <0.05 was considered statistically significant.

**Results**

**Diagnostics**

According to the European Association of Neuro-Oncology (EANO) guidelines, the main symptom of VS is unilateral hearing loss (94%), with 83% of patients experiencing tinnitus [11]. Indications for performing brain MRI may include detection of an interaural difference of ≥10 dB at two or more adjacent frequencies or ≥15 dB at one frequency on audiogram [12]. Additionally, patients may experience difficulty understanding speech in the affected ear, while only minor asymmetry will be detected on the audiogram. In 10–15% of patients, symptoms may begin with dizziness, described as episodes of unsteady gait worsening in the dark without hearing loss or tinnitus [13]. Unfortunately, the diagnosis of VS in Ukraine cannot be compared with data from leading countries. In our observations, 75% of tumors are of large or extremely large size (≥T3b) [14]. Therefore, the issue of VS in Ukraine differs significantly from that in developed countries and requires a specialized multidisciplinary approach.

**Surveillance, surgery, facial nerve function**

When a VS is detected, the question arises regarding the treatment strategy, considering the size of the tumor and the existing symptoms. Several studies [15-18] recommend adhering to an observation and waiting strategy until active interventions are initiated, especially if the size of the VS is small or medium (according to the classifications of W.T. Koos [10], J. Regis [19], and M. Samii [20]), and options for microsurgery or radiation are considered only in cases of tumor growth. According to E. Zanoletti et al. [21], primary surgical treatment of small VS, especially those <1 cm in cysternal dimension, is necessary to achieve better preservation of facial nerve function compared to tumors sized 1-2 cm.

In the United States, over the last 50 years, a cross-sectional study of VS treatment showed a decrease in the proportion of microsurgical treatment from 88-86% in the 1970s-2000s to 44% in the last decade, an increase in the proportion of observation from 7% in the 1990s to 14% in the 2000s and to 33% in the 2010s, and an increase in radiosurgery from 7% in the 1990s to 28% in the last decade [22].

In Ukraine, patients undergoing VS treatment are mostly treated at Romodanov Neurosurgery Institute and Kolomichenko Otolaryngology Institute. However, while Romodanov Neurosurgery Institute before 2017 observed only large and extremely large VS, T4a-b according to the Hanover classification [20], requiring surgical treatment, earlier diagnosis of VS at Kolomichenko Otolaryngology Institute allowed the adoption of a “wait-and-scan” strategy since 2003. For example, in the Department of Ear Microsurgery and Otoneurosurgery of Kolomichenko Otolaryngology Institute, 373 patients with VS aged 18 to 79 years (mean age: 54 years) were examined from 2003 to 2023. Among the patients, there were 144 (38.6%) males and 229 (61.4%) females. The first stage of VS according to the Koos was diagnosed in 153 (41%) cases, the second stage in 112 (30%), the third stage in 67 (18%), and the fourth stage in 25 (6.8%) cases. Intralabyrinthine VS was detected in 9 (2.4%) patients, with 2 of them having combined intracanalicular tumors. Most patients (239; 64.1%) are under observation with regular MRI monitoring. The first follow-up examination after tumor detection was performed at 6 months, and subsequent follow-ups were conducted every 12 months for 5 years. In the absence of signs of tumor growth, subsequent follow-up examinations are conducted every 2 years. According to our preliminary data, the level of vascular endothelial growth factor (VEGF) and transforming growth factor beta-1 (TGF-1β) may serve as indicators of tumor growth. Surgery was performed in 110 (29.5%) patients. Various surgical approaches were used, including translabyrinthine, retrosigmoid, and middle fossa approaches. The choice of approach depends on the tumor size, its location in the internal auditory canal, and hearing status. Stereotactic radiosurgery or radiotherapy was performed in 24 (6.4%) patients, primarily based on patient choice. According to the Subtentorial Neurooncology Department data, out of 27 patients from the study group from 2019 to October 2023, 7 (25.9%) underwent surgery, and 5 (18.5%) underwent radiation therapy due to progressive growth or symptoms.

At the dawn of microsurgery, its negative impact on patients’ quality of life was noted, but with the improvement of intraoperatively controlled microsurgery, this negative impact decreased [20]. Both observation and radiosurgery are effective treatment options for small-sized VS, while surgical treatment provides a high level of facial nerve preservation, acceptable preservation of hearing, and sufficient tumor removal [23]. Based on our own experience, we have come to the conclusion, which is consistent with the opinions of other clinicians [23], that surgical treatment should be considered as an option for initial treatment of symptomatic small VS in younger patients, while observation or radiosurgery should be considered for elderly individuals. High-quality
Microsurgical treatment is only possible in specialized institutions with standardized approaches, where a large number of such surgeries have been performed, ensuring a lower frequency of facial nerve function disturbances and other complications, as well as a shorter length of stay in the medical facility [24]. We are of the opinion that delaying the removal of a VS should be avoided, as its growth and expansion into the internal auditory canal to 14—20 mm significantly complicates the achievement of expected microsurgical results [25]. Our experience with the vast majority of VS T4a-b according to the Hannover classification [20] indicates the high complexity of removing such tumors and higher risks of postoperative complications. According to our statistical data, a inversely weak correlation was established between the radicality of removal and tumor size according to the Koos \( r=0.262, p<0.001 \), tumor sizes on magnetic resonance imaging (MRI) scans \( r=0.310, p<0.001 \), and age \( r=0.128, p=0.005 \). This confirms the increased surgical complexity for larger tumors and in older patients. The tumor stage according to the Koos classification did not affect the functional status before and after surgery \( p=0.131 \) and \( p=0.757 \), respectively, likely due to the predominance of patients with Koos III—IV VS in our sample. Tumor size on MRI scans affected the patient's functional status preoperatively but not postoperatively \( p=0.011 \) and \( p=0.429 \), respectively, and this also applied to the effect of age \( p=0.014 \) and \( p=0.796 \). The preoperative functional status in patients with sporadic VS was weakly directly correlated with postoperative status \( r=0.192, p=0.001 \). Consequently, the earlier the tumor is removed (based on patient age and tumor size), the better the functional status.

For small and medium-sized VS, besides surgery can be used radiotherapy or observation. In larger VS microsurgical treatment is preferred. In case of incomplete resection and recurrences radiosurgical approach is method of choice. Stereotactic radiosurgery (SRS) has been a common treatment strategy for small and medium-sized VS (stage III according to Koos) for over 20 years [26,27]. The radiosurgical community continues to debate the use of radiosurgery for large (stage IV according to Koos, or \( \geq 2.5 \) cm) VS, both primarily diagnosed and with continued growth. For such VS, microsurgical resection is recommended in most cases [28]. In some cases of extremely large VS or perifocal edema, the volumetric impact of the tumor leads to the development of hydrocephalus, requiring cerebrospinal fluid shunting procedures. The prevalence of large VS in Ukraine, with 75% of patients in our material classified as T4a-b according to the Hannover classification at the time of seeking medical care, necessitated the establishment of a cerebrospinal fluid shunting system in 37 (10.3%) cases (obstructive hydrocephalus or increased pressure communicative hydrocephalus) before surgery and in 6 (1.7%) cases after surgery. Data on VS resection in the setting of intracranial hypertension and occlusive hydrocephalus before 2016 indicate a significantly higher incidence of complications, worse postoperative functional outcomes and lower survival rates.

Currently, there is no consensual opinion regarding the optimal tumor removal extent and algorithm for subsequent application of radiosurgery, but a residual volume of 6.4 cm³ is considered to be the limit for demonstrating the greatest difference in progression-free survival when performing postoperative radiosurgery [29].

The prerequisites for incomplete removal of VS include the absence of a cerebrospinal fluid cap at the apex of the internal auditory canal above the tumor, older patient age, and larger tumor size [30], especially in the case of large VS [31]. Stage IV according to the KOOS classification, the presence of cysts, dense adhesions with brainstem structures and cranial nerves, haemorrhage are correlated with worse long-term outcomes in facial nerve function recovery [32—36]. Long duration of preoperative symptoms, profound deafness, and anterosuperior location of the facial nerve relative to the tumor negatively impact facial nerve function recovery after surgery, and in the case of large tumors (3.0—3.9 cm), the presence of dizziness or balance disturbances was associated with relatively better facial nerve function recovery [37]. The results of the study by L. Mastronardi et al. [38] indicate greater difficulties in removal due to adhesions of "tumor capsules", larger tumor sizes, vascularization, higher risk of intraoperative bleeding and higher (according to the House—Brackmann facial nerve function evaluation scale [39]) level of facial nerve dysfunction in the remote period in a group of patients aged 15—30 compared to a group of patients aged 31—40. Our experience and literature data [40] suggest that VS density directly influences facial nerve functional preservation immediately after surgery. Enlargement of the internal auditory canal on CT, rather than signal intensity on T2-weighted images, determines whether the tumour is soft or hard [40], but these data, given the studies of W.R. Copeland et al. [41], cannot be definitive. Intraoperative monitoring is necessary and nowadays standard to preserve the function of nerve structures and improve the resection volume [11, 42—47].

Our experience indicates that the possibility of gross total resection, safe from a functional standpoint, largely depends on the tumor's vasculature and arachnoidal membrane adhesions to the brainstem/facial nerve, hearing and cochlear portion preservation, the individual mutual location/relationship of neurovascular structures and experience of the surgeon. In our personal series of 363 cases of VS operated on from 2017 to October 2023, gross total resection from the level of the apex of the internal auditory canal was performed in 270 (75.2%) cases (total resection in 127 (35.4%) cases, subtotal in 143 (39.8%)), no statistically significant difference in the possibility of total removal depending on tumor density was found. Tumor vascularization intensity significantly affects safe dissection ability from the facial and VIIth nerve cochlear portion. According to our experience, the stiffness of arachnoid adhesions to tumor tissue and adjacent brain structures, the presence of cysts in the tumor, and intense vascularization of the tumor stroma negatively affected the possibility of radical VS removal. The most common stroma variants of VS based on macroscopic characteristics are soft tissue, yellow, aspirating, avascular or relatively dense nodular, gray-cherry, with moderate vascularity non-aspirating. No statistically significant differences were found in the possibility of total resection.

While most foreign authors report facial nerve function preservation rates at HB I—III for tumors
≥T3b to be 15–20% [48–50], then according to our data, this indicator in the early postoperative period under the same tumor parameters reaches 84.6%. In our case series, for VS removals <25 mm in size, facial nerve function at HB I-II was observed in the early postoperative period, with restoration to HB I within 6 months for all patients. According to our data, patient age had weak positive correlation with postoperative impairments on the HB (r=0.181, p=0.007). Intraoperative facial nerve monitoring has been standard in the Subtentorial Neurooncology Department since 2012, which presumably, based on accumulated experience, led to no influence of tumor size based on MRI data and Koos on postoperative facial nerve function impairments on the HB (p=0.197 and p=0.905, respectively).

Combined strategy (subtotal resection followed by radiosurgery) is associated with good clinical and functional outcomes and tumor control compared to gross total resection [51] and do not affect the timing and extent of postoperative facial nerve function recovery [52]. Residual tumor volume >95 mm³, internal auditory canal expansion, large tumor size (>3 cm), NF2 syndrome, presence of edema on preoperative MR1 and preoperative symptoms caused by the trigeminal nerve were predictors of postoperative progression and the need for further intervention. The latter three criteria and large tumor size were also associated with poorer progression-free survival [53–56]. While literature data suggest that trigeminal nerve involvement symptoms in VS are extremely rare, in our case series, concomitant trigeminal neuralgia was observed in 17 (4.7%) out of 359 patients, and symptoms of trigeminal nerve sensory disturbances on the affected side were observed in 91 (25.3%) patients. This is evidently due to the prevalence of our observations of large VS with significant trigeminal nerve compression. Pain syndrome regression in the postoperative period was achieved in all patients. Hypesthesia as a new symptom in the early postoperative period was recorded in 23 (6.4%) patients (BNI NS II–III) with gradual regression and sensory recovery (BNI NS I), both in cases of primary and postoperatively impaired sensitivity, in the majority of cases.

Postoperative mortality in VS surgical treatment is approximately 0.5% [57], according to our data since 2017 – 0.84% (3 cases), consistent with literature data.

Our experience demonstrates that over the past 6 years, progressive VS growth necessitated radiosurgery in 9 (4.4%) patients (from the primarily operated group), all of whom were young (not older than 47 years). Facial nerve function deterioration was observed in 2 patients after radiotherapy.

Radiosurgery

Over the past 20 years, approaches to performing stereotactic radiosurgery (SRS) have been fundamentally altered and significantly improved. Optimization of the dosage regimen, specifically reducing the radiation dose to VS to 12.0–13.0 Gy, has led to a decrease in the number of post-radiation reactions and complications. For instance, while in the 1970s, facial nerve dysfunction in the early post-SRS period was observed in 33-38% of cases, by the 1990s, this decreased to <2% [58–69]. The primary goal of radiosurgical treatment of VS patients is to control tumor growth while preserving quality of life and avoiding worsening neurological deficits in the future. In literature, tumor growth control refers to stability in tumor size or reduction as per post-radiation neurovisualization monitoring [70–74].

The "Marseille group" scientists [68, 75], in long-term observation of 2991 cases of SRS application in VS patients, recorded a high level of tumor growth control – 97.5%. In 0.5% of cases, transient post-radiation facial nerve dysfunction was observed, while another 0.5% experienced trigeminal nerve involvement. The frequency of useful hearing preservation during a 3-year observation period was 78.0%. A noteworthy publication from 2021 [76] retrospectively analyzed treatment outcomes in 1447 VS patients, of whom 100 had Grade I hearing preservation according to Gardner-Robertson (GR). Among these patients, 67 experienced a downgrade from GR Grade I to II during SRS, and 33 during follow-up. Over the long-term observation, the frequency of preserved hearing (GR I–II) was 80%, 63%, and 51% at 3, 5, and 10 years respectively. Functionally satisfactory hearing was recorded in 40%, 33%, and 20% of patients at 3, 5, and 10 years respectively. The authors also concluded that the shorter the observation period for a patient with preserved and functionally satisfactory hearing (Grade I GR) in the presence of VS before treatment, the better the hearing preservation outcomes in the long term after SRS. Our data support this conclusion.

In a literature review spanning 2010–2020, A.R. Savardekar et al. [77] noted that regardless of treatment strategy for VS <3 cm (microsurgery or radiosurgery), hearing preservation after 5 years was possible in only about half of the cases. Facial nerve dysfunction in the remote period was more common after surgical treatment (10%) than after radiosurgery (2%), while a higher level of tumor growth control was achieved with microsurgery (98% and 92%). Similar conclusions were noted by V.K. Yakkala et al. [78]. T. Hasegawa et al [79] suggested that patients aged ≥48 years with ≥9.8 mm compression of the middle cerebellar peduncle are at higher risk with lower tumor growth control.

In the last 3 years, the radiosurgical and neurosurgical community has not recommended the "wait-and-scan" strategy due to the risk of life-threatening complications associated with tumor progression [1]. Numerous papers provide compelling evidence for the high effectiveness of using SRS in VS patients as a standalone, alternative to surgery, or adjuvant treatment (radiation on the residual tumor part in the postoperative period) [70, 80–82].

An analysis of local control after SRS for stage III and IV Koos VS was carried out. Out of 177 patients with VS, 65 (36.7%) had stage III, and 112 (63.3%) had stage IV. Female patients predominated (118 (66.6%)). The youngest patient was 19 years old, the oldest was 86 years old, with a mean age of 50.1 years. Follow-up data were obtained for 159 patients.

Stereotactic radiosurgery was performed using the Trilogy linear accelerator (USA, 6MeV) in the Department of Neuroradiology and Radioneurosurgery of Romodanov Neurosurgery Institute from November 2010 to March 2019. Primarily diagnosed tumors were
treated in 110 (62.1%) patients, 67 (37.9%) had residual postoperative tumors.

Out of 67 patients who underwent radiosurgery as a second stage. after VS resection (combined treatment), 20 (29.8%) received radiation within 3 months after the operation, while in other cases, it was administered ≥3 months later.

At the time of radiosurgery, the volume of the irradiation target (VS) ranged from 1.33 to 21.60 cm³ (average 7.38 cm³), in patients with primarily diagnosed VS ranging from 1.33 to 21.60 cm³ (average 7.08 cm³). Among them, those with stage III Koos ranged from 1.33 to 15.20 cm³ (average 4.58 cm³), and those with stage IV ranged from 1.8 to 21.6 cm³ (average 8.82 cm³). For postoperative patients, the target volume ranged from 1.4 to 21.0 cm³ (average 7.86 cm³): stage III ranged from 1.40 to 12.86 cm³ (average 5.64 cm³), and stage IV ranged from 1.43 to 21.0 cm³ (average 9.05 cm³).

The assigned dose to the radiation target ranged from 10 to 14 Gy (average 12.2 Gy). The dose was delivered on average to 97.8% of the irradiation target volume (range 86 to 100%). Radiation techniques used were Dyn Arc + IMRT in 97 (54.8%) patients, IMRT in 49 (27.7%), Arc cone in 19 (10.7%), and MLC Dyn Arc in 12 (6.8%).

In our opinion, the assessment of local control should be conducted in groups with follow-up periods of up to 24 months and more than 24 months. Currently, it is widely accepted that within the first 24 months after radiosurgery, tumors may undergo changes, accompanied by size increase as a manifestation of transient radiation reaction (pseudoprogression).

Out of 159 patients, 106 (66.66%) were followed up for more than 24 months, 20 (12.57%) for more than 60 months. The longest observation period was 90 months. Among the 106 patients observed for more than 24 months, VS decreased in size or remained stable (achieving local control) in 90, including 7 with stage III Koos and 22 with stage IV.

Local control was achieved in 131 (82.4%) out of 159 patients.

**Hearing preservation**

In addition to preserving the anatomical integrity and function of the facial nerve, the patient's quality of life after surgery is influenced by hearing preservation and the presence or absence of tinnitus. The most significant predictor of hearing preservation is tumor size [83]. Better preoperative hearing, tumor growth from the upper portion of the vestibular nerve, middle cranial fossa approach, a shorter period of hearing loss, and normal intraoperative I-wave were determined as prognostic factors of functional hearing preservation [84–88]. Studies indicate [89] that microsurgery offers preferable outcomes in patients with class A hearing. Other researchers [90] also note the correlation of hearing preservation to internal acoustic meatus tumor filling. They proposed the TFIAC (tumor filling the inner auditory canal) scale to assess this relationship. According to their data, microsurgery in patients with preserved hearing before surgery with TFIAC II (25–50% tumor filling in the inner auditory canal) is the preferred treatment option considering postoperative hearing preservation.

In our case series, out of 359 patients operated on since 2017, 100 had functional hearing preoperatively, and among them, 56 (56%) retained it postoperatively.

**Tinnitus**

The prognosis for tinnitus regression in patients with VS is better after translabyrinthine compared to radiosurgical microsurgery. Postoperative tinnitus is also less likely in patients with worse preoperative hearing. The onset of tinnitus postoperatively was more common in patients with better preoperative hearing who had tumors resected by translabyrinthine approach [91]. A study of 40 patients found that the presence of mid-frequency and high-frequency tinnitus and louder tinnitus preoperatively were associated with a worse prognosis than the presence of low-frequency and quieter tinnitus when using the translabyrinthine approach for tumor resection [92]. Larger tumor size and female sex have been recognized by some authors as statistically significant factors in predicting the absence of postoperative tinnitus [93]. We do not have statistical data on tinnitus. Studying treatment outcomes in the long term will provide such data.

**Quality of Life**

The patients quality of life without tumor progression/reccurrence is the main goal of VS treatment [42]. For most patients without VS progression the quality life is sufficiently high in "wait-and-scan" strategy that validates its effectiveness [94]. To assess the patients life quality general scales (SF-36, EORTC QLQ, PROMIS-10) and specialized scales (PANQOL and Mayo VSQOL Index) are used [8, 9, 95–97]. Spontaneous pathological vestibular disorders and their impact on quality of life are assessed using the Dizziness Handicap Inventory (DHI) [98] and the International Classification of Functioning, Disability and Health (ICF) [99]. Subjective vestibular disorders (balance function impairment, nausea, vomiting) associated with dizziness are assessed using the ICF [100].

When determining quality of life, it is important to assess the functions of the vestibular portion of the VIII nerve, the degree of hearing impairment, trigeminal nerve dysfunction, and particular attention is paid to signs of facial nerve dysfunction, which are evaluated using the House-Brackmann scale [39].

Often, cranial nerve dysfunction, which is the focus of physicians' attention, is not prioritised in patients' own quality of life assessments. Lack of energy, anxiety, headaches and balance disturbances are the strongest predictors of physical and mental quality of life deterioration according to the SF-36 and PANQOL scales in VS patients. Greater awareness, support for recovery, coping with anxiety, headache, balance problems and assistance in informing, assessing and treating patients with VS may improve quality of life [101-103]. Some studies’ drawback [17, 18, 102, 104] is that they do not include patients with tumours >3 cm in size. Usually 3 cm is a critical tumour size, exceeding which is associated with deterioration of patients' quality of life [105], so it is important to evaluate this parameter in patients with VS, especially in Ukraine due to the prevalence of tumours of this size. In the study by M.K. Turel et al. [106] revealed that patients with large (>3 cm) or giant (>4 cm) VS have lower quality of life scores on all domains compared to the general population. More than 60% of
them showed clinically significant improvement on the Health-related quality of life (HR-QOL) questionnaire 1 year after surgery, which was maintained at follow-up. Older age and “symptom overload” are associated with worse quality of life [107]. The lowest level of satisfaction with treatment was registered in the group of patients with combined treatment methods (surgical and radiosurgery) [94], which is probably due to the need for both two-stage prolonged treatment and treatment outcomes.

The diagnosis of “vestibular schwannoma” is often of concern to the patient. For tumour sizes that do not require urgent surgery, a short follow-up period allows patients to accept the diagnosis more calmly, receive information about treatment options, and decide on further tactics [108]. In general, satisfaction with the results of treatment is higher in patients who underwent SRS and observation, but a high level of satisfaction after all types of treatment has also been recorded [109]. VS total resection is associated with better quality of life according to the general SF-36 and PROMIS-10 questionnaires and the disease-specific PANQOL questionnaire both in the postoperative period and in the long term. Regarding mental health assessment, there may be a psychological advantage to removing the entire tumour with microsurgical resection, which would improve overall well-being [110]. Also, microsurgery may reduce patient anxiety, probably related to the psychological benefit of tumour removal [111]. However, prospective and retrospective assessment of an individual’s quality of life may lead to different results, which may not be reliable due to individual psychological factors [112]. The choice of treatment should be justified and unbiased. Developments in this direction available in the literature [113] should help patients in the future.

Analysis of studies examining the quality of life of patients with VS after SRS suggests that radiosurgical treatment provides a high quality of life [68-71, 114-116]. R. Whitmore et al. [114] compared the quality of life of patients with VS 5 years after surgical treatment and SRS. Overall quality of life was higher in patients treated with SRS. There is insufficient data on quality of life ≥10 years after VS treatment, which requires further studies.

To use the scales for assessing the quality of life of patients with VS in Ukraine, the PANQOL and Mayo VSQOL Index scales were translated into Ukrainian independently by three neurosurgeons, then a member of the Department of Ukrainian Language and Literature at the Taras Shevchenko National University of Kyiv made a generalised version from the three translations. Twenty patients with VS were asked to answer the questionnaire questions. Five (<1%) questions out of 66 (26 questions of the PANQOL scale and 40 of the Mayo VSQOL Index scale) required clarification, i.e. the content of the translated scales was understandable for this category of patients. The final consolidated version in Ukrainian was translated into English by a certified translator of the English language department of the Taras Shevchenko National University of Kyiv; another independent translator compared the translated version with the original corresponding to the FACIT standards adaptation [117]. Taking into account the requirements of the Mayo VSQOL Index authors, we obtained written permission to translate their scale.

To improve the quality of life of patients with VS diagnosed in Ukraine, we initiated the study of treatment outcomes in the long term using PANQOL (Table 1) and Mayo VSQOL Index scales (Table 2) with the follow-up period from 2001 to 2022 of patients treated on the basis of the Subtentorial Neurooncology Department and Radiosurgery Department of Romodanov Neurosurgery Institute (since 2010), as well as a group of “wait-and-scan” patients, who after verification of VS were observed during 2010-2021 and, if necessary, treated at the Department of Ear Microsurgery and Otoneurosurgery of Kolomiichenko Otolaryngology Institute or referred for surgical treatment to the Romodanov Neurosurgery Institute if the size of VS ≥T2 increased according to the control examination data.

The number of patients treated in the Subtentorial Neurooncology Department in the period from 2001 to October 2023 was 1100, 41 of them came to the clinic with continued tumour growth (unfortunately, there is no data on all primary operated patients), repeated surgical treatment was performed in 37 patients, radiation treatment of VS progression - in 3 patients. Combination of surgery and subsequent radiation with repeated surgery of continued growth - 1 case. After radiosurgical treatment in the clinic, removal of VS was performed due to neoplasm progression in 10 patients, after radiotherapy - in 1 patient. Unfortunately, the data do not reflect the real statistics for the whole sample, as there are known cases of patients choosing other neurosurgical clinics and radiosurgery centers after detecting continued VS growth.

According to the data of the Radiosurgery Department for 2010-2021, radiotherapy was performed in 359 cases, of which in 2014-2021 after surgical intervention - in 87 patients, in 128 - as an independent treatment option, of which in 44 cases the tumour size was Koos stage I, in 29 - stage II, in 22 - stage III, in 33 - stage IV. Data of Neuroradiology and Radioneurosurgery Department regarding combined treatment contain information about a part of patients who underwent treatment at the Subtentorial Neurooncology Department.

Since 2022, the Radioneurosurgery Department has been working on assessing the long-term outcomes of combined treatment (tumor removal and SRS) in patients with VS (excluding patients with neurofibromatosis) from November 2010 to November 2022. Out of 79 VS patients, 33 (41.8%) experienced VS progression, while in 46 (58.2%), the residual part of the tumor was subjected to radiation. Among the 33 patients with VS progression, 21 (63.6%) had tumor size <3.0 cm, and 12 (36.4%) had tumor size ≥3.0 cm. Among the 46 patients with residual VS after surgery, 34 (73.9%) had tumor size <3.0 cm, and 12 (26.1%) had tumor size ≥3.0 cm.

The target volume for VS in 79 postoperative patients ranged from 1.38 to 16.14 cm³ (mean volume: 8.34 cm³). The prescribed radiation dose to the target ranged from 10 to 13 Gy (mean dose: 12.17 Gy). The dose was delivered on average to 98.28% of the target volume (from 91 to 100%). Radiation techniques included Dyn Arc + IMRT in 48 (60.8%) patients, IMRT in 25 (31.6%), Arc cone in 2 (2.5%), and MLC Dyn Arc in 4 (5.1%). The longest follow-up period was 96 months.

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<tr>
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<td>В мене є неприємне відчуття страху наше ось-ось маєтрапитись щось жахливе</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>16</td>
<td>В мене час від часу бувають тривожні думки</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>17</td>
<td>В мене є відчуття загальмованості</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>18</td>
<td>В мене є неприємне відчуття «смоктання під ложечкою»</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>19</td>
<td>В мене бувають раптові відчуття паніки</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>20</td>
<td>В мене є відчуття ізоляції через мій діагноз невриноми</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>21</td>
<td>В мене є складності із зосередженням під час читання або перегляду телевізора</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>22</td>
<td>Я щасливий більш нетерплячим (ою)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>23</td>
<td>Мені не вистачає енергії та життєвих сил</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>24</td>
<td>В мене є складності із запам'ятовування інформації</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>25</td>
<td>Я маю чудове здоров'я</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>26</td>
<td>Я очікує погіршення стану свого здоров'я протягом наступного року</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
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</table>
Table 2. Mayo VSQOL Index, ukrainian variant

<table>
<thead>
<tr>
<th>№</th>
<th>Reactant</th>
<th>Ukrainian (Ukraine)</th>
<th>Ukrainian (Ukraine)</th>
<th>Ukrainian (Ukraine)</th>
<th>Ukrainian (Ukraine)</th>
<th>Ukrainian (Ukraine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>У мене є труднощі з безпекою через проблеми зі слухом (наприклад, я не чую димову сигналізацію або мені важко почити транспорт, що наближається)</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Троян/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>2</td>
<td>Мені важко розбирати мову на фоні навколишнього шуму, або коли говорю декілька людей водночас</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Троян/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>3</td>
<td>Мої проблеми зі слухом змушують мене відчувати себе відокремлено, коли я у групі людей</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Троян/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>4</td>
<td>Я хвилююся, що втрачу слух і на інше вухо (де немає вестибулярної шваноми)</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Троян/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>5</td>
<td>Мої проблеми зі слухом перешкоджають можливості приймати участь у соціальній активності або активному відпочинку</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Троян/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>6</td>
<td>Внаслідок запаморочення або порушення рівноваги я маю проблеми, коли повертаю швидко голову або дивлюсь вгору</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Троян/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>7</td>
<td>Через запаморочення та порушення рівноваги для мене складно змінити напрям руху під час ходьби</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Троян/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>8</td>
<td>Через запаморочення та порушення рівноваги мене непокоїть, що довколишні люди вважатимуть, ніби я перебуваю під впливом наркотичних речовин чи алкоголю</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Троян/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>9</td>
<td>Через моє запаморочення та порушення рівноваги я не відчуваю себе впевнено за кермом</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Троян/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>10</td>
<td>Напади запаморочення та порушення рівноваги стають на заваді у виконанні моєї фізично навантаженої діяльності: заняття спортом, танці, робота на присадибній ділянці</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Троян/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>11</td>
<td>Біль, дискомфорт і шум у вусі/-хах</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Троян/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>12</td>
<td>Мене турбує важкість у голові, тиск або головний біль, пов’язані з моїм станом</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Троян/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>13</td>
<td>Через біль, пов’язаний з моїм станом, я відчуваю дративість або депресію</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Троян/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>14</td>
<td>Біль, пов’язаний з моїм станом, заважає моїй щоденній діяльності</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Троян/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>15</td>
<td>Мій шум у вусі/-хах заважає мені зосередитися</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Троян/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
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Continuation of the Table 2. Mayo VSQOL Index, ukrainian variant

<table>
<thead>
<tr>
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<th>Шум у вусі/-хах заважає мені засинати</th>
<th>Зовсім ні</th>
<th>Дуже незначно</th>
<th>Трохи/певною мірою</th>
<th>Досить сильно</th>
<th>Дуже сильно</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>Проблеми з обличчям чи очима</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Я соромлюсь своїх проблем з обличчям, що спричинені моїм станом</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Трохи/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>18</td>
<td>Слабкість м’язів обличчя негативно впливає на якість моєго життя та щоденнє самопочуття</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Трохи/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>19</td>
<td>Мене турбує те, що моє око надмірно сльозиться або стає сухим</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Трохи/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>20</td>
<td>Мене турбує те, що моє око надмірно сльозиться або стає сухим</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Трохи/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>21</td>
<td>Вплив на фізичне, емоційне та соціальне благополуччя</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Я відчуваю подразнення або біль в очі</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Трохи/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>23</td>
<td>Мешканцією мені важко виконувати мої звичайні справи через втому</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Трохи/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>24</td>
<td>Я більше не отримую задоволення від речей, які зазвичай мене радували</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Трохи/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>25</td>
<td>У моїй голові виникають тривожні думки</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Трохи/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>26</td>
<td>Мій стан негативно вплинув на мій погляд на життя</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Трохи/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>27</td>
<td>Я відчуваю, ніби мій мозок гальмує</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Трохи/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>28</td>
<td>Мешканцією мені важко знайти потрібні слова під час розмови чи письма</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Трохи/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>29</td>
<td>Мешканцією мені важко знайти потрібні слова під час розмови чи письма</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Трохи/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
</tbody>
</table>

Труднощі з мисленням та пам’яттю

<table>
<thead>
<tr>
<th></th>
<th>Мешканцією мені важко знайти потрібні слова під час розмови чи письма</th>
<th>Зовсім ні</th>
<th>Дуже незначно</th>
<th>Трохи/певною мірою</th>
<th>Досить сильно</th>
<th>Дуже сильно</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>Мешканцією мені важко знайти потрібні слова під час розмови чи письма</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Трохи/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>31</td>
<td>Мешканцією мені важко знайти потрібні слова під час розмови чи письма</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Трохи/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>32</td>
<td>Мешканцією мені важко знайти потрібні слова під час розмови чи письма</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
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<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
<tr>
<td>33</td>
<td>Мешканцією мені важко знайти потрібні слова під час розмови чи письма</td>
<td>Зовсім ні</td>
<td>Дуже незначно</td>
<td>Трохи/певною мірою</td>
<td>Досить сильно</td>
<td>Дуже сильно</td>
</tr>
</tbody>
</table>
Continuation of the Table 2. Mayo VSQOL Index, ukrainian variant

<table>
<thead>
<tr>
<th>Question</th>
<th>Option 1</th>
<th>Option 2</th>
<th>Option 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>34 Я зовсім припинив/-ла працювати і зараховав/ала непрацездатність/незначну непрацездатність/таку незначну непрацездатність</td>
<td>Так</td>
<td>Ні</td>
<td>Дуже незначну</td>
</tr>
<tr>
<td>35 Я зовсім припинив/-ла працювати і зараховав/ала непрацездатність/незначну непрацездатність/таку незначну непрацездатність</td>
<td>Так</td>
<td>Ні</td>
<td>Дуже незначну</td>
</tr>
<tr>
<td>36 Я зовсім припинив/-ла працювати і зараховав/ала непрацездатність/незначну непрацездатність/таку незначну непрацездатність</td>
<td>Так</td>
<td>Ні</td>
<td>Дуже незначну</td>
</tr>
<tr>
<td>37 Я зовсім припинив/-ла працювати і зараховав/ала непрацездатність/незначну непрацездатність/таку незначну непрацездатність</td>
<td>Так</td>
<td>Ні</td>
<td>Дуже незначну</td>
</tr>
</tbody>
</table>


Discussion

Advances in technology and changing priorities in assessing the outcomes of patients with VS, obtaining an incomplete desired outcome when using assessment scales necessitates the search for new assessment tools. The diagnosis-specific PANQOL quality of life assessment scale was created in 2010 [8] and the Mayo VSQOL Index in 2022 [9]. The developers of the latter, based on a literature review, concluded that the PANQOL scale does not identify clinically meaningful differences between treatment methods. The Mayo VSQOL Index scale was developed to determine whether this was indeed the case and whether there was a methodological error.

However, the Mayo VSQOL Index scale is also not exhaustive because of a number of issues that, in our opinion, need further research and development. For example, it is possible to assess mental status and cognitive functions (thinking and memory) due to the presence of VS alone without taking into account other diseases, specific activities of the patient. What is the significance of the age factor? There are no prognostically significant predictors of progressive growth of VS, the optimal terms of dynamic MRI-control of both first detected and operated or irradiated VS have not been determined, there are no clearly defined clinical-morphological-MRI-correlations, which are crucial for treatment strategy justification, prognosis and quality of life assessment. Obtaining such data will help substantiate treatment method selection and enhance treatment satisfaction.

Since the quality of life of patients with large VS (KoosIV/T4) is significantly impaired and life-threatening obstructive hydrocephalus often develops, the treatment strategy for large VS is not debated, and primarily involves surgical removal or installation of a CSF shunt system mainly at the initial stage. However, even with "total" resection, according to the literature, the incidence of progression is less than 10%, but most studies used insufficiently sensitive imaging studies, and the postoperative follow-up period rarely exceeds 5-10 years, which reduces the number of recurrences detected [54]. Probably, the definition of "total resection" does not always correspond to truly total resection or terminologically is not standardised. In our opinion, there is a necessity for a more precise definition of "total" resection, which may explain the indicated incidence of progression. Considering personal experience of VS prolonged growth, attention should be paid to the area of tumour remnants - intracanalicular or cisternal region, which is also not well defined regarding potential continued growth.
Due to the risk, albeit small, of VS progression in "total resection" cases, MRI control should be standardised. In cases of subtotal or partial VS resection, postoperative follow-up of these patients is mandatory in the treatment algorithm. According to the CNS Guidelines, the time limit for late MRI follow-up is 1 year after surgery, and more frequent follow-up is desirable if total resection has not been performed. Annual MRI examination may be appropriate during 5 years after VS surgical resection [12] due to the highest incidence of potential prolonged growth during this follow-up period. There are also recommendations for MRI at 3–6 months and 1 year after total resection with the follow-up every 2–5 years if there is no evidence of recurrence. For non-total resection, annual MRI follow-up is recommended. If MRI shows signs of prolonged growth or new mass lesion, a repeat MRI is recommended after 6 months for prolonged growth verification [42]. Consequently, the timing at which MRI examination should be performed is justified insufficiently. In our experience, out of 1100 VS, there are at least 5 cases (documented) with intensive growth of incompletely resected VS, doubling their size within 3 months. In the clinic it is usually accepted to perform control MRI at 3, 6, 12 and 24 months after surgical treatment of these neoplasms in the absence of prolonged growth signs, in future followed by intervals of 2 years.

The provided data underscore the relevance of determining prognostic factors for the progressive course of VS. Among the molecular biomarkers predicting rapid continued growth in patients with VS and NF2, merlin protein is frequently mentioned. In its normal state, merlin acts as a suppressor of VS growth. However, mutations in the NF2 gene cause it to lose this function, resulting in tumor growth. Proliferation markers, particularly Ki-67, widely used in histological tumor studies, do not demonstrate the probability of rapid prolonged growth in VS. It has been established that in univariate analysis comparing two groups with and without tumor growth, the Ki-67 index did not significantly differ [55]. Other important factors contributing to tumor growth in VS include VEGF, fibroblast growth factors, platelet-derived growth factors, and neurotrophic growth factor [118].

Studies conducted in various research centers have shown that the increase in VS volume depends not on the level of cell proliferation but on several factors: activation of neoangiogenesis, intratumoral hemorrhage, cyst formation (and their transformation), and changes involving various inflammatory pathways [31, 119, 120]. Another important factor in VS progression is stromal factors – alternatively activated macrophages, which may predominate among proliferating cells in sporadic VS [119, 121]. However, a clear interdependence between different signaling pathways of tumor progression has not been established, justifying the need for further study of VS morphogenesis to develop targeted interventions that inhibit its growth.

According to our preliminary data, the expression levels of VEGF and TGF-1β in VS tissue can be considered as indicators of tumor progression. Studies involving a series of VS observations, categorized for determining proliferative potential of VS (average 2.8% Ki-67 proliferation index), have revealed a low degree of malignancy. However, cases of indirect signs of chronic tissue hypoxia in the tumor and co-expression of indicator of VEGF indicating rapid VS progression have been identified. According to inter-group comparative analysis, the proportion of VEGF AN-immunopositive cells constitutes 70.0 (63.6; 73.5) % (p = 0.0001, Mann-Whitney criterion), indicating an indirect sign of metabolic disturbances – tissue hypoxia [122].

Further studies are needed to examine clinical and morphological correlations: searching for correlations between MRI features and morphological markers of VS growth, which will contribute to optimizing diagnostic and therapeutic algorithms, improving long-term treatment outcomes, and reducing financial burdens on this patient category. Data on a fivefold increase in VS detection [123] frequency over the last decades, particularly about 25% incidentally detected cases with minimal or absent symptoms, create an even greater dilemma regarding treatment and observation tactics, especially with existing practice recommendations, which are not only non-comparable in Ukraine but also in the USA [124] and other countries [125], leading to unjustified treatment and associated problems [126].

The problem of choosing the optimal treatment method remains unresolved. Currently, it is chosen based on the physician's experience rather than guided by other principles. Even consultations with multiple specialists do not guarantee optimal treatment strategy selection, although it reduces the likelihood of errors.

Therefore VS patients treatment is a medical and social problem that needs an early detection. If "wait and scan" strategy is chosen, criteria and markers of VS progression would be highly effective in tumor control that need additional research. VS treatment requires not only educating family doctors and specialists but also implementing social campaigns regarding the need for self-monitoring when minor symptoms typical of VS appear, and early diagnosis using imaging methods. Given the lengthy course of VS and examples from advanced countries, establishing a VS patient association in Ukraine as an informational and educational organization to connect with specialists involved in treating this patient category is necessary, as well as developing optimal treatment algorithms to ensure their quality of life.

Conclusions

Existing criteria and quality of life assessment scales for neuro-oncology patients do not adequately reflect the situation for patients with VS, necessitating the development of specialized scales such as PANQOL and the Mayo VSQOL Index. The implementation and validation of specialized scales are necessary to assess the quality of life of this patient category in Ukraine. The patient category with primarily diagnosed VS in Ukraine still significantly differs from that in developed countries. Therefore, evaluating the quality of life to choose the optimal treatment strategy should be conducted by categories: among individuals without pronounced compressive-occlusive symptoms (i.e., up to T4a/Koos III), and those with existing symptoms requiring only surgical treatment. Quality of life assessment in patients T4a-b/Koos IV should be used not for comparison to other VS patients but to quality of surgical treatment determine and the level of care provided for those patients by different clinics and specialists. Adapted PANQOL and the Mayo VSQOL Index scales should
be used to assess the quality of life surgically treated patients (T1-T3/Koos I-III) in comparison with patients who have undergone other treatment strategy and among surgically treated patients, to justify VS patients care in departments and specialized centers with a high VS surgery volume (more than 25-30 per year) that could provide a high level quality of life postoperatively.

We hope that consistency of professional information, self-awareness, and responsibility will improve the early diagnosis and treatment outcomes of VS. The "wait-and-scan" strategy is advisable for managing patients with newly detected asymptomatic VS. Patients with VS T1-T3 under dynamic observation and signs of tumor growth can be operated on, and in the presence of contraindications, radiation therapy is applied. For VS T4a-b, it is necessary to remove the tumor, and if total safe removal is impossible, decompression of brain structures should be provided with subsequent dynamic monitoring, and if necessary, radiation therapy is applied. VS should be removed with mandatory intraoperative neuromonitoring. The choice of surgical approach depends on the surgeon's training and experience. Evaluating the quality of life of VS patients should be conducted using specialized scales such as PANQOL and the Mayo VSQOL Index in a large series of cases and over the longest possible observation periods to form an optimal treatment strategy. VS removal surgeries should only be performed in specialized centers with extensive experience in treating such tumors.

There is a need to determine the diagnostic algorithm and treatment strategy for VS involving multidisciplinary teams, and the creation of educational information platforms.

Disclosure
Conflict of interest
The authors declare no conflicts of interest or financial involvement in the preparation of this article Ethical approval
All procedures performed on patients comply with the ethical standards of institutional and national ethics committees, the 1964 Declaration of Helsinki and its amendments or similar ethical standards.

Informed consent
Informed consent was obtained from each of the patients for conducting the research and publishing the data and accompanying images.

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References


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Peculiarities of angiospasm and ischemic complications in ruptures of cerebral arterial aneurysms against the background of occlusive-stenotic lesions of cerebral arteries

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Objective – to determine the effect of occlusive-stenotic lesions of cerebral arteries on angiospasm and ischemic complications in patients with ruptured arterial aneurysms against the background of occlusive-stenotic lesions of cerebral arteries.

Materials and methods. A retrospective study of the medical histories of 1,147 patients with cerebral artery aneurysms from 2006 to 2022 was conducted. 63 patients were included in the study group because they met the following criteria: surgical treatment; rupture of saccular aneurysms (SAs); the presence of occlusive-stenotic lesions was proven using instrumental examination methods. Patients of the control group had to meet the following criteria: surgical treatment; rupture of SAs; the absence of occlusive-stenotic lesions was proven by means of instrumental examination methods; the gender and age distribution had to match the study group. Of the 126 patients included in this study, there were 76 men (60.32%) and 50 women (39.68%). The age of the patients varied from 31 to 77 years. The average age of patients-55.9±0.76 years; men – 54.3±0.94 years, women – 58.3±1.19 years.

Results. A percentage predominance of patients with high cerebral blood flow velocity (>200 cm/s, which is equal to the velocity with severe grade III vasospasm of the cerebral arteries) in the study group (32.56%) compared with the control group (24.24%) was revealed.

Conclusions. The predominance of men among patients of the study group (60.32%) was established. The average age of men with occlusive-stenotic lesions was younger than that of women (men – 54.3±0.94 years, women – 58.3±1.19 years). The difference in age is the largest in the 2nd subgroup of the study group where the severity of stenosis is 50-75% (men - 48.3 years; women - 62 years). Ruptures of arterial aneurysms of the middle cerebral artery occur more often in the presence of stenoses (study group - 25.4%, control group - 12.7%). The neurological status of patients with a hemorrhagic stroke, as a result of the rupture of an arterial aneurysm, is significantly aggravated by occlusive-stenotic lesions due to the occurrence of chronic brain ischemia. The worst prognosis for life and health was in men with a ruptured arterial aneurysm against the background of a 50-75% stenotic lesion and severe vasospasm of the cerebral arteries.

Key words: angiospasm; ischemic complications; ruptures of arterial aneurysms; occlusive-stenotic lesions; cerebral arteries; surgical treatment

Cerebral arterial aneurysms are mostly congenital pathologies that are treated exclusively by surgical methods (transcranial [1–3], endovascular [4–13], and their combinations). The prevalence of cerebral arterial aneurysms is 1–5% in the population. For a long time, cerebral arterial aneurysms have no clinical manifestations and are asymptomatic, but the incidence of subarachnoid hemorrhage (SAH) due to their rupture is 6–10 cases per 100,000 people per year. Aneurysmal disease of the cerebral vessels [3, 4, 6, 14–19] of [3, 4, 14–17], but they are less affected by atherosclerosis due to the angioprotective effect of estrogens. The above etiological factors explain the rarity of the combination of occlusive-stenotic lesions with cerebral arterial aneurysm rupture [5, 6, 10, 15, 18, 19]. Risk factors of cerebral arterial aneurysm rupture include arterial hypertension, endocrine disorders, reduced functional capabilities of the cardiovascular system, and the progressive decline associated with the aging process.

The neurological status of patients after the rupture of a cerebral arterial aneurysm is significantly influenced by angiospasm caused by SAH [2, 3, 15, 16, 18] and the presence of stenotic lesions [1–22], as they impair cerebral hemodynamics [3, 7, 20, 21] and lead to secondary ischemic brain lesions [4, 11, 12, 16, 18, 22].

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The severity of ischemic lesions will be greater with less compensatory and adaptive collateral blood supply [13, 20, 22], involving the common carotid arteries, extracranial and intracranial segments of the internal carotid artery (ICA), vertebral artery, basilar artery (BA), anterior (AComm) and posterior communicating arteries (PComm), anterior cerebral artery (ACA), middle cerebral artery (MCA), and posterior cerebral arteries (PCA), and the external carotid arteries. With adequate blood flow compensation, occlusive-stenotic lesions of the arteries [3, 5, 13, 20, 22] may be incidental findings during angiography [4, 18, 20, 22] or may have clinical manifestations in the form of cerebral infarctions and transient ischemic attacks [8, 14, 18].

The severity of neurological manifestations depends on the extent and form of hemorrhagic stroke, the degree of stenosis [5, 8, 14, 20], the severity of angiospasm, and the volume of secondary ischemic lesions. The most severe neurological status is observed with massive SAH with parenchymal hemorrhage and ventricular tamponade combined with critical stenosis or occlusion of cerebral arteries against the background of grade III angiospasm.

The impact of angiospasm against the background of occlusive-stenotic lesions of the cerebral arteries and major cervical arteries on the manifestations of cerebral arterial aneurysm rupture is poorly studied. This causes difficulties in forming an adequate treatment plan. Studying the features of this pathology will contribute to the pathogenetically grounded optimization of the treatment protocol for this category of patients and improve the results of surgical treatment, for which there is no alternative in this type of cerebrovascular pathology.

Objective: To determine the impact of occlusive-stenotic lesions of the cerebral arteries on angiospasm and ischemic complications in patients with ruptured cerebral arterial aneurysms.

Materials and Methods

Study Object

The study object encompasses the clinical features of acute cerebrovascular accidents of both hemorrhagic and ischemic types caused by the rupture of cerebral artery aneurysms, amid angiospasm and occlusive-stenotic lesions of the cerebral and main arteries of the neck.

To test the hypothesis regarding the causal relationship between occlusive-stenotic lesions of the cerebral arteries and the main arteries of the neck and the clinico-morphological characteristics of stroke, a retrospective study was conducted in two parallel groups.

Study Participants

A retrospective analysis was conducted on case histories of 1147 patients with cerebral artery aneurysms from 2006 to 2022. Out of these, 126 patients who underwent neurosurgical treatment for ruptured cerebral artery aneurysms were selected. The study group included 63 patients who met the following criteria: surgical treatment, rupture of saccular aneurysms, and the presence of occlusive-stenotic lesions confirmed by instrumental methods. The control group included 63 patients who met such criteria as: performed surgical treatment, rupture of saccular aneurysms, he absence of occlusive-stenotic lesions which are confirmed instrumental methods.

Informed and voluntary written consent for participation in the study and data publication was obtained from all patients.

The study was approved by the Ethics and Bioethics Committee of the Romodanov Institute of Neurosurgery, National Academy of Medical Sciences of Ukraine (Minutes No.3 dated December 16, 2020).

Inclusion Criteria

The inclusion criteria for the study group were: undergone surgical treatment, rupture of saccular aneurysm, and presence of occlusive-stenotic lesions confirmed by instrumental methods. For the control group, the criteria were: undergone surgical treatment, rupture of saccular aneurysm without occlusive-stenotic lesions confirmed by instrumental methods.

Group Characteristics

Among the patients involved in the study, males predominated (76 males, 60.32%). In both the study group (n=63) and the control group (n=63), there were 38 males and 25 females each. The patients' ages ranged from 31 to 77 years, with a mean age of 55.90±0.76 years. The mean age of male patients was 54.30±0.94 years, and the mean age of female patients was 58.30±1.19 years. The groups were comparable in terms of sex ratio and age.

Study Design

All patients were examined uniformly. Upon hospitalization, neurological status was assessed (including general brain symptoms, meningeal and focal symptoms such as motor, speech, mental disorders, and dysfunction of pelvic organs) alongside a general examination of organs and systems. The clinical examination of patients involved a neurosurgeon, ophthalmologist, otolaryngologist, therapist, and other specialists as needed. If hospitalization occurred soon after hemorrhage, the examination was conducted urgently.

To determine the severity of the patients' condition upon hospitalization and before surgery, assessments were made using the Hunt-Hess scale, World Federation of Neurological Surgeons (WFNS) scale, National Institutes of Health Stroke Scale (NIHSS), and Glasgow Coma Scale (GCS). Neuroimaging methods were essential to objectify and determine the anatomical form, size, and location of intracranial hemorrhage. Angiographic examination was the gold standard for detecting aneurysms and stenoses. Key parameters evaluated during the examination of brain vessels included aneurysm location, shape, size, neck width relative to the aneurysm dome and parent artery, number of chambers in aneurysm, dome direction, and the presence and severity of angiospasm [23], occlusive-stenotic lesions and compensatory collateral blood flow.

To detect subarachnoid hemorrhage (SAH), parenchymal or intraventricular hemorrhage, midline structure shifts, ischemic lesions, and cerebral edema, the presence of occlusive-stenotic lesions confirmed by instrumental methods. The control group included 63 patients who met such criteria as: performed surgical treatment, rupture of saccular aneurysms, he absence of occlusive-stenotic lesions which are confirmed instrumental methods.

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To detect subarachnoid hemorrhage (SAH), parenchymal or intraventricular hemorrhage, midline structure shifts, ischemic lesions, and cerebral edema, and
computed tomography (CT) was used [14, 16]. Multislice CT (MSCT) with angiography is a universal method allowing simultaneous detection of saccular aneurysms, arterial stenoses, SAH, parenchymal or intraventricular hemorrhage, midline structure shifts, ischemic lesions, and cerebral edema. Magnetic resonance imaging (MRI) of the brain is highly sensitive for detecting ischemia and is desirable for further examination of patients with occlusive-stenotic lesions and concurrent vasospasm.

Intraoperatively, contact Doppler ultrasound is used to assess the radicality of aneurysm clipping during microsurgical transcranial surgery and diagnose occlusive-stenotic arterial lesions along with the aneurysm. Ultrasound examination of the head and neck vessels is necessary to assess the functional state of cerebral hemodynamics, determine the presence and sufficiency of collateral blood flow in occlusive-stenotic lesions, and diagnose and monitor cerebral vasospasm. This non-invasive method can be repeated multiple times.

All patients underwent standard laboratory tests in intensive care units and during preoperative preparation, with particular attention to water-electrolyte balance and the blood coagulation system. Lumbar puncture and cerebrospinal fluid sampling for general analysis were performed for diagnostic and therapeutic purposes.

To objectify the findings of neuroimaging (MSCT, MRI), the Fisher Scale Revisited was used for SAH and the Graeb Modified Scale for blood breakthrough into the ventricular system.

Statistical Analysis

The data obtained were processed using the Statistica software package (StatSoft). Quantitative data (age) are presented as arithmetic mean (M) and standard deviation (SD). Nonparametric criteria of statistical analysis methods were used: the Kruskal-Wallis H test for comparing groups by age and gender, and Pearson’s χ² test for assessing consciousness impairment (GCS) and severity of condition in SAH patients (WFNS and Hunt-Hess scales).

A critical level of statistical significance (p) was considered ≤0.05.

Results and Discussion

Based on cerebral angiography, MSCT angiography, ultrasound of the head and neck vessels, and medical documentation, occlusive-stenotic lesions of the cerebral arteries, major neck arteries, or their combined involvement were confirmed in all patients in the study group.

The study group was divided into five subgroups based on the severity of occlusive-stenotic lesions (Fig. 1). The largest number of patients was recorded in subgroup 1 (21 patients with mild stenosis (up to 50%)) and subgroup 5 (19 patients with changes in the cervical-para-cervical area of the aneurysm).

Data on gender and age ratio in subgroups of the study and control groups are presented in Table 1. It was found that the average age in the presence of occlusive-stenotic lesions is lower in men compared to women (54.3 and 58.3 years, respectively). The difference in average age is most pronounced in subgroup 2 of the study group (stenosis 50-75%): men - 48.3 years, women - 62.0 years. This indicates the atherogenic influence of androgens and the angioprotective effect of estrogens.

The data regarding the affected cerebral arteries are presented in Fig 2. In both groups, aneurysms of the ACA-AComA complex predominated.

When stenoses are present, ruptures of MCA aneurysms occur more frequently (study group – 25.4%, control group – 12.7%).

In the majority of cases, the clinical manifestations of a ruptured cerebral arterial aneurysm were typical: an acute onset without prodromal symptoms, developing general and focal neurological symptoms. Sudden severe headaches, vomiting (often repeated), meningeal signs, and pronounced autonomic disturbances were common. The objectification and quantitative assessment of neurological disorders were performed using the GCS, WFNS, and Hunt-Hess scales (Tables 2-4).

When assessing the severity of the patients’ condition according to the Hunt-Hess scale, no significant difference was observed between the study and control groups, but according to the WFNS scale, more patients in the control group had grade II and moderate impairment on the GCS.

![Figure 1. Distribution into subgroups by severity of occlusive stenotic lesion: CPAA - cervical-paracervical area of the aneurysm](http://theunj.org)
Table 1. Distribution by gender and age in subgroups of the study and control groups (M±SD)

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Sex</th>
<th>Average age, years</th>
<th>Study group</th>
<th>Control group</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Men</td>
<td>56,40±2,13</td>
<td>54,30±0,94</td>
<td></td>
<td>0,91</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>56,60±2,96</td>
<td>58,30±1,19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Men</td>
<td>48,30±2,51</td>
<td>54,30±0,94</td>
<td></td>
<td>0,91</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>62,00±5,06</td>
<td>58,30±1,19</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>p=0,32</strong>*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Men</td>
<td>56,00±4,04</td>
<td>54,30±0,94</td>
<td></td>
<td>0,91</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>–</td>
<td>58,30±1,19</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>p=0,32</strong>*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Men</td>
<td>58,40±2,58</td>
<td>54,30±0,94</td>
<td></td>
<td>0,91</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>55,0±1,0</td>
<td>58,30±1,19</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>p=0,32</strong>*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Men</td>
<td>53,72±3,11</td>
<td>54,30±0,94</td>
<td></td>
<td>0,91</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>58,25±1,85</td>
<td>58,30±1,19</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>p=0,32</strong>*</td>
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</table>

*According to the Kruskal-Wallis H test.

Figure 2. Distribution of pathology by pools of cerebral arteries: PICA - Posterior inferior cerebellar artery; SCA - Superior cerebellar artery
Table 2. Level of consciousness according to Glasgow Coma Scale during hospitalization

<table>
<thead>
<tr>
<th>Level of consciousness</th>
<th>Study group (n=63)</th>
<th>Control group (n=63)</th>
<th>Statistical method</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Abs.  %</td>
<td>Abs.  %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clarity of consciousness (15 points)</td>
<td>36  57,1</td>
<td>32  50,8</td>
<td>Criterion $\chi^2$ Pearson</td>
<td>0,47</td>
</tr>
<tr>
<td>Moderate loss of consciousness (13-14 points)</td>
<td>18  28,6</td>
<td>23  36,5</td>
<td>Criterion Fisher</td>
<td>0,22</td>
</tr>
<tr>
<td>Deep silencing of consciousness (11-12 points)</td>
<td>7 11,1</td>
<td>7 11,1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sopor (9-10 points)</td>
<td>1  1,6</td>
<td>0  0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Coma 1 (7-8 points)</td>
<td>1  1,6</td>
<td>0  0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Coma (5-6 points)</td>
<td>0  0</td>
<td>1  1,6</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 3. Evaluation according to the WFNS scale

<table>
<thead>
<tr>
<th>Grade</th>
<th>Study group (n=63)</th>
<th>Control group (n=63)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Abs.  %</td>
<td>Abs.  %</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>28 44,4</td>
<td>29 46,0</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>9  14,3</td>
<td>17 27,0</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>18 28,6</td>
<td>19 30,2</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>8  12,7</td>
<td>7 11,1</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>0  0,0</td>
<td>1  1,6</td>
<td></td>
</tr>
</tbody>
</table>

*According to Fisher's test.

Table 4. Evaluation according to the Hunt–Hess scale

<table>
<thead>
<tr>
<th>Grade</th>
<th>Study group (n=63)</th>
<th>Control group (n=63)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Abs.  %</td>
<td>Abs.  %</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>15 23,8</td>
<td>20 31,7</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>27 42,9</td>
<td>24 38,1</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>18 28,6</td>
<td>17 27</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>2  3,2</td>
<td>1  1,6</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>1  1,6</td>
<td>1  1,6</td>
<td></td>
</tr>
</tbody>
</table>

*According to Fisher's test.

There were 5 fatalities in the study group (5 men) (Table 5) [15] and 2 deaths in the control group (both men).

Focal neurological manifestations of cerebral lesions in the acute period of arterial aneurysm rupture are due to anatomical localisation of the haemorrhage, local ischaemia resulting from cerebral vasospasm due to subarachnoid hemorrhage (SAH), and aggravated by chronic cerebral ischaemia due to occlusion.

Cerebral vasospasm was diagnosed using Doppler ultrasound of the head and neck vessels (Table 6).

A predominance of patients with high cerebral blood flow velocity (200 cm/s, corresponding to the velocity during grade III cerebral artery vasospasm)
was observed in the study group (32.56%) compared to the control group (24.24%).

Data on ischemic lesions detected by CT before and after the surgery are presented in Table 7.

Patients in the study group were more vulnerable to ischemic complications compared to the control group.

The most severe prognosis for life and health occurs when arterial aneurysm rupture occurs in men against the background of 50-75% stenosis and grade III cerebral artery vasospasm. The best prognosis is observed in young women without concomitant occlusive-stenotic lesions of cerebral arteries and major arteries of the neck, and without vasospasm.

It was found that men predominated among patients in the study group (60.32%). The average age of men with occlusive-stenotic lesions was lower than that of women (men - (54.30±0.94) years, women - (58.30±1.19) years). The age difference was most pronounced in the subgroup of the study group with 50-75% stenosis (men - 48.3 years, women - 62 years). Age and gender differences were identified, which may indicate the atherogenic influence of androgens and the angio-protective effect of estrogens.

When assessing the severity of patients' condition according to the Hunt-Hess scale, no significant difference was noted between the study and control groups. However, according to the WFNS scale, more patients in the control group had grade II severity and moderate impairment according to the GCS.

The assumption regarding the "opposing" influence of concomitant occlusive-stenotic lesions on the risk of arterial aneurysm rupture depending on the aneurysm's location [1,15] is based on the relationship between pressure gradient on the vascular wall, blood flow direction, and resistance of the arterial wall. Arterial aneurysm rupture is considered a disturbance of hemodynamic equilibrium in the affected arterial segment [3, 5–10, 14, 20, 21].

The development of cerebral vasospasm is associated with the direct effect of blood on the sympathetic plexus of arteries, the toxic action of hemoglobin breakdown products on arteries, the influence of catecholamines, platelet degradation products, leukotrienes, and eicosanoids. A higher proportion of patients with high cerebral blood flow velocity (>200 cm/s) was detected in the study group (32.56%) compared to the control group (24.24%). This is likely due to decreased vascular wall elasticity (cerebral atherosclerosis and hypertensive angiopathy), lower sensitivity to selective L-type calcium channel blockers, and greater disruption of cerebral blood flow regulation mechanisms (myogenic, humoral, nervous, metabolic) in conditions of hemorrhagic stroke in patients of the study group.

### Table 5. Mortality in subgroups of the study group (n=63)

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Survived</th>
<th>Died</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>21</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>19</td>
<td>0</td>
</tr>
</tbody>
</table>

### Table 6. Severity of cerebrovascular spasm, %

<table>
<thead>
<tr>
<th>Group</th>
<th>Absence of angiospasm</th>
<th>Grade I angiospasm</th>
<th>Grade II angiospasm</th>
<th>Grade III angiospasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study (n=63)</td>
<td>11,63</td>
<td>18,60</td>
<td>37,21</td>
<td>32,56</td>
</tr>
<tr>
<td>Control (n=63)</td>
<td>18,18</td>
<td>15,15</td>
<td>42,42</td>
<td>24,24</td>
</tr>
</tbody>
</table>

### Table 7. Ischemic lesions in the preoperative and postoperative period

<table>
<thead>
<tr>
<th>Group</th>
<th>The presence of ischemia in the preoperative period</th>
<th>Occurrence of ischemia in the postoperative period</th>
<th>Total preoperative and postoperative period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study (n=63)</td>
<td>21 (16,7%)</td>
<td>15 (11,9%)</td>
<td>36 (28,6%)</td>
</tr>
<tr>
<td>Control (n=63)</td>
<td>13 (10,3%)</td>
<td>10 (7,9%)</td>
<td>23 (18,2%)</td>
</tr>
<tr>
<td>That's all</td>
<td>34 (27,0%)</td>
<td>25 (19,8%)</td>
<td>59 (46,8%)</td>
</tr>
</tbody>
</table>

Note. The percentage of 126 is given.
Conclusions
Arterial aneurysm ruptures of the middle cerebral artery occur more frequently in the presence of stenoses (in the study group - 25.4%, in the control group - 12.7%).

Gender differences were identified in patients who experienced arterial aneurysm rupture against the background of occlusive-stenotic lesions, with men predominating (60.32%).

Neurological status in patients with hemorrhagic stroke due to arterial aneurysm rupture is significantly exacerbated by vasospasm and occlusive-stenotic lesions due to chronic cerebral ischemia. The most severe prognosis is observed in men with arterial aneurysm rupture against the background of 50-75% stenotic lesions and severe cerebral artery vasospasm.

Disclosure
Conflict of interest
The authors declare no conflicts of interest or financial involvement in the preparation of this article

References
Treatment of schizencephaly: A brief review and case study

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Introduction: Schizencephaly is a rare disease. It is a poorly understood pathology. The clinical signs are variable and the diagnosis is made by elimination. The treatment is varied with poor results. Corticosteroids are not commonly used medications.

Case Presentation: The observation concerns a 5-month-old child, born with a motor deficit in the right hemibody. His parents had an unremarkable medical history. After brain imaging for epileptic seizures, the child is referred for neurosurgery 5 months later. The diagnosis of schizencephaly was mentioned. Antiepileptic treatment associated with corticosteroid therapy for two weeks was started. Motor physiotherapy began at the same time. At 6 months after start of treatment, the evolution was satisfactory marked by a clear improvement in the motor deficit and a complete cessation of seizures.

Conclusions: Due to its rarity, the diagnosis of schizencephaly is made by elimination. Brain MRI is the best radiological examination. Corticosteroid therapy combined with physiotherapy can have an impact on good progress. Treatment should be early.

Keywords: schizencephaly; epilepsy; hemiparesis; malformation; pediatric neurosurgery

Schizencephaly is a rare congenital disorder of cerebral cortical development [1]. Due to insufficient knowledge of this condition, several definitions had been proposed. The most recent which seems to be the synthesis of the previous definitions is from Naïdich et al [2]. It includes a trans-mantle column of dysplastic gray matter extending from the ependyma to the pia mater without a cleft containing CSF [2]. A recently discovered condition, schizencephaly was first described at the end of the 19th century [3]. The term was first introduced by Yakovlev and Wadsworth 1946 [4] to designate a malformative lesion due to a deviation from normal development and not secondary to destruction of the mature cortex as in porencephaly. The prevalence of this disease is estimated at approximately 1.5 per 100,000 babies born alive, according to estimates from a review of four million births in California [5]. According to Howe et al. a combined live birth and stillbirth rate of 1.48 per 100,000 was found in a population of over 2.5 million in the United Kingdom [6]. Its etiology is still subject to debate. Treatment is symptomatic with poor results. Corticosteroids are not commonly used in the treatment of schizencephaly. The objective was to report the first case of type 3 in our practice treated effectively with corticosteroids and physiotherapy. We do not have statistical data on this pathology on a hospital level, much less on a national scale.
deficit rated at 1/5 in the right upper limb and 0/5 in the right lower limb. The rest of the exam was unremarkable. The brain CT performed revealed the presence on the left side of the brain a a fronto-parietal cleft causing the left lateral ventricle to communicate with the ipsilateral pericerebral space through a dehiscence of the brain parenchyma (Figure 1).

The absence of the septum pellucidum was also noted. This combination suggests type 3 Schizencephaly. The brain MRI requested was not carried out due to financial accessibility, availability (because it is done in a private hospital) and the difficulty of carrying out (the examination is carried out under anesthetic sedation in patients less than 1 year old). Electrophysiological examinations were not carried out because they are not available. At the end of a concern meeting, a treatment based on valproic acid 10 mg/kg divided into one dose every 12 hours per day for a period of 6 months was proposed by the neuropediatrician; under his directive and also on the instructions of the physiotherapist, corticosteroid therapy based on methylprednisolone 0.5 mg/kg only in the morning was implemented for two weeks. The child continued his motor rehabilitation of his right half body. This treatment was started in the child at 5 months old. At 6 months of evolution when the child was 11 months old, we noted a recovery of the motor deficit. This was 5/5 in the right upper limb and 4/5 in the right lower limb with remission of seizures under antiepileptic treatment. The child did not present any delay in psychomotor development.

Figure 1. The cleft of the brain tissue of the hypodense density of the left fronto-parietal area, which communicates with the left lateral ventricle. Nonenhanced CT

Discussion

Etiology and risk factors

Many etiologies have been mentioned for the occurrence of schizencephaly. Work between 2010 [7] and 2013 [8] had aroused interest in genetic anomalies even if the first reports by Merello et al. in 2008 linking schizencephaly to mutations in the EMX2 gene have not been confirmed [9]. The majority of cases of schizencephaly are sporadic and not familial, and in most cases no cause is found [10]. Schizencephaly is thought to be due to “a defect in growth and differentiation of a circumscribed part of the brain wall” [11]. According to Griffiths, this disease would have its origins in the first trimester of pregnancy, more precisely the first 2 months after conception [12]. The theory of pinning of the ependyma and the pia mater, refined by Naidich [2], which are anatomically very close during the first trimester is not shared by Griffiths who finds it difficult to explain the banks largely open openings and loss of volume frequently present in schizencephaly (type 3) [12]. Further evidence against the pinning theory is the consistent presence of abnormal cortex lining the clefts, which indicates an etiological factor in the second trimester: “...Coincidental polymicrogyria suggests that the timing is between the fourth and the sixth month [12]. Chen states that the primary etiology is due to “in utero vascular insufficiency” [13]; this vascular etiology was found in the work of Nabavizadeh et al. [14]. There is now clinical, morphological and experimental evidence in favor of a destructive origin of these lesions” [11]. Among the risk factors recognized for the occurrence of schizencephaly, transplacental infections by cytomegalovirus [11] and recently by Zika virus [15] have been well documented. No notion of genital infection was found in the patient’s mother. Our observation would relate to a sporadic case of schizencephaly.

Clinical aspects

The clinical presentation of schizencephaly is very variable. In their 10-year study in Thailand, the authors found that the most common clinical features of schizencephaly were motor disability, developmental disorders and epilepsy [16]. Some authors claim that gravity is closely linked to the size of the cleft [17]. According to Denis et al. children with unilateral schizencephaly present hemiparesis and mild mental retardation [17]. Maurine et al. [1] had reported the existence of a correlation between clinic and imaging. They found that patients with closed-cleft schizencephaly were more likely to have mild to moderate clinical signs than those with open clefts. That children with unilateral schizencephaly more frequently presented a mild or moderate course than those with bilateral lesions. Single lobe involvement accounted for 88% of those with mild results and 53% of those with moderate results [1]. We do not share these statements in the sense that the case reported in our observation presented type 3 schizencephaly (open cleft), but did not have the severe neurological form. Apart from hemiparesis which was regressive and comitiality improved under treatment, the child had no other signs (delay in psychomotor development, axial hypotonia, and microcephalus). However, the lesion was located between the frontal
and parietal lobes. Perhaps the unilateral attack had something to do with it.

**Diagnostic aspects**
The diagnosis of schizencephaly is raised by neuroradiology. The absence of a consensual definition meant that this diagnosis was established by elimination when made in early childhood. The ideal is to make the diagnosis during the antenatal period. Magnetic resonance imaging (MRI) is the best of choice. In utero magnetic resonance imaging (iMRI) is now used for prenatal detection of brain abnormalities, including schizencephaly [4]. In the United Kingdom, less than half of cases of schizencephaly were detected prenatally [6].

As this examination is difficult to access in our context, we relied on brain CT-scan to make the diagnosis. This examination is a good tool for uncovering the cleft, its location and its extent. It made it possible to detect the absence of the septum pellucidum in our patient. According to Maurine et al. found it in 45% of patients in their study [1]. The absence of septum pellucidum is associated with "open cleft" schizencephaly (type3) [12]. The reasons for the association of schizencephaly with the absence of the septum pellucidum are not yet known with certainty [12]. Although MRI is essential for diagnosis of schizencephaly [18]; also, it can highlight the abnormal existence of ventricular diverticulum which hinder the free circulation of cerebrospinal fluid [19]. A high-performance brain CT scan can be an important means of clarifying confusion, as was the case in our observation. The stereoelectroencephalography (SEEG) can be used to identify seizure foci in patients whose clinical symptoms do not correspond to imaging results and/or routine electroencephalogram (EEG) results [20].

**Classification**
Griffiths P.D. in his work on schizencephaly proposed a classification which takes into account all the definitions of the anomaly reported in the literature [12]. This classification is recorded in Table 1.

**Therapeutic aspect**
Treatment is symptomatic. There is no cure for the disease. Short-term corticosteroid therapy was used in our study because of its anti-inflammatory effect. According to Becker et al. corticosteroids have been used for the treatment of patients with epilepsy for more than 6 decades, based on the hypothesis of inflammation in the genesis and/or promotion of epilepsy [21]. We have not had any document relating to the use of corticosteroids in the treatment of schizencephaly. In the event of an epileptic seizure, antiepileptic treatment may be administered depending on the patient’s weight and the type of seizure. In the event of partial seizures, carbamazepine should be preferred. For other forms of seizures, all other antiepileptic drugs can be used at the minimum effective and tolerated dose. When monotherapy is not effective, a combination of antiepileptic drugs can be used. In our observation, valproic acid had been used successfully. For refractory

Table 1. Classification of schizencephaly according to P.D. Griffiths [12]

<table>
<thead>
<tr>
<th>Nomenclature used in this article</th>
<th>Schizencephaly (type 1)</th>
<th>Schizencephaly (type 2)</th>
<th>Schizencephaly (type 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nomenclature if a cleft is required for the diagnosis of schizencephaly</td>
<td>Trans-mantle heterotopion</td>
<td>Closed lip schizencephaly</td>
<td>Open lip schizencephaly</td>
</tr>
<tr>
<td>Nomenclature if a cleft is NOT required for the diagnosis of schizencephaly</td>
<td>Closed lip schizencephaly</td>
<td>Open lip schizencephaly</td>
<td>Open lip schizencephaly</td>
</tr>
</tbody>
</table>

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epilepsy, high-dose steroids may be administered before possible surgical treatment [18]. In cases of drug resistance, which concerns a third of patients, epilepsy surgery can be offered. This can be the resection either of the schizencephalic cleft alone, or of the cleft and the surrounding epileptogenic tissue, or of temporal or fronto-temporal lobectomy. Also, surgery may consist of the removal of abnormal intraventricular diverticulum which can lead to intracranial hypertension [19]. This surgery is done endoscopically. In case of failure, we will convert to open surgery. Preventive treatment of epilepsy is not permitted. Functional rehabilitation is necessary to hope for recovery from the motor deficit. In our patient, over a period of 6 months after start of treatment, recovery was good. We cannot say with certainty whether this therapeutic effectiveness is due to rehabilitation or corticosteroid therapy or to the combined effect of the two methods.

**Prognostic aspects**

The prognosis is variable and depends on the extension of the cleft, its extent and the association with other craniocerebral malformations. Children with a severe motor deficit associated or not with drug-resistant epilepsy will present a very poor outcome. Open lip clefts were associated with poor seizure control, and a larger cleft was related to a younger age at seizure onset [22].

**Conclusions**

Schizencephaly is a rare congenital pathology that is most often diagnosed in the second instance. Brain neuroimaging is essential for the diagnosis of this disease. Corticosteroid therapy can be included in symptomatic treatment. Multidisciplinary care must begin as early as possible in order to hope for a favorable outcome.

**Disclosure**

Ethical Considerations

Compliance with ethical guidelines: Ethical considerations, anonymity and patient modesty were respected.

**Informed consent**

We obtained parental consent for the use of the child's medical data.

**Conflict of interest**

No conflict of interest.

**Funding**

No funding received.

**References**

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Application into clinical practice of a minimally invasive surgical approach to the removal of hyperostotic cranio-orbital meningiomas. This publication is based on the analysis of a clinical case of 49-year-old woman with exophthalmos, and the absence of neurological deficits. A non-standard approach to remove a cranio-orbital hyperostotic meningioma through a minimally invasive orbito-zygomatic approach was used.

The main principle of proposed surgical approach was to remove first the hyperostosis, followed by the areas of dura mater involved by the tumor, according to the "outside-in" principle. According to the intraoperative process and the results of MRI control, it was possible to achieve total removal of both the affected dura mater and the hyperostotic lesion.

The minimally invasive transorbital approach opens a wide corridor for surgery of the para and retroorbital space and allows using the "outside-in" method, to remove not only hyperostosis but also the area of damage to the dura mater.

**Key words:** meningioma; hyperostotic lesion; orbit; minimally invasive surgery

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**Introduction**

Meningiomas are the most common primary tumors of the central nervous system (CNS), accounting for about one-third of all primary tumors of the brain and spinal cord [1].

The incidence of meningioma progressively increases with age. The average age at diagnosis is 65 years. Meningiomas are more common in women, with a female-to-male ratio of 2–3:1 [2].

En plaque meningiomas account for 2–9% of all meningiomas [3]. This is a special type of meningiomas that infiltrate the dura mater diffusely, forming a thin layer that precisely follows the contours of the inner surface of the skull. The term "en plaque" was first used by Cushing and Eisenhardt [4, 5] to describe this special type of growth, distinguishing it from the more common exophytic type. These tumors are characterized by invasion into the adjacent bone, leading to the development of distinct hyperostosis. Although bony hyperostosis is a well-known feature of all types of meningiomas, in plaque meningiomas, bone invasion is much more intense and results in clinical manifestations. This is particularly evident in meningiomas of the greater wing of the sphenoid bone, which typically present with progressive exophthalmos. Hyperostotic bone should be considered as part of the neoplastic process, as the pathology demonstrates invasion of meningiomatous cells into Haversian canals [6]. Standard surgical approaches for removing such neoplasms are the pterional and FTOZ approaches, but significant trauma and cosmetic defects after surgery induce the search for more gentle and minimally invasive tactics.

**Case report**

A female patient born in 1973 presented with complaints of protrusion of the left eye. Previously she consulted an ophthalmologist, no abnormalities were detected in visual organ. Magnetic resonance imaging (MRI) of the brain with intravenous contrast was performed, revealing a hyperostotic meningioma of the greater wing of the sphenoid bone on the left with deformation of the left orbit and secondary exophthalmos (Fig. 1). The patient underwent surgery using a minimally invasive orbito-zygomatic approach with total resection of the affected area of the sphenoid wing and subsequent brow ridge plasty.

**Method description**

A linear incision of approximately 4 cm in length was made in the area of the left eyebrow. The frontal and zygomatic bones were exposed.

Using a bone saw, the frontal process of the zygomatic bone and partially the brow ridge were removed (Fig. 2). Holes for screws, which would secure the bone flap to minimize cosmetic defects, were pre-marked. The bone tissue with altered structure was immediately visualized.

Using dynamic retraction of the orbital soft tissues on one side and the temporal muscle on the other, gradual drilling (with a high-speed microdrill) of the altered bone was performed until visualization of the...
basal dura mater of the frontal and temporal poles, which served as the locus of tumor growth (Fig. 3). The dura mater of the temporal pole was coagulated, then microsurgically dissected within the unaltered tissue, allowing for total removal of the neoplasm (Simpson grade 1) (Fig. 4).

The dura mater defect was closed with a piece of fascia lata and sealed using BioGlue adhesive (Fig. 5).

To prevent enophthalmos, the bone defect was lined with layers of adipose tissue from the lateral surface of the thigh and also sealed with BioGlue adhesive. The bone flap was fixed with a titanium plate and microscrews (Fig. 6). The wound was closed in layers with a cosmetic suture.

The patient was activated on the day of surgery. There was no postoperative neurological deficit. Moderate periorbital edema was observed, which regressed by the 5th day. The patient was discharged 3 days after the surgical intervention. A follow-up brain MRI was performed the next day after the surgery, revealing no residual neoplasm or hyperostosis (Fig. 7).

A follow-up examination was conducted after 3 months. The exophthalmos has regressed, palpebral fissures were fully symmetrical, and there were no neurological symptoms (Fig. 8).

Discussion

Despite the fact that en plaque meningiomas with hyperostosis account for only 2-9% of all meningiomas, they remain a challenge in neurosurgery. Although the soft tissue component of tumors is usually small, the bony hyperostosis extending into the orbit, potential invasion of the cavernous sinus, and extension into the infratemporal region pose challenges for achieving...
Figure 4. Defect of the dura mater after total removal of the neoplasm

Figure 5. Sealing of the dura mater defect with BioGlue adhesive

Figure 6. Fixation of the bone flap with a titanium plate
In a study conducted in 2021, it was concluded that adequate and meticulous drilling of the lateral and/or superior walls of the orbit, removal of any intraorbital pathological soft tissue components, and all available hyperostotic bone are key factors contributing to complete resection and regression of proptosis. Postoperative complications identified in this study included visual impairment, hemiplegia, ophthalmoplegia, facial numbness, hematomas, and trigeminal nerve injury [13]. Hence, the use of surgical techniques that ensure atraumatic, complete removal, and absence of cosmetic defects was our primary goal. The technique of minimally invasive orbito-zygomatic approach has several advantages over traditional surgical tactics, primarily cosmetic and atraumatic. Considering the characteristics of en plaque meningiomas, particularly the pronounced hyperostosis of the adjacent bone, this method entails step-by-step removal of the tumor, starting from the hyperostosis rather than the asymptomatic soft tissue component. Therefore, we propose to call this technique "outside-in". Additionally, such a direction of removal provides complete and constant control during surgery over intra-orbital structures, minimizing the risk of iatrogenic injury. However, the minimally invasive approach is feasible only in cases of limited intradural involvement.

Conclusions
The use of minimally invasive transorbital approach using the "outside-in" technique for resection of cranio-orbital hyperostotic meningiomas is a safe and convenient method of surgical treatment.

Disclosure
Conflict of interest
The authors declare no conflicts of interest.
Informed consent
The patient provided informed consent for the publication of data and images.

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Figure 7. Follow-up MRI 24 hours after the operation

Figure 8. Regression of exophthalmos at the follow-up examination. The patient gave written informed consent to publish the full face photo without anonymisation.


