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Vestibular Schwannomas: implementation of PANQOL and Mayo VSQOL 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 VSQOL 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 Kolomiichenko 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 VSQOL 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 Kolomiichenko 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 5 (18.5%) 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

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(both general practitioners and subspecialists - otologists, neurologists) regarding VS, especially its most typical symptoms, and low oncological alertness.

Since the issue of VS in developed countries is more social than medical, such a tendency is likely to be observed in Ukraine as well. Relevant services should be prepared for a "wait-and-scan" strategy and not spend resources on unjustified treatment when it is not needed. Over the past years, the radiosurgical and neurosurgical community has not been as united in recommending the "wait-and-scan" strategy due to the risk of life-threatening complications associated with tumor progression [1]. There is a need for markers that can predict the progressive growth of VS, which is important for preventing abandoned cases of extremely large VS and for choosing the appropriate tactic for newly detected VS.

Understanding the state of the problem and trends in assistance planning through specialized test systems will contribute to improving the quality of life of patients with VS.

Prevalence of Vestibular Schwannomas

Sporadic vestibular schwannoma (vestibular schwannoma, VIIIth cranial nerve neuroma, acoustic neurinoma, vestibular neurolemmoma) is one of the most common neoplasms of the cerebellopontine angle, arising in the internal auditory canal, at the border between oligodendrocytes and myelin-producing schwann cells. The term "vestibular schwannoma," proposed by R. Eldridge and D. Parry in 1992 [2], is more commonly used based on histogenesis since in 90% of observations VS is formed from cells of the vestibular portion of the VIII cranial nerve, and only in 10% from the acoustic (auditory) portion.

According to the study [3], the frequency of VS varies from 1 case per 2000 adults to 1 case per 500 individuals over 70 years old. Sporadic VS accounts for 95% of all observations, with the remaining occurring in patients with neurofibromatosis type II. In developed countries, it is often an incidental finding on magnetic resonance imaging (MRI) due to other pathologies, indicating a transition from the era of microsurgery and radiosurgery to the era of "chronic disease control" [4,5]. In patients over 70 years old, VS have smaller sizes at the time of detection and a slower growth rate compared to tumors in younger patients [6]. Over the past 40 years, the incidence of VS has steadily increased from 3 to 34 cases per 1 million population per year primarily due to improved access to enhanced diagnostics and detection of more tumors in elderly individuals. Meanwhile, the diagnostic tumor size has decreased from 26 to 7 mm, and the diagnostic peak has shifted from 49 to 60 years [7].

According to our data, the average size of initially diagnosed VS in 2017 was 32.3 mm, in 2018 - 29.6 mm, in 2019 - 31.2 mm, in 2020 - 31.1 mm, in 2021 - 25.6 mm, in 2022 - 21.85 mm, and in 2023 - 22.4 mm, indicating a trend towards improved diagnosis, but its indicators are still worse than those abroad.

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 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 Kolomiichenko 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

Diagnosics

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 Kolomiichenko Otolaryngology Institute. However, while Romodanov Neurosurgery Institute before 2017 observed only large and extremely large VS, T4a–b according to the Hannover classification [20], requiring surgical treatment, earlier diagnosis of VS at Kolomiichenko Otolaryngology Institute allowed the adoption of a "wait-and-scan" strategy since 2003. For example, in the Department of Ear Microsurgery and Otoneurosurgery of Kolomiichenko 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, an 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 recurrence radiosurgery 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 ≥ 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 arachnoid 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 VIIIth 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

$\geq T3b$ 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 $>95 \text{ mm}^3$, internal auditory canal expansion, large tumor size ($>3 \text{ cm}$), NF2 syndrome, presence of edema on preoperative MRI 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 $<3 \text{ cm}$ (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 $\geq 9.8 \text{ mm}$ 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 chances of preserving class B hearing according to the AAO-NHS scale, while SRS is associated with better 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 retrosigmoid 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/recurrence is the main goal of VS treatment [42]. For most patients without VS progression the life quality 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 Otoneurology of Kolomiichenko Otolaryngology Institute or referred for surgical treatment to the Romodanov Neurosurgery Institute if the size of VS $\geq T2$ 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 Radioneurology Department regarding combined treatment contain information about a part of patients who underwent treatment at the Subtentorial Neurooncology Department.

Since 2022, the Radioneurology 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.

Table 1. The Penn Acoustic Neuroma Quality-of-Life Scale, ukrainian variant

UKRAINIAN (UKRAINE)						
 PANOOL						
Будь ласка, вкажіть наскільки Ви погоджуєтесь чи не погоджуєтесь із кожним твердженням. Обведіть колом ТІЛЬКИ ОДНУ цифру в кожному рядку						
П.І.П.:						
	Зовсім не погоджуюсь	Не погоджуюсь	Нейтрально	Погоджуюсь	Абсолютно погоджуюсь	
1	Втрата слуху впливає на мої особисті стосунки	1	2	3	4	5
2	Я маю труднощі у спілкуванні через порушення слуху	1	2	3	4	5
3	Мені важко концентруватись через дзвін, шум та інші сторонні звуки у вухах/вусі	1	2	3	4	5
4	У мене значні проблеми через запаморочення	1	2	3	4	5
5	Я відчуваю нестійкість чи інші порушення рівноваги	1	2	3	4	5
6	Я маю відчуття обертання чи падіння коли стою чи ходжу	1	2	3	4	5
7	Через запаморочення чи порушення рівноваги я маю складності при зміні напрямку під час ходіння	1	2	3	4	5
8	Маю складності із пересуванням по дому в темряві	1	2	3	4	5
9	Через порушення рівноваги мені здається, що люди подумують ніби я сп'янілий (а)	1	2	3	4	5
10	Мені довелось змінити поведінку на людях через проблеми з рухливістю обличчя	1	2	3	4	5
11	Я маю відчуття дискомфорту, зуду чи надмірну сльозотечу в одному з очей	1	2	3	4	5
12	Через проблеми з обличчям змінилась моя мова	1	2	3	4	5
13	Я здійснив менше своїх планів, ніж хотів, через свій діагноз невриноми	1	2	3	4	5
14	В мене є головний біль на стороні пухлини	1	2	3	4	5
15	В мене є неприємне відчуття страху наче ось-ось має трапитись щось жахливе	1	2	3	4	5
16	В мене час від часу бувають тривожні думки	1	2	3	4	5
17	В мене є відчуття загальмованості	1	2	3	4	5
18	В мене є неприємне відчуття «смоктання під ложечкою»	1	2	3	4	5
19	В мене бувають раптові відчуття паніки	1	2	3	4	5
20	В мене є відчуття ізоляції через мій діагноз невриноми	1	2	3	4	5
21	В мене є складності із зосередженням під час читання або перегляду телевізору	1	2	3	4	5
22	Я став/стала більш нетерплячим (ою)	1	2	3	4	5
23	Мені не вистачає енергії та життєвих сил	1	2	3	4	5
24	В мене є складності із запам'ятовуванням інформації	1	2	3	4	5
25	Я маю чудове здоров'я	1	2	3	4	5
26	Я очікую погіршення стану свого здоров'я протягом наступного року	1	2	3	4	5

Table 2. Mayo VSQOL Index, ukrainian variant**Mayo VSQOL Index****UKRAINIAN (UKRAINE)**

Мета цього опитування — зрозуміти, як діагноз вестибулярної шванноми або її лікування вплинуло на якість Вашого життя. Будь ласка, відмітьте одну відповідь стосовно кожного твердження, яка б найкраще відповідає Вашому стану після встановлення діагнозу вестибулярної шванноми або її лікування. Якщо Ви не стикались із ситуацією, наведеною у твердженні, виберіть “Зовсім ні”.

Проблеми зі слухом: будь ласка, дайте відповіді на твердження стосовно проблем зі слухом. Якщо Ви використовуєте слуховий апарат, будь ласка, дайте відповіді, враховуючи його використання.						
1	У мене є труднощі з безпекою через проблеми зі слухом (наприклад, я не чую димову сигналізацію або мені важко почути транспорт, що наближається)	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
2	Мені важко розібрати мову на фоні навколишнього шуму, або коли говорять декілька людей водночас	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
3	Мої проблеми зі слухом змушують мене відчувати себе відокремлено, коли я у групі людей	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
4	Я хвилююся, що втрачу слух і на інше вухо (де немає вестибулярної шванноми)	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
5	Мої проблеми зі слухом перешкоджають можливості приймати участь у соціальній активності або активному відпочинку	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
Запаморочення та порушення рівноваги						
6	Внаслідок запаморочення або порушення рівноваги я маю проблеми, коли повертаю швидко голову або дивлюсь вгору	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
7	Через запаморочення та порушення рівноваги для мене складно змінити напрям руху під час ходьби	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
8	Через запаморочення та порушення рівноваги мене непокоїть, що довколишні люди вважатимуть, ніби я перебуваю під впливом наркотичних речовин чи алкоголю	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
9	Через запаморочення та порушення рівноваги я боюся впасти чи травмуватися	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
10	Через моє запаморочення та порушення рівноваги я не відчуваю себе впевнено за кермом	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
11	Напади запаморочення та порушення рівноваги стають на заваді у виконанні мною фізично навантаженої діяльності: заняття спортом, танці, робота на присадибній ділянці	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
Біль, дискомфорт і шум у вусі/-хах						
12	Мене турбує важкість у голові, тиск або головний біль, пов'язані з моїм станом	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
13	Через біль, пов'язаний з моїм станом, я відчуваю дратівливість або депресію	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
14	Біль, пов'язаний з моїм станом, заважає моїй щоденній діяльності	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
15	Мій шум у вусі/-хах заважає мені зосередитися	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно

Continuation of the Table 2. Mayo VSQOL Index, ukrainian variant

16	Шум у вусі/-хах заважає мені засинати	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
Проблеми з обличчям чи очима						
17	Я соромлюсь своїх проблем з обличчям, що спричинені моїм станом	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
18	Слабкість м'язів обличчя негативно впливає на якість мого життя і щоденне самопочуття	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
19	Мене турбує те, що моє око надмірно сльозиться або стає сухим	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
20	Я відчуваю подразнення або біль в оці	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
Вплив на фізичне, емоційне та соціальне благополуччя						
21	Я відчуваю, що мій загальний стан здоров'я поганий	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
22	Мій стан заважає моїй повсякденній діяльності	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
23	Мені важко виконувати мої звичайні справи через втому	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
24	Я більше не отримую задоволення від речей, які зазвичай мене радували	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
25	У моїй голові виникають тривожні думки	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
26	Мій стан негативно вплинув на мій погляд на життя	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
27	Я хвилююсь, що мій стан погіршиться	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
28	Мій стан робить мене роздратованим або нетерплячим	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
29	Мій стан погіршив мої стосунки з членами родини чи друзями	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
Труднощі з мисленням та пам'яттю						
30	Мені важко знайти потрібні слова під час розмови чи письма	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
31	Мені важко зосередитися на зустрічах або світських зборах	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
32	Мені важко запам'ятовувати	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
33	Я відчуваю, ніби мій мозок гальмує	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно

Continuation of the Table 2. Mayo VSQOL Index, ukrainian variant

Задоволення або жаль/шкодування: будь-ласка, дайте відповідь на твердження наведені нижче стосовно вашого досвіду лікування вестибулярної шваноми						
34	Я задоволений лікуванням, яке я отримав/-ла з приводу вестибулярної шваноми	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
35	Я відчуваю, що я отримав/-ла достатньо об'єктивної/неупередженої інформації, щоб зробити правильний вибір як лікувати мою вестибулярну шваному	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
36	Я відчуваю, що моя команда лікарів прислухалась до моїх думок і побажань, коли формувала рекомендації щодо лікування моєї вестибулярної шваноми	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
37	Я б рекомендував/-ла таку ж тактику лікування вестибулярної шваноми, яку я отримав/-ла, для своїх друзів або членів родини, якщо б вони опинились у такій же ситуації	Зовсім ні	Дуже незначно	Трохи/певною мірою	Досить сильно	Дуже сильно
Вплив на працездатність: будь ласка, вкажіть чи вплинули обмеження, зумовлені діагнозом вестибулярна шванома або її лікуванням, на Вашу можливість продовжувати працювати?						
38	Я був/була змушений/-а просити про поступки на роботі (наприклад, робити більше перерв, забезпечити синхронний переклад під час зустрічей, надати спеціальне обладнання для безпечного утримання рівноваги)	Так	Ні	Не звертався/-лась		
39	Мені довелося повністю змінити сферу діяльності	Так	Ні	Не звертався/-лась		
40	Я зовсім припинив/-ла працювати і зараз повністю непрацездатний/-а	Так	Ні	Не звертався/-лась		

* From: Carlson ML, Lohse CM, Link MJ, Tombers NM, McCaslin DL, Saoji AA, Hutchins M & Yost KJ. Development and validation of a new disease-specific quality of life instrument for sporadic vestibular schwannoma: the Mayo Clinic Vestibular Schwannoma Quality of Life Index. J Neurosurg. 2022 Sep 2;1-11; used with permission of the Mayo Foundation for Medical Education and Research, all rights reserved.

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, is it 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- β 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 II), 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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