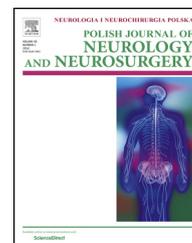


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## Original research article

# Surgery for sporadic vestibular schwannoma. Part I: General outcome and risk of tumor recurrence



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## ABSTRACT

**Background:** Vestibular schwannomas are slow growing, benign tumors. There are three possible management options: surgery, radiation treatment or active surveillance. The aim of this study was to assess the general outcome and risk of tumor recurrence.

**Materials and methods:** The study included 220 consecutive patients (134 women, 86 men; the age ranged from 18 to 74) operated with the retrosigmoid transmeatal approach. The largest extrameatal diameter of the tumor ranged from 8 to 72 mm (mean 30 mm). According to the Samii grading scale, the tumors were classified as follows: T2–12 (6%), T3–51 (23%) and T4–157 (71%). Gross total resection was performed in 217 patients and neartotal in 3.

**Results:** Two hundred and eighteen (99.1%) patients were discharged home in a satisfactory neurological condition (GR or MD in GOS). One (0.5%) patient died due to brainstem infarction. One (0.5%) patient had unchanged severe cerebellar syndrome in comparison to the preoperative period (SD in GOS). In long-term follow-up, one patient went blind within a few months after surgery. Including the results of further neurosurgical procedures for CSF leak, shunt implantation, tumor regrowth and facial nerve reanimation, 98.6% of the patients were fully independent but with different neurological deficits. Tumor recurrence was observed in 5 (2.3%) patients during the follow-up period (mean term: 6.4 years). The average time to recurrence diagnosis was 8.8 years. All those patients were operated on again without any adjuvant therapy and there was no further re-growth at mean follow-up of 5.2 years.

**Conclusions:** Complete removal of VS is usually curative and poses very low risks of severe disability (if audio-facial sequels are not included), mortality and long-term recurrence. For recurrent tumors, carefully tailored revision surgery without irradiation offers a high efficacy with low risk of complications.

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## 1. Introduction

Almost 100 years has passed since the publication of a monograph by Harvey Cushing [1] and vestibular schwannoma (VS) is still a subject of interest in many medical specialties. Currently, the number of publications on this topic exceeds 250 per annum. Otolaryngology, neurosurgery, radiosurgery and basic sciences collaborate and compete with each other leading to a sharp increase of our knowledge about the natural course of the disease and has improved the treatment outcomes in recent decades.

Vestibular schwannomas are benign tumors, which are detected more frequently between the fourth and sixth decade of life. Currently, there are three possible management options: surgery, radiation treatment or active surveillance. A trend toward less radical VS surgery is seen again now, which can be justified by the benign and slow growing nature of the tumor, as well as by the reduction of the risk of facial (CNVII) and auditory nerve dysfunction [2,3]. In these cohorts, nerve function preservation is exquisite, but only extended follow-up of 10–20 years can confirm the rationale of this approach. A literature review on the effectiveness of incomplete resections showed that the risk of VS recurrence is proportional to the size of the tumor remnant [2]. Similarly, observation and radiosurgery offer high chances of excellent function preservation during the first years after diagnosis, but do not eradicate the tumor and imply a number of potential problems in the future.

On the other hand, in centers of excellence the results of total VS removal via the retrosigmoid approach (RSA) are nowadays comparable. Excellent functional outcome, including hearing preservation with near-zero recurrence and mortality rates can be achieved after complete excision of small VS [4–6]. For medium-to-giant VS, the RSA offers also good facial nerve function (House–Brackmann (HB) grades I–II), low morbidity and mortality rates [5–9]. A recent meta-analysis on large (>3.0 cm) VS surgery via the RSA demonstrated that good postoperative facial nerve function and mortality rates were 63% and 0.9%, respectively, while the gross total resection (GTR) was achieved in 79% [9].

The principles of vestibular schwannoma treatment in our Department are based on the ideas put forward by Samii [10]. This means that the main goal of the treatment is to assure a permanent cure by complete tumor resection, as most patients are middle-aged and still have a long life expectancy. At the same time, however, attempts are made to preserve facial and auditory nerve function with the use of continuous electrophysiological monitoring.

The average size of diagnosed VS in developed countries decreased from 30 mm to 10 mm during the last 30 years [11]. Thanks to earlier detection and advances in surgery, including methods of intraoperative neurophysiological monitoring, the operative safety of VS surgery greatly improved. Function preservation, especially of the facial and auditory nerves, are currently in the spotlight. The overall treatment results or post-operative complications are currently published more rarely than previously. However, it should be kept in mind that VS surgery takes place in the immediate vicinity of vital structures and the procedure “*ex definitione*” is fraught with the

risk of serious complications. Therefore, the objectives of this study were: (1) analysis of the overall early and late results after vestibular schwannoma surgery, (2) assessment of the tumor recurrence rate.

## 2. Materials and methods

This series of papers is devoted to the results of surgery for sporadic vestibular schwannoma over a period of 22 years. Perioperative management, surgical equipment and technique were changing during the analyzed period. On the one hand, this makes it difficult to analyze the general outcome, but, on the other hand, it creates an opportunity to depict the gradual progress in the treatment results. Consecutive papers in this series of papers will present different aspects of vestibular schwannoma treatment results, complications, and preservation of facial and auditory nerve function.

### 2.1. Patients

This retrospective analysis includes 220 consecutive patients operated on for sporadic VS in the years from 1990 to 2011. Patients with neurofibromatosis type II were not enrolled in the study. Two hundred and thirteen patients were not treated previously for VS and 7 patients were previously ineffectively treated in other centers. This subgroup includes 5 patients after subtotal resections, 1 patient after stereotactic radiosurgery and 1 patient after prior surgery and radiosurgery. There were 134 women and 86 men, ranging in age from 18 to 74 years old (mean – 47 y.o., median – 48 y.o.). Preoperative testing included MR imaging with contrast medium, bone window CT of petrous pyramids, Auditory Brainstem Response, Pure Tone Average, Word Recognition Score, and Electromyography of the facial nerve.

### 2.2. Symptoms

The symptomatology of VS in the study group is shown in Table 1. Unilateral or asymmetric hearing loss was found in 97.8% of patients at admission.

One patient with tumor progression after two prior subtotal resections in other centers was admitted in a fairly serious condition. He was unable to walk and presented with psychomotor slowing and severe cerebellar syndrome. Another patient with tumor progression, referred from another center after incomplete resection, presented with sustained right limbs paresis. The remaining 218 patients were admitted in good general condition, without limb weaknesses. The symptomatic period ranged from 0 to 30 years (mean – 3.6 years, median – 2 years).

### 2.3. Tumors

The largest extrameatal diameter of the tumor ranged from 8 to 72 mm (mean – 30.1 mm; median – 30 mm). According to various definitions of “large VS”, the tumor diameter exceeded 20 mm in 174 (79.1%) tumors, 25 mm in 136 (61.8%) and 30 mm in 99 (45%). The average size of the first 110 tumors was 32.1 mm, while the average size of the last 110 tumors was

**Table 1 – Signs and symptoms in the analyzed group.**

Symptoms	Number of patients	%
Tinnitus	120	54.5
Hypoacusis	155	70.5
Deafness	60	27.3
Vertigo	46	20.9
Cerebellar symptoms	57	25.9
Trigeminal nerve symptoms	65	29.5
	Including:	
	- Neuralgia – 6	
	- Neuralgia and hypoesthesia – 6	
	- Hypoesthesia – 32	
	- Paresthesia – 14	
	- Paresthesia and hypoesthesia – 3	
	- Hyperaesthesia – 2	
	- Lack of conjunctival and corneal reflexes only – 2	
CNVII weakness	40	18.2
Headaches	30	13.6
Hydrocephalus	10	4.5
	Including:	
	- Acute – 6	
	- Normotensive – 4	
Lower cranial nerves paresis	8	3.6
Optic disk swelling	6	2.7
	- With decreased vision – 4	
	- Without visual disturbances – 2	
Other	5	2.2
Asymptomatic tumor	1	0.5

**Table 2 – Tumor stage according to Samii grading scale [12].**

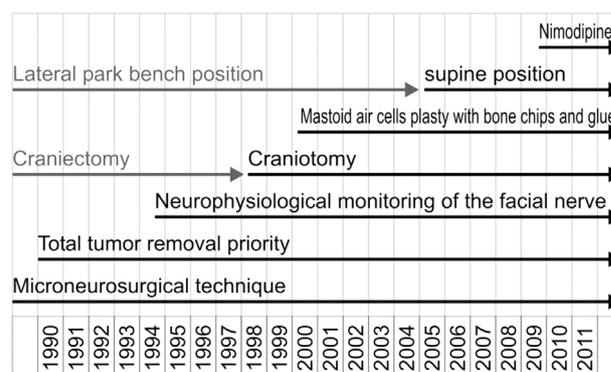
Tumor stage	Number	%
T1 (Tumor is purely intrameatal)	0	0.0
T2 (Tumor is intra- and extra-meatal)	12	5.5
T3A (Tumor is filling the cerebellopontine angle cistern)	23	10.5
T3B (Tumor is reaching the brain stem)	28	12.7
T4A (Tumor is compressing the brain stem)	45	20.5
T4B (Tumor is severely dislocating the brain stem and the 4th ventricle)	112	50.9

28.1 mm. The tumor volume ranged from 0.2 cm<sup>3</sup> to 113 cm<sup>3</sup> (mean 14.6 cm<sup>3</sup>, median 9.4 cm<sup>3</sup>). According to the Samii grading scale [12], the tumors were classified as follows: T1–0, T2–12 (5.5%), T3–51 (23.2%) and T4–157 (71.4%, Table 2). The structure of the tumor was solid in 185 (84.1%) cases, and cystic in 35 (15.9%). Internal auditory canal (IAC) enlargement was observed in 185 (84.1%) cases. Histological examination revealed Antoni type A in 67 (30.4%), Antoni type B in 29 (13.2%) and mixed type, Antoni A + B in 124 (56.4%) patients [13].

#### 2.4. Surgery

Removal of the tumor was performed via the retrosigmoid approach (RSA) with the opening of the IAC in 217 patients. In 3 patients, a translabyrinthine approach (TLA) was used. The majority of patients (89%) were operated on by a senior neurosurgeon (AM). Since a priority was to cure the patient from the neoplasm, the surgery sought to complete tumor removal macroscopically. In 217 (98.6%) cases, the tumor was completely removed. In 3 cases, small fragments of tumor

strongly attached to the facial nerve (2) or the brain stem (1) were left (near-total resection, NTR). The surgical technique evolved slightly during the analyzed period (Fig. 1). During the first 94 procedures, the lateral park bench position was used. Since 2005, patients were positioned supine with the head rotated toward the healthy side (123 procedures). Sitting or semi-sitting position was not used, because of neurosurgeon preferences and to avoid the risks associated with this position (mainly venous air embolism). Craniectomy was performed during the first 30 procedures. From 1998 to the present, craniotomy (the last 190 procedures) with small bone flap covering the lateral part of occipital bone was used. The base of mastoid process is then removed with a high speed drill until the border of sigmoid sinus is visible. The approach included wide opening the internal auditory canal with a high speed drill and rongeurs. Over the whole analyzed period, the microsurgical technique was employed and the priorities of

**Fig. 1 – Evolution of surgical technique in the analyzed period.**

the procedure were total tumor removal including intrameatal part while trying to preserve auditory and facial nerves. At the end of surgery, the dura was closed watertight and the bone flap was restored (the last 190 procedures). Open mastoid air cells were protected with wax in all patients. In addition, since 2000, the clearance after partial mastoid process removal was filled by autologous bone chips with fibrin glue. Intraoperative neurophysiological monitoring of the facial nerve was routinely used since 1994. Since August 2009 (the last 50 procedures), vasoactive perioperative prophylaxis was routinely employed for blood supply protection of the facial and cochlear nerves. For this purpose, nimodipine was administered orally at a dose of 60 mg every 6 h from 3 days before surgery to 7 days after surgery. In justified cases, i.e., if deep CNVII weakness (HB grades IV-VI) occurred despite anatomical continuity preservation, intravenous infusion of nimodipine was started at a dose of 2 mg/h (=10 ml/h) after surgery.

### 2.5. Outcome evaluation

The treatment results were assessed twice: at discharge and at a distant period, at least 6 months after surgery. The results were appraised in three categories: (1) general early outcome according to the Glasgow Outcome Scale (GOS) [14], (2) general long-term results according to the Karnofsky Performance Status Scale (KPS) [15], (3) risk of tumor recurrence.

Postoperative unilateral deafness and CNVII weakness do not constitute a substantial limitation in normal activity according to the GOS scale and it does not worsen the outcome. For this reason, the auditory and facial nerve functions were evaluated separately. Cerebellar symptoms and lower cranial nerves palsy present at discharge were classified as a moderate disability in GOS.

## 3. Results

### 3.1. Early outcomes

In the analyzed series, 218 (99.1%) patients left hospital in satisfactory condition (GR or MD in the GOS scale). These patients were independent without limb weaknesses (Table 3). Patients in the GR group had unilateral hearing loss and/or facial nerve weakness and/or trigeminal nerve symptoms. Patients in the MD group additionally had cerebellar symptoms and/or swallowing problems. One patient had a prior minor hemiparesis and one had impaired vision that worsened after surgery.

One patient was moved to the neurological ward for further rehabilitation. The patient was already bedridden, dependent, with severe cerebellar syndrome and with weakness of the cranial nerves from VII to XII. He was operated on for massive tumor progression (grade T4B) after two non-radical surgeries at another center. The postoperative course in our department was uneventful, and the patient's condition improved slightly (withdrawing cerebellar syndrome). At discharge, he could walk with assistance (SD in the GOS scale).

One patient died shortly after surgery as a result of brain stem stroke. Mortality rate in the series was 0.5%.

**Table 3 – General early and late outcome.**

Glasgow Outcome Scale [4]		
	Number	%
GR	187	85.0
MD	31	14.1
SD	1	0.5
VS	0	0.0
D	1	0.5
Karnofsky Performance Scale [5]		
	Number	%
100	0	0.0
90	184	83.6
80	29	13.2
70	4	1.8
60	1	0.5
0	1	0.5
N/A	1	0.5

Abbreviations: GR – good recovery; MD – moderate disability; SD – severe disability; VS – vegetative state, D – Death, N/A – not available.

### 3.2. Long-term results

The follow-up period ranged from ½ to 18 years (mean – 6.4 years, median – 6.0 years). Out of 220 patients, one patient died in the early postoperative period and one lost to follow-up.

In long-term follow-up, including the results of further neurosurgical procedures for CSF leak, shunt implantation, tumor regrowth and facial nerve reanimation, all but one patient (Karnofsky Performance Scale 70–100: 98.6%) were fully independent but with different neurological deficits (Table 3). One patient went blind. The blindness appeared gradually after the patient was discharged home. Four patients had persistent severe cerebellar symptoms (KPS 70), 29 did not achieve satisfactory facial nerve function or had permanent LCN palsy (KPS 80). One hundred and eighty-four patients were qualified as KPS 90, had unilateral deafness or hearing loss and a satisfactory function of the facial nerve (HB grades I-III), including results of facial nerve anastomosis.

### 3.3. Tumor recurrence

Regrowth of the tumor was observed in 5 patients (Table 4). There were 2 women and 3 men, ranging in age from 18 to 49 years old (mean – 38) in this group. In all 5 patients, the tumor was completely removed macroscopically during the initial procedure. The risk of recurrence in the analyzed series was 2.3% during mean follow-up of 6.4 years. The average time from surgery to recurrence diagnosis was 8.8 years.

All of these patients were operated on again. In four, the tumor was removed using a different surgical approach than initially, i.e., TLA in three and MFA in one. One patient was operated on via RSA again. The recurrent tumor was removed totally (GTR) in all 5 patients.

In three patients, the recurrent tumor was located mainly in IAC with a minor extension to the posterior fossa. Therefore, TLA was applied during the second surgery with the aid of an ENT team. The size of these tumors was 19 mm, 15 mm and

**Table 4 – Patients with tumor recurrence.**

Patient	Tumor size and grade before treatment	Initial surgery (approach, extent of resection)	Time to tumor recurrence	Treatment for tumor recurrence	CNVII function in follow-up (HB)
1	35 mm, T4B	RSA, GTR	9 years	TLA, GTR	Grade III
2	50 mm, T4B	RSA, GTR (+end-to-end CNVII anastomosis)	6 years	TLA, GTR	Grade III
3	42 mm, T4B	RSA, GTR	4 years	TLA, GTR	Grade II
4	60 mm, T4B	RSA, GTR (+HFA)	10 years	MFA, GTR	Grade III
5	25 mm, T4A	RSA, GTR (+HFA)	15 years	RSA, GTR	Grade III

Abbreviations: T – tumor stage according to Samii scale; CNVII – facial nerve; HFA – hypoglossal to facial nerve anastomosis; GTR – gross total resection; RSA – retrosigmoid approach; TLA – translabyrinthine approach; MFA – middle fossa approach; HB – House–Brackmann facial nerve function grading scale.

15 mm. In one of these patients, CNVII was not preserved during the first surgery but “end-to-end” anastomosis was performed during the same procedure. At the time of the second operation, the final proximal CNVII stimulation (after the tumor removal) showed response from the facial muscles. The anatomical continuity of the facial nerve was preserved also in two remaining patients. The postoperative course was complicated with transient otorrhea in one patient. The CSF leak was stopped effectively with a sponge dressing of the external auditory canal, without additional invasive procedures.

In one patient, the tumor re-grew from the IAC into the petrous apex, reached the petrous portion of the internal carotid artery and destroyed the anterior surface of petrous bone with extradural extension into the middle cranial fossa. The size of the tumor was 33 mm and showed no significant progression into posterior cranial fossa. During the second operation, MFA was used and total tumor resection was performed. Because HFA was previously performed with satisfactory results, there was no need to look after the CNVII during revision surgery. The postoperative course was uneventful.

In one case, the recurrent tumor was removed by RSA, because it originated not from the internal auditory canal but was located exclusively in the cerebellopontine angle. Initially, tumor re-growth was observed and it increased from 9 mm to 14 mm in one year. The facial nerve was not preserved during the first surgery and HFA was performed shortly thereafter. During the second surgery, the tumor was totally removed without further complications.

In long-term follow-up, all 5 patients maintained their quality of life and satisfactory CNVII function, which they presented before the revision surgery. One patient had grade II HB and 4 had grade III HB, including 3 patients after previously performed HFA. Follow-up after second surgery ranged from 3 to 7 years (average 5.2 years). No further recurrence was noted.

Near total resection was performed in 3 of 220 patients. In one case, a small tumor layer was left on the brainstem surface, in one on the CNVII trunk in the cerebellopontine angle and in one on the CNVII in *porus acusticus internus*. Follow-up MRI, performed 2 years after surgery, showed no recurrence or identifiable tumor remnant in two patients. In the third patient, follow-up data were not available.

#### 4. Discussion

The early treatment outcome of vestibular schwannoma in our series can be considered to be satisfactory as the mortality rate was only 0.5%. The postoperative condition of other patients, admitted in good condition to the hospital, did not deteriorate below MD level in GOS (99.5%). From the perspective of the same Department, the mortality rate was substantially reduced from 50.0% to 0.5% from the 60s of the twentieth century to the present [16]. This is thanks to a number of factors. Early detection of tumors and, therefore, treatment of smaller and less symptomatic tumors are both essential. The use of modern equipment during surgery, including operating microscopes, microtools, ultrasonic aspirators and neurophysiological monitoring, improves the precision and safety of the treatment. Of considerable importance, in addition to the neurosurgeon's learning curve, is the increasing experience of the whole team involved in the treatment of VS. In other words, current success is the result of the combined progress of neuroscience, anesthesiology, and neurorehabilitation.

Perioperative mortality of vestibular schwannoma surgery is currently estimated in the literature at about 0.3–1.1% [12,17–20]. A US population study revealed the factors that reduce the risk of death after surgery. They were: younger age, Caucasian race, having private insurance, and operation performed by a surgeon who performs this kind of surgery more than twice a year [18]. Yamakami et al., in a VS treatment outcome meta-analysis estimated the risk of severe disability and death after surgery at 2.9% and 0.63%, respectively [21].

In our series, at mean follow-up of 6.4 years, including the results of any follow-up treatments (for HCP, CSF leak, tumor re-growth, etc.), the general condition of 98.6% of patients was satisfactory. These patients were independent, with no need for assistance (KPS: 70–100).

In 84% of patients, the only deficits were unilateral hearing loss and/or minor CNVII paresis (HB grades II–III). On the one hand, such a presentation of the results indicates the very high efficacy and safety of microsurgery. On the other hand, the Karnofsky scale is not a sensitive indicator of the quality of life after VS treatment. Currently, the function of facial and auditory nerves are in the spotlight, which will be discussed separately.

The risk of VS re-growth in the analyzed series was 2.3% during the mean follow-up of 6.4 years. The risk of tumor

recurrence after surgery in meta-analysis from recent years is estimated to be around 0.7–6.2% [21,22]. Ahmad et al. showed, on a series of 2400 surgically treated VS, that the risk of tumor recurrence is 0.7%, 1.8% and 0.05%, respectively for RSA, MFA and TLA [22]. A literature review by Ansari et al. indicates that the risk of tumor recurrence is higher after RSA than MFA (6.2% vs. 1.1%;  $p = 0.045$ ), possibly because MFA is useful only for smaller tumors and because of better insight into the internal auditory canal bottom [23].

In case of small recurrence detection, active observation may be applied initially for tumor growth rate tracking. Some prefer radiosurgical treatment of tumor recurrence [24]. Another optional strategy is a subsequent non-radical VS excision while trying to preserve CNVII function as long as possible. However, in the series of Freeman et al., revision surgery is associated with a higher risk of postoperative complications (23%), subsequent re-growth and deepening of CNVII weakness (HB grades IV–VI: 54%), as compared to the initial surgery [25].

Considering the treatment modality for VS recurrence, we should take into account the quality of life (QOL) before and after any further treatment. A patient's awareness of a growing tumor despite prior treatment may play a major role. Recent research by Carlson et al. suggests that VS diagnosis itself has a greater impact on health related QOL than any treatment modality [26]. This may mean that surgical eradication of the tumor may positively influence a patient's awareness of freedom from the disease. This thesis seems to be confirmed in papers on QOL in observed, irradiated and surgical groups. While QOL remains stable during observation and after radiosurgery, it significantly improves in surgical groups after treatment, especially in the composite mental dimension [27,28]. Therefore, our general strategy for recurrent VS is radical surgery using tailored approaches together with modern FN reconstruction techniques, if needed.

In our series, revision surgery is an effective and safe treatment option. The recurrent tumor was completely removed in all 5 patients, and no subsequent re-growth was noted in further follow-up of 5.2 years on average. The only complication was CSF leak, which was eliminated with non-invasive methods in 1 patient. The facial nerve function was maintained at the same level as before revision surgery in all 5 patients. However, the assessment of safety in this regard is hampered by previously performed extratemporal CNVII anastomosis in two patients.

A different approach than the first one was applied in four patients, because of the location of tumor recurrence in the internal auditory canal or tumor extension into the petrous apex. The important advantage of using a different approach is also to avoid dissection across the postoperative scar, which is strongly tied with cranial nerves as well as cerebellum and brain stem surface [25].

A literature review on the effectiveness of incomplete resections showed that the risk of VS recurrence is proportional to the size of the tumor remnant [2]. This confirms the legitimacy of complete tumor removal. On the other hand, in our study, all VS recurrences occurred after macroscopically complete removal. The possible cause of recurrence could be an invisible tumor remnant in the IAC bottom. The risk of

missing this part of the tumor can be minimized by endoscopic control of the IAC bottom at the end of procedure [29].

Bennett et al. postulate that, in patients after complete resection of sporadic VS, there is no need for further follow-up MRI, if an examination a year after the procedure shows no pathological enhancement [30]. In the cited series, none of the 10 linear enhancements progressed over time but two tumor recurrences progressed out of three nodular enhancements. The linear contrast enhancement of the dura around the IAC is usually transient and demonstrates an evolution of postoperative scar. However, nodular enhancement suggests a tumor remnant or recurrence [31].

The interval between initial surgery and recurrence diagnosis was 8.8 years on average in our series. This fact indicates the need for long-term surveillance even after GTR [22]. Our recommendation is to perform the first follow-up MRI half a year after surgery for tumor remnant exclusion in the IAC bottom. In the light of the presented results, it is reasonable to perform follow-up imaging even 5 and 10 years after surgery. This is also supported by two other arguments. Firstly, most schwannomas are characterized by very slow growth. Secondly, effectiveness should be verified in the same way for radiotherapy, observation and surgery, therefore the follow-up schedule should be comparable for all three management modalities [24].

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## 5. Conclusions

Complete removal of VS via the retrosigmoid approach is usually curative and poses very low risks of severe disability (if audio-facial sequelae are not included), mortality and long-term recurrence. Thus, it should be considered as a first-line strategy option especially for larger tumors. For recurrent tumors, carefully tailored revision surgery without irradiation offers a high efficacy with low risk of complications.

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## Conflict of interest

None declared.

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All authors report no any actual or potential conflict of interest including any financial, personal or other relationships with other people or organizations within three years of beginning the submitted work that could inappropriately influence, or be perceived to influence, their work.

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## Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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