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OTOLOGY: VESTIBULAR SCHWANNOMAS (RA FRIEDMAN AND M SCHWARTZ, SECTION EDITORS)

Treatment of Small Vestibular Schwannomas

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Abstract

Purpose of Review Vestibular schwannomas (VS) are benign neoplasms that arise from the Schwann cells enveloping the vestibular division of the eighth cranial nerve. These tumors typically exhibit indolent growth and commonly cause audiovestibular dysfunction. If allowed to grow large enough, VS can cause brainstem compression and become fatal. Treatment options include observation with serial imaging, radiotherapy, and microsurgical resection. This review will summarize the literature regarding treatment outcomes for patients with small VS.

Recent Findings Advances in diagnostic imaging have allowed for earlier and more frequent detection of small VS. Management of small VS remains controversial and is influenced by physician preference. Recent studies have summarized outcomes in small VS in conservative, radiosurgery, and microsurgery cohorts. Additional data on quality of life, volumetry, and morphometry allow for more informed decision-making in the treatment of small VS.

Summary In this article, we review contemporary literature describing outcomes of each treatment modality, with emphasis on tumor control, facial nerve function, hearing preservation, and quality of life.

Keywords Vestibular schwannoma · Acoustic neuroma · Facial nerve outcomes · Hearing preservation · Radiosurgery · Observation · Quality of life

Introduction

Vestibular schwannomas (VS) are benign neoplasms arising from the Schwann cells of the vestibular division of the cochleovestibular nerve. The most common tumor of the internal auditory canal and cerebellopontine angle, VS is estimated to occur with an incidence of 1.1–4.2 per 100,000 person-years [1–5]. On average, VS tumors exhibit growth (in maximal tumor diameter) at a rate of 1 mm/year [6]. Over the past 15–20 years, tumor size at the time of diagnosis has decreased [1]; according to a recent analysis of the Surveillance, Epidemiology, and End Results (SEER) database, between 2004 and 2011, the percentage of tumors measuring 0–1 cm in maximal diameter increased from 12.3 to 20.8% [1], mirroring a trend toward increasing use of magnetic resonance imaging (MRI) and a concurrent rise in diagnosis of incidental VS [6].

In spite of robust literature analyzing VS outcomes, the management of small tumors remains controversial [7–11]. Numerous factors may influence treatment recommendations, including patient age, general health, hearing quality, tumor size, location (intrameatal vs. extrameatal), and patient preference. Yet, many high-volume VS centers asymmetrically tend toward either radiosurgery or microsurgery, suggesting that institutional bias may be the strongest factor predicating management decisions.

In the present discussion, we review contemporary literature describing outcomes of treatment of small VS, with

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particular attention to tumor control, facial nerve and hearing preservation, and quality of life. Definitions of small VS are not uniform in the literature. In general, most authors consider small VS to include intracanalicular tumors and tumors with limited extension into the cerebellopontine angle (CPA). Throughout this review, care is taken to describe size criteria when discussing the relevant literature.

Observation for Small VS

There is little controversy regarding the value of intervention for large VS causing symptomatic brainstem compression; if allowed to progress, brainstem compression can ultimately become fatal, and surgical resection is indicated as a life-preserving measure. By contrast, the management of small VS, particularly in patients with minimal symptomatology, is contentious. There has been a recent trend toward conservatism in the management of small tumors [1]. Presumably, this shift reflects mounting evidence showing that a significant proportion of small VS do not grow significantly over time. There is also continuing debate regarding the role of hearing preservation surgery for small and/or non-growing VS. These issues and the relevant contemporary literature will be discussed in the ensuing sections.

Observation: Tumor Growth

To date, the most robust epidemiologic data on the natural history of VS have originated in Denmark, where a prospective national database of VS patients has been maintained since 1976 [4, 12–16]. Literature on long-term outcomes of observation presented here draws heavily on these studies. In a recent paper examining long-term tumor growth and hearing in a Danish population of patients with intracanalicular VS, the investigators found that, at a mean length of follow-up of 9.5 years, tumor growth occurred in 37% (n = 58) of patients, shrinkage occurred in 3% (n = 5), and stable tumor size occurred in 60% (n = 93). (Tumor growth was defined as having ≥ 2-mm growth in any tumor diameter in 3 planes [coronal, axial along the internal auditory canal, and perpendicular to the axis of the internal auditory canal]). Twenty-three percent (n = 36) of patients developed growth to extrameatal extension (i.e., progression of growth from the internal auditory canal into the cerebellopontine angle) during the study period, and 15% of patients (n = 23) failed conservative treatment, with 22 patients being treated surgically and 1 patient treated with radiotherapy [17].

Whereas in the aforementioned study only 23% of intracanalicular tumors developed extrameatal extension over nearly 10 years of follow-up, a previous report on the same cohort showed that growth to extrameatal extension occurred in 19% of patients after 4.6 years of observation [18], suggesting that the vast majority of intracanalicular tumors that grow will do so within the first 5 years after diagnosis. However, a separate study of 361 VS patients showed that, of 68 tumors confined to the internal auditory canal at the time of diagnosis, 16.2% (n = 11) demonstrated delayed growth, defined as ≥ 2-mm enlargement in linear diameter first detected at least 5 years after initial MRI. Interestingly, for tumors within the internal auditory canal, those that demonstrated early growth had a higher median growth rate than those with delayed growth (1.40 vs. 0.45 mm/year, $p < 0.001$) [19].

There is some evidence that delayed tumor growth may occur less frequently in elderly VS patients compared to younger patients. In a retrospective study of 112 patients ≥ 70 years of age and mean follow-up of 82 months (range 60–144 months), 29% of VS displayed growth, but no tumors grew after 42 months from the time of diagnosis. The authors therefore argued that, in these patients, initial MRI at 6 months after diagnosis, followed by annual MRI for 3 years, is warranted to monitor tumor growth; thereafter, for patients whose tumors remain stable, consideration could be given to discontinuing serial imaging [20].

Importantly, many large studies of tumor growth in untreated VS have used linear dimensions, not volumetric changes, to define tumor enlargement. This methodology has been criticized because serial linear measures of tumor diameter can underestimate volumetric growth [21]. In a single-center retrospective analysis of 3-dimensional volumetric growth in patients with untreated VS, Lees et al. found that, in 232 patients with intracanalicular tumors, 69.8% (n = 162) demonstrated volumetric growth at a median follow-up of 1.1 years, whereas only 45.3% (n = 105) demonstrated linear growth [22•]. Increasingly, many authors argue that serial volumetric measurement of VS is superior to traditional linear measurement in describing tumor growth over time. Contemporary studies have shown considerable variation in choice of measurement technique [23–26]. Future investigation is warranted to establish a consensus definition of volumetric growth and a consistent methodology for measuring VS tumor volume.

Observation: Hearing Preservation

Over the past decade, numerous series have advanced our understanding of the natural history of hearing in untreated VS. Hearing results are commonly reported according to the 1995 American Academy of Otolaryngology – Head & Neck Surgery (AAO) criteria [27] or the Gardner-Robertson scale [28], both of which classify hearing quality according to pure tone average (PTA) and word recognition score (WRS). Some studies report hearing outcomes according to WRS class as defined by Meyer et al. [29]. While there is controversy regarding what constitutes serviceable (or preserved) hearing, generally speaking, favorable hearing is commonly defined by a combination of PTA cutoff at 50 dB and WRS cutoff at

50%, corresponding to AAO class A/B hearing, Gardner-Robertson I/II, and WRS class I/II. In 2018, Hunter et al. performed a retrospective evaluation of long-term hearing of 466 patients with untreated VS and serviceable hearing (PTA ≤ 50 dB and WRS ≥ 50%) at presentation. Kaplan-Meier rates of maintaining serviceable hearing at 5 and 10 years after diagnosis were 66% and 44%, respectively [30]. The authors did not report hearing outcomes according to tumor size but analyzed tumor diameter as a risk factor for progression to nonserviceable hearing. After accounting for demographic and clinical variables, regression analysis showed tumor size did not predict rapidity of progression to nonserviceable hearing. These findings agree with those of a recent systematic review of the Congress of Neurological Surgeons, in which tumor size, age, and sex did not predict development of nonserviceable hearing during observation [31]. By contrast, a literature review by Sughrue et al. found that patients with larger tumors were more likely to maintain hearing during observation [32]. It is possible that differences in outcomes are attributable to differences in statistical modeling, as the publication by Sughrue et al. failed to control for follow-up time.

Although multiple studies have evaluated hearing preservation in observed small or intracanalicular VS [29, 33, 34], very few have reported long-term (≥ 10-year) hearing outcomes. In addition to examining tumor growth, the aforementioned report by Kirchmann et al. evaluated long-term hearing results in a population of 156 patients with intracanalicular VS. Seventy-three patients had AAO class A/B hearing (PTA < 50 dB and WRS > 50%) at the time of diagnosis. Among them, only 34% (n = 25) had serviceable hearing (AAO class A/B) at 10-year follow-up. Of 99 patients who had a word recognition score (WRS) > 50% at the time of diagnosis, 58% (n = 57) maintained serviceable hearing (i.e., > 50% WRS) at 10-year follow-up [17]. Patients with normal speech discrimination (100% WRS) also fared significantly better than patients who presented with mild loss of speech discrimination (WRS 70–98%). The mean rate of WRS loss was 1.86%/year for patients with normal WRS at diagnosis and 6.19%/year for patients who presented with mild loss of speech discrimination [17], and rate of WRS loss appeared to be independent of tumor size. In a larger study of 491 Danish VS patients with WRS 70% at the time of diagnosis, long-term hearing preservation (after 10 years of observation) was significantly higher among those with 100% speech discrimination at the time of diagnosis compared to those with only a small loss of speech discrimination at the time of diagnosis (69% vs. 38%, respectively) [14].

The relationship between tumor growth and progression to nonserviceable hearing has been investigated, but findings are inconsistent. In a retrospective study of 213 patients with VS and serviceable hearing, Patel et al. found no significant association between volumetric tumor growth at progression to nonserviceable hearing [35]. Similarly, a prospective longitudinal study of 72 conservatively managed VS found that deterioration of pure tone thresholds and speech discrimination occurred independently of tumor growth rates [36], and several other studies have reported similar findings [37–39]. By contrast, a small retrospective study of 31 observed VS showed that tumor growth rate correlated with rate of decline in hearing (decline in PTA in dB/year) [40].

For the population of VS patients with small tumors, the relationship of tumor growth and hearing loss is similarly unclear. In perhaps the most illuminating study to date, Patel et al. found that larger tumor volume at diagnosis was associated with worse hearing by PTA ($p < 0.001$) and decreased speech discrimination ($p = 0.014$). However, tumor volume at diagnosis was not associated with progression to nonserviceable hearing after controlling for PTA and WRS [35]. Similarly, Sakamoto et al. found no correlation between rapidity of hearing decline and tumor size [40]. By contrast, in 2016, van Linge published a retrospective series in which tumor growth was associated with more accelerated hearing loss in intracanalicular tumors compared to tumors extending to the CPA [41]. In an investigation of 49 patients with non-growing VS, however, Graamans et al. found no significant differences in rapidity of hearing loss between patients with small (3–10 mm) or medium (11–20 mm) tumors. There was also no significant difference in rates of hearing loss between intracanalicular and extrameatal tumors [38]. Among these series, there are methodological differences relating to measurement of tumor size and growth, and studies are generally small. Larger, prospective series are warranted to illuminate the relationship between tumor size, growth, and progression of hearing loss in VS patients.

Radiosurgery for Small VS

Radiation has proven a safe option for achieving tumor control in small VS, with high rates of tumor control within 5–10 years of treatment. While nonsurgical, radiation is not without risk. Contrary to resection, radiation cannot eliminate the presence of the tumor; rather, radiotherapeutic success is generally defined by cessation of tumor growth. Continued VS growth is a risk of radiotherapy, as are dizziness, hearing loss, trigeminal neuropathy, and hydrocephalus. Table 1 summarizes a large collection of reported outcomes related to radiotherapy for VS. Benefits of radiation therapy for treatment of small tumors include its low risk of facial nerve morbidity, which may be as low as < 1% in patients with tumor volume ≤ 1.5 cm^3 [67], as well as low rates of other cranial nerve deficits [68] and high rates of tumor control with minimal downtime. Disadvantages include the need for long-term serial imaging post-treatment, as well as the risk of regrowth, and the unavailability of long-term outcomes beyond 10 years after treatment.

Table 1 Microsurgery outcomes in treatment of small VS

Reference	Approach	*n*	Tumor size	Follow-up	Degree of resection	Tumor control	Preop serviceable hearing	Serviceable hearing preservation rate	Postoperative AAO-HNS classification		Facial nerve function at last follow-up		Complications		
									A	B	HBI	HB II	CSF leak	Infection	Other
Arts et al. (2006) [42]	MCF	73	Range: 0.3–1.8c-m	Mean: 4 months	–	–	62 (85%)	45 (72%)	21 (33%)	24 (39%)	61 (85%)	8 (11%)	–	1 (1%)	4 (5%) aseptic meningitis; 1 (1%) transient expressive aphasia
Brackmann et al. (2000) [43]	MCF	333	Mean: 1.12cm	Mean: 14 days	–	–	300 (90%)	188 (62%)	108 (36%)	80 (26%)	–	–	–	–	–
Ginzkey et al. (2013) [44]	MCF	89	Mean: 2.154cm^3	–	–	–	65 (82%)	48 (74%)	25 (39%)	23 (35%)	82 (89%)	3 (3%)	–	–	–
Gjurić et al. (2001) [45]	MCF	735	–	Mean: 5 years	97%GTR	99.7% at 5 years	423 (58%)	188 (26%; 52% for IAC tumors)	114 (23%)	74 (15%)	463 (63%, 78% for tumors < 1 cm)	129 (18%; 9% for IAC tumors)	16 (2.2%)	9 (1.2%)	3 (0.4%) mortality; 2 (0.3%) CPA hematoma; 2 (0.3%) temporal lobe contusion; 1 (0.1%) seizures; 45 (5.7%) transient neurologic deficits
Goddard et al. (2010) [46]	MCF	101	Range: 0.52–1.1-2cm	Mean: 10.6 weeks	–	–	92 (91%)	56 (44%)	27 (26%)	29 (29%)	–	–	–	–	–
Hillman et al. (2010) [47]	MCF	88	Max: 0.8cm	Mean: 3 months	–	–	59 (67%)	35 (59%)	32 (54%)	3 (5%)	63 (72%)	14 (16%)	–	–	–
Hilton et al. (2011) [48]	MCF	78	Mean: 1.2cm	Mean: 4 years	–	93.60%	78 (100%)	51 (65%)	22 (28%)	29 (37%)	–	–	–	–	–
Meyer et al. (2006) [29]	MCF	127	Range: 0.2–1.4c-m	> 12 months	–	–	124 (77%)	61 (57%)	45 (36%)	16 (21%)	140 (86%)	17 (10%)	9 (5.6%)	–	2 (1.2%) aseptic meningitis; 2 (1.2%) aphasia; 2 (1.2%) seizures
Raheja et al. (2016) [49]	MCF	60	Mean: 0.72cm	Mean: 15.1 months	–	–	49 (81%)	38 (77%)	14 (30%)	23 (47%)	50 (76%)	9 (14%)	0	3 (3.8%)	0
Goel et al. (1992) [50]	Retrosigmoid	12	< 1 cm, Koos grades I–II	Median: 2.5 years	–	100%	All subjects	13 (31%)			–	–	–	–	–
Post et al. (1995) [51]	Retrosigmoid	56	–	Mean: 2.5 years	89% GTR	96%	46 (82%)	18 (39%)			89%	7%	18%	–	–

Table 1 (continued)

Reference	Approach	*n*	Tumor size	Follow-up	Degree of resection	Tumor control	Preop serviceable hearing	Serviceable hearing preservation rate	Postoperative AAO-HNS classification		Facial nerve function at last follow-up		Complications		
									A	B	HBI	HB II	CSF leak	Infection	Other
Rowed et al. (1997) [52]	Retrosigmoid	23	Koos grade I	5 years	100% GTR	0% requiring treatment	All subjects	11 (48%)	4(17%)	7(30%)	96%		–	–	–
Lee et al. (2002) [53]	Retrosigmoid	34	< 1.5 cm	Mean: 24 months	94% GTR, 2%NTR	100%	20 (59%)	5 (15%)	5(15%)	0(0%)	87%	-	11%	6% meningitis, 4% wound infection	3% cerebellar contusion
Chee et al. (2003) [54]	Retrosigmoid	29	< 2cm	Mean: 113.4 months	100% GTR	100%	All subjects	23 (79%)	11 (37%)	12 (41%)	–	–	–	–	–
Mohr et al. (2005) [55]	Retrosigmoid	128	< 1.5cm	–	–	–	77 (60%)	77 (60%)	20 (26%)	10 (13%)	–	–	–	–	–
Betchen et al. (2005) [56]	Retrosigmoid	142	Mean: 1.53cm	Mean: 7 years	–	–	All subjects	38 (27%)			97%		19%	2% meningitis	–
Yamakami et al. (2009) [57]	Retrosigmoid	44	Koos grade I or < 1.5cm	Mean: 48 months	100% GTR	100%	All subjects	36 (81%)	19(43%)	17(39%)	100%	–	–	–	–
Phillips et al. (2010) [58]	Retrosigmoid	23	Mean: 0.52cm	–	83% GTR, 17% NTR	–	All subjects	11 (48%)			–	–	–	–	–
Tawfik et al. (2020) [59•]	Retrosigmoid	153	Mean: 1.4cm	41.6 months	99.3% GTR	100%	141 (92%)	64(41%) overall, 52/97 (54%) for tumors < 1.5cm			–	–	–	–	
Sameshima et al. (2010) [60]	Retrosigmoid, MCF	125 (43 MCF, 82 RS)	Mean: 1.24cm	–	100% GTR	0% requiring treatment	All subjects	93 (74%), MFC: 33 (76.7%), RS: 60 (73.2)	37(29.6%) MCF: 16 (37%), RS: 21(26%)	39(31.2%) MCF: 17 (39.5%), RS: 39(47.5%)	99%	1%	5%	4% meningitis	–
Tringali et al. (2010) [61]	Retrosigmoid	278	Koos grades I–II	–	–	100%	213(77%)	87 (41%)			90%	–	–	–	–
Mazzoni et al. (2012) [62]	Retrosigmoid	200	–	Mean: 14 years	–	–	189 (95%)	47 (25%)	12 (6%)	35 (19%)	–	–	–	–	–
Nguyen et al. (2012) [63]	Retrosigmoid	185	Mean: 0.72cm	–	–	–	53 (29%)	40 (75%)	14 (26%)	26 (49%)	–	–	–	–	–
Freitas et al. (2012) [64]	Retrosigmoid, MCF	82	Mean: 0.8cm	> 1 year	100% GTR	–	All subjects	20 (24%)			97%	-	8%	1% meningitis	1% hydrocephalus requiring shunting
Yamakami et al. (2014) [65]	Retrosigmoid	36	Koos grade I or < 1.5cm	Mean: 81 months	100% GTR	100%	All subjects	26 (72%)			100%	–	0%	0%	–
Anaizi et al. (2016) [66]	Retrosigmoid, MCF	80	Koos grades I and II	Mean: 34 months	89% GTR, 11%NTR	–	39 (49%)	14 (37%), MCF: 1 (25%), RS: 13 (37%)			95%	–	5%	–	–

Radiosurgery: Tumor Control

In recent years, a number of series have shed light on tumor control after radiosurgical treatment of small VS. In a 2017 single-center retrospective analysis of long-term tumor control in 49 patients with intracanalicular VS, all subjects underwent single session linear accelerator (LINAC) or Cyberknife-based stereotactic radiosurgery with a mean marginal dose of 12.6 ± 0.6 Gy (range, 11.0–14.0 Gy). Mean follow-up was 65 months, and 100% of patients required no further treatment [69]. Several series have reported long-term tumor control outcomes after Gamma Knife radiosurgery (GKRS) for intracanalicular VS, with 97–100% of patients requiring no further treatment after primary GKRS (see Table 1) [70–74]. As tumor size increases, however, radiosurgical tumor control declines [75].

To date, there is insubstantial literature describing tumor control outcomes of treatment of small/intracanalicular VS in the long term (> 10 years after treatment). Furthermore, some authors have taken issue with reported tumor control outcomes in the radiosurgical literature. Many authors define radiosurgical tumor control as requiring no further treatment, not as an absence of further tumor growth. This definition is problematic because long-term series have shown that the majority of untreated small or intracanalicular tumors do not grow [14, 17, 18]. Battaglia et al. performed a retrospective review of 111 conservatively managed VS patients and compared their average tumor growth rate to a meta-analysis of reported tumor control outcomes after radiosurgery. In their series, the mean growth rate of untreated tumors was 0.7 mm/year, and 87% of tumors grew < 2 mm/year. Defining tumor control as growth < 2 mm/year, the authors found no significant difference in tumor control between untreated and radiosurgically managed VS [76]. Reflecting the fact that observation, compared to radiosurgical treatment, is not harmful for stable, small VS tumors, in 2018 the Congress of Neurological Surgeons published evidence-based guidelines on the role of radiosurgery and radiation therapy for VS, recommending observation over treatment for patients with non-growing small VS (< 2 cm) and no tinnitus [31]. The exception for patients with tinnitus was based on a small number of studies suggesting that tinnitus at presentation may have implications for management. In a survey of the Acoustic Neuroma Association, Van Gompel et al. found that tinnitus worsened over time in the cohort of survey recipients whose tumors were observed (n = 289) compared to those whose tumors were treated by surgery or radiosurgery (n = 1138) [77]. In addition, a retrospective study of 180 untreated VS tumors found that tinnitus at presentation increased the odds of tumor growth nearly threefold [78]. It should be noted, however, that some evidence suggests radiosurgery may have no benefit to tinnitus. In a large study of 379 patients who underwent GKRS and had median long-term follow-up of 69.5 months, there was no significant symptom improvement in patients who presented with tinnitus [79].

Radiosurgery: Hearing Preservation

Numerous prospective and retrospective series have reported hearing preservation outcomes after primary radiotherapy for VS (Table 1). In general, patients with VS and good hearing who undergo radiosurgery have good hearing in the near term after treatment but tend to demonstrate accelerated hearing loss over time. Animal models and temporal bone specimens from postirradiated patients have suggested that the stria vascularis, outer hair cells, and spiral ganglion cells may be most susceptible to injury from ionizing radiation [80, 81]. Proposed mechanisms for injury include direct damage to cochlear primary sensory cells and injury to auditory nerve fibers, and ischemic injury of the cochlea [82].

Long-term hearing preservation outcomes (> 10 years) in patients treated with radiosurgery are not commonly reported. In a 2013 report of 44 VS patients with serviceable hearing at the time of radiosurgery, 36 developed nonserviceable hearing at a mean of 4.2 years following treatment, and Kaplan-Meier estimated rates of serviceable hearing at 1, 3, 5, 7, and 10 years following radiosurgery were 80%, 55%, 48%, 38%, and 23%, respectively [83]. Similarly, a systematic review of 47 papers with 4689 patients, 47% of whom had serviceable hearing, found that rates of post-radiosurgical hearing preservation were 73% at < 2 years, 48% at 5–10 years, and 23% at > 10 years of follow-up [84]. In a separate systematic review by the Congress of Neurological Surgeons, the overall probability of maintaining serviceable hearing following stereotactic radiosurgery at 10 years was determined to be > 25–50% [31].

In the same systematic review, the authors evaluated literature reporting patient- and tumor-related factors influencing progression to nonserviceable hearing after stereotactic radiosurgery using ≤ 13 Gy at the tumor margin and found the most consistent positive predictors of hearing preservation include good pre-treatment pure tone thresholds and good preoperative speech discrimination, as well as smaller tumor size, marginal tumor dose ≤ 12 Gy, and cochlear dose ≤ 4 Gy. Notably, age and sex were not found to be strong predictors of hearing preservation outcome [31]. Notably, many of these positive risk factors for hearing preservation after radiosurgery are also favorable predictors for untreated or surgically resected VS. While several reports have suggested that higher cochlear dose is an unfavorable risk factor for hearing [85–88], one report found that cochlear dose was not significantly associated with time to nonserviceable hearing after accounting for baseline differences in a multivariate model [89].

Microsurgery for Small VS

Although recent literature suggests a trend toward conservatism in the management of patients with VS, particularly those with small tumors [1], microsurgical resection remains an efficacious option. Microsurgery is the only treatment option

that provides the opportunity for tumor removal. As previously discussed, many authors define radiosurgical success by the absence of reintervention, thereby allowing for continued tumor growth after radiosurgery to be classified as a favorable outcome. While microsurgical resection could be viewed as the most aggressive option for treatment of small VS, there is substantial evidence to support its safety and efficacy.

Microsurgical resection of VS can be accomplished via three classical routes: the translabyrinthine, middle cranial fossa, or retrosigmoid approaches. In the translabyrinthine approach, the VS is accessed by a transmastoid route. A labyrinthectomy is performed to achieve a wide exposure of the entire length of the internal auditory canal (IAC); because ablation of the vestibular apparatus renders the ear deaf, the translabyrinthine approach is a hearing-sacrificing operation. In the middle cranial fossa and retrosigmoid approaches, the IAC and CPA can be accessed without entrance into the membranous labyrinth, offering the opportunity to preserve residual hearing. Any of the three principal approaches may be appropriate for resection of small VS. In general, advantages of the translabyrinthine exposure include minimal cerebellar and temporal lobe retraction and early identification of the facial nerve. Disadvantages include the need to sacrifice hearing. The middle cranial fossa approach provides good exposure of the length of the IAC while affording the chance to preserve residual hearing. However, this approach necessitates temporal lobe retraction and provides a limited view of the CPA. Conversely, the retrosigmoid approach provides a more limited view of the lateral third of the IAC, particularly when preservation of hearing is a principal goal of surgery. Bony drilling through the posterior semicircular canal and vestibule permits more generous retrosigmoid exposure of the fundus of the IAC but is highly likely to render the ear deaf. Yet, the retrosigmoid approach affords a generous view of the medial portion of the IAC and CPA.

Microsurgery: Tumor Control and Morbidity

In general, tumor control rates after microsurgical resection are excellent, especially when gross total tumor resection is achieved. Table 2 includes a list of publications examining various surgical outcomes. Series reporting tumor control outcomes after resection of small tumors consistently demonstrate that absence of disease recurrence is achievable in > 95% of cases at long-term follow-up, with excellent facial nerve preservation and low rates of surgical complications [45, 50, 52–54, 57, 65]. Among studies reporting tumor control at ≥ 5 years of follow-up, results consistently show ≥ 95% rates of tumor control, defined either as radiographic absence of disease or no need for additional treatment [45, 54, 65].

A recent large series by Schwartz et al. reported outcomes of 107 patients who underwent translabyrinthine resection for small (< 1 cm of extension into the CPA) VS. In that report, gross total resection was achieved in 97% of patients, and short-term (1-year) tumor control, defined as the absence of radiographic disease and need for additional treatment, was achieved in 100% of patients. By more stringent criteria (gross total resection, absent radiographic disease, and no additional treatment), the tumor control rate was 95.6% [110]. House-Brackmann (HB) [111] 1 grade facial nerve function was achieved in 97.2% of cases, and good (HB 1–2) function was achieved in 99.1% of cases. Postoperative cerebrospinal fluid (CSF) leak occurred in 4.6% ($n = 5$). Four of five patients with CSF leaks manifested with CSF rhinorrhea and were managed with blind sac closure of the external auditory canal and Eustachian tube obliteration. One patient presented with CSF drainage from the postauricular wound and was managed with oversewing the site of leakage and placement of a lumbar drain. No patient developed meningitis [110]. In general, these favorable outcomes are recapitulated across the literature, with the exception that some have reported lower CSF leak rates in the range of 0–2% [112, 113].

While serious surgical complications such as meningitis, stroke, seizures, or death are uncommon, the risks of these devastating events should not be minimized or discounted. Due to the infrequency of these events, predisposing risk factors for major postoperative complications are poorly studied. Patients considering surgical VS removal should be counseled about the possibility of these events. In the authors' opinion, microsurgical resection nevertheless remains appropriate for patients desiring complete tumor removal. The presence of serviceable hearing complicates surgical decision-making, as even surgical approaches that afford the opportunity to conserve hearing still place audition at risk. Yet, patients with small VS and serviceable hearing should be counseled on the option of surgical removal and the potential for hearing preservation, and clinicians should provide honest estimates of the estimated chances of surgical preservation and loss, as well as other risks.

Microsurgery: Hearing Preservation

Numerous studies have reported hearing preservation results after either middle fossa or retrosigmoid VS resection. Hearing preservation rates after resection of small tumors vary widely between studies (15–81%) [53, 54, 57, 59•, 114]. Some of the variability in outcomes may be attributable to heterogeneity in tumor size and quality of preoperative hearing between study populations. Small tumor size, good preoperative hearing (as measured by PTA and WRS), and a fundal CSF fluid cap have been shown to be consistent favorable predictors of postsurgical hearing preservation [31]. A recent publication by the Congress of Neurological Surgeons included a systematic review of hearing preservation outcomes in VS patients and evidence-based guidelines suggesting that patients with small- and medium-sized tumors be

Table 2 Radiosurgery outcomes in treatment of small VS

Reference	*n*	Tumor size	Dose strategy	Tumor control	New facial nerve dysfunction	New trigeminal nerve dysfunction	Hydrocephalus	Hearing	Follow-up
Baschnagel et al. (2013) [90]	40	Median: 0.23cm^3	12.5Gy	100%	0%	0%	-	93% (q year), 77% (3years), and 74% (5years)	Median: 25 months
Breivik et al. (2013) [91]	13	Mean: 3.9cm^3	12Gy	94% no additional tx	0%	0%	-	36% retained SH	Mean:55 months
Carlson et al. (2013) [83]	44	Median: 0.715cm^3	12–13Gy	-	-	-	-	80% (1 year), 55% (3 years), 48% (5 years), and 23% (10 years)	Median: 9.3 years
Chopra et al. (2007) [92]	216	Median: 1.3cm^3	13Gy	98% @10y	0% paresis, 1% HFS	-	-	56.6% (60/106)	Median: 5.7 years
Flickinger et al. (2001) [93]	190	Median: 2.7 cm^3	13Gy	97% @5 years	1%	3% at 5 years	-	81% (61/75)	Median: 30th
Flickinger et al. (2004) [94]	313	Median: 1.1cm^3	13Gy	99%	0%	4%	7%	79% (218/246) retained SH	Median: 24 months
Han et al. (2012) [95]	119	Mean: 1.95cm^3	12Gy	-	-	-	-	68.5% (12 months), 62.5% (24 months), 59.9% (36 months), and 56.2% (60 months)	Mean: 55 months
Hasegawa et al. (2005) [96]	317	-	13.2Gy	91%	6% (high dose), 1% transient in low dose	4% high dose group, 2% low dose group	-	68% (50/74) retained SH	Median: 7.8 years
Hasegawa et al. (2011) [97]	117	Median: 1.9cm^3	12Gy	98% no growth	-	-	-	55% (3 years), 43% (5 years), and 34% (8 years)	Median: 74 months
Iwai et al. (2003) [68]	51	Median: 3.6 cm^3	≦12Gy	96%	0% paresis, 6% HFS	0%	6%	56% (10/18) retained SH	Median: 60 month s
Kim et al. (2011) [98]	41	Mean: 1.5cm^3	12Gy	88% no growth; 98% no surgery	0%	0%	-	61% (25/41) retained SH	Median: 30 months
Kim et al. (2013) [74]	60	Mean: 0.34cm^3	12.2Gy	88% no growth; 100% no additional treatment	-	-	-	70% (1 year), 63% (2 years), and 55% (5 years)	Median: 42 months
Lasak et al. (2008) [86]	33	Mean: 1.48cm^3	12–13Gy	94% no growth; 100% no surgery	3% transient HFS	3%	-	90% (9/10)	Median: 24 months
Litvack et al. (2003) [99]	134	-	12Gy	97%	2% transient paresis, 6% transient HFS	6% transient	3%	62% (29/47) retained SH	Mean: 32 months
Lunsford et al. (2005) [100]	829	Mean: 2.5cm^3	13Gy	97% no additional treatment at 10 years	0%	0.20%	0.80%	79%	-
Massager et al. (2007) [101]	82	-	12Gy	99% (no growth)	-	-	-	65% (39/60) retained SH	Median: 2 years
Myrseth et al. (2009) [10]	60	Mean: 1.6cm	12Gy	98% no surgery	0%	-	0%	76% (1yr) and 68% (2yr)	2 years (all)
Paek et al. (2005) [102]	25	Median 3.0cm^3	12Gy	92% no growth; 100% no surgery	0%	0%	0%	52% (13/25) retained SH	Median: 45 months
Petit et al. (2001) [103]	35	Median: 1.8 cm	12Gy	100%	4% transient, 0% permanent	0%	-	100% with GR grade I or II at baseline retained GR grades I–III at follow-up	Median: 3.5 years
Pollock et al. (2006) [11]	46	Mean: 1.5cm^3	12.2Gy	96% no surgery	0%	2%	4%	63% retained SH	Mean: 42 months
Prasad et al. (2000) [104]	96	Mean: 2.7cm^3	13Gy	94%	2%	4%	0%	58% (21/36) retained SH	Mean: 4.3 years

Table 2 (continued)

Reference	*n*	Tumor size	Dose strategy	Tumor control	New facial nerve dysfunction	New trigeminal nerve dysfunction	Hydrocephalus	Hearing	Follow-up
Régis et al. (2002) [105]	97	-	12–14Gy	97% no surgery	0%paresis, 3% HFS	4%	3%	50% retained SH	-
Regis et al. (2010) [106]	34	Mean:1.125cm^3	12Gy	97%	-	-	-	77% (3 years), 70 (4 years), and 64 (5 years)	Mean: 46 months
Sun et al. (2012) [107]	190	Median: 3.6 cm^3	≦14Gy	90% no growth	14% transient paresis, 1% permanent	21% transient, 3% permanent	3%	86% (19/22)	Median: 109 months
Tamura et al. (2009) [108]	74	-	12Gy	93% no additional treatment	1%	10%	-	70%	Median: 48 months
Yomo et al. (2012) [109]	154	Mean: 0.73cm^3	12.1Gy	95% no additional treatment	1%	1%	1%	58%	Mean: 60 months

counseled that the probability of maintaining serviceable hearing is moderately low (> 25–50%) immediately after surgery, moderately low (> 25–50%) at 2 years, moderately low (> 25–50%) at 5 years, and moderately low (> 25–50%) at 10 years [31]. These guidelines should be interpreted with caution, however. Hearing preservation surgery is technically challenging, and it is possible that differences in surgical experience—in addition to the aforementioned factors—account for much of the heterogeneity in published hearing preservation results. Numerous series have reported rates of early postoperative hearing preservation that far exceed the figures published by the Congress of Neurological Surgeons. In reviewing a series of 89 patients, Ginzkey et al. found that 74% of patients with preoperative AAO class A/B hearing maintained class A/B hearing after middle fossa resection of their tumors [44]. Several other series have also reported hearing preservation rates > 70% after middle fossa or retrosigmoid resection [42, 49, 54, 65, 115••] and a common theme across these series is that favorable hearing outcomes are most consistently achieved in patients with good preoperative hearing and small tumors. These features, in addition to the presence of a fundal fluid cap, are the most consistent positive predictors of hearing preservation after VS resection [31].

There is controversy regarding the durability of hearing preservation after both radiosurgery and microsurgery. Delayed hearing loss has been reported to occur in 11–30% of patients after surgical VS resection [48, 116–119]. Very few studies have examined hearing outcomes ≥ 10 years after surgery. Perhaps the best study is the 2018 publication by Ahmed et al., in which audiometric results were evaluated for patients up to ≥ 12 years after surgery. Contrary to many other series, the authors also corrected for decline in contralateral hearing (in an attempt to control for age-related hearing decline). Durability of hearing preservation was high up to 3–5 years (67% preservation of AAO class A/B hearing, 91% preservation of WRS class I or II) after surgery but declined thereafter. Speech discrimination was significantly less prone to decline than pure tone thresholds. At 9–11 years, AAO class A/B hearing was preserved in 68% of patients, whereas WRS class I or II was preserved in 88% [115••]. (Rates of preservation declined at follow-up ≥ 12 years, but due to loss of follow-up, only 11 patients were analyzed in this group.)

In another recent publication, Roche et al. reported audiometric outcomes in 13 patients who had hearing preservation after middle fossa resection of small VS and mean follow-up of 14 years. In this small series, the rates of change in PTA and WRS were not statistically different between operated and non-operated ears (within subjects), and the authors concluded that preserved hearing is maintained in the majority of patients > 10 years after surgery [120].

It should be noted that one of the barriers to obtaining and interpreting long-term hearing preservation data is the

possibility of selection bias and loss to follow-up. It is conceivable that patients who elect to continue presenting for audiometric testing ≥ 10 years after surgery have hearing outcomes that differ substantially from patients who are lost to audiometric follow-up. Bearing these problems in mind, contemporary literature does suggest that preserved hearing after surgical resection tends to endure over the long term.

Quality of Life in Patients with Small VS

Over the past decade, robust literature has emerged describing quality of life outcomes in patients with small VS. A 2018 report retrospectively compared quality of life between treatment modalities (microsurgery, radiotherapy, and observation) in 168 patients with small VS (intracanalicular or extrameatal without brainstem contact) at a mean of 66 months between management and questionnaire completion. Quality of life was measured using four questionnaires: the Short-Form Health Survey 36 (SF-36), Hearing Handicap Inventory, Tinnitus Handicap Inventory, and Dizziness Handicap Inventory Short-Form. The authors found no difference in quality of life measures between treatment groups on any of the four administered questionnaires [121]. Importantly, vertigo appeared to be the principal cause of deterioration in quality of life in the management of small VS, which is consistent with other reports [122, 123], but its prevalence did not differ between groups before or after treatment [121].

In 2015, Carlson et al. published an international multicenter study comparing long-term quality of life between VS patients who underwent microsurgery, stereotactic radiosurgery, and observation, comparing outcomes to a group of nontumor controls. All VS patients had small- or medium-sized tumors (i.e., less than 3 cm in maximal diameter), and a total of 642 respondents were analyzed with a mean time interval of 7.7 years between treatment and survey completion. Surveys included the SF-36, the 10-item Patient-Reported Outcomes Measurement Information System short form (PROMIS-10), the Glasgow Benefit Inventory (GBI), and the Penn Acoustic Neuroma Quality-of-Life (PANQOL) scale. While patients who underwent radiosurgery or observation reported better total PANQOL scores and more favorable PANQOL facial, balance, and pain subdomain scores than the microsurgical cohort ($p < 0.02$), for the majority of survey instruments, differences in scores between the nontumor control group and patients with VS were greater than differences between individual treatment groups. The authors concluded that differences in long-term quality of life outcomes after microsurgery, radiosurgery, and microsurgery for VS are small, and in fact, it is the diagnosis of VS, rather than the treatment strategy, that most significantly influences quality of life [1].

Soulier published a similar study comparing PANQOL scores in 807 VS patients treated with observation, radiotherapy, or microsurgery at a tertiary referral center in the Netherlands. (The PANQOL is a 26-item questionnaire with seven subdomains—hearing, balance, anxiety, energy, pain, face, and general health—and represents the only disease-specific quality of life instrument for VS.) Four hundred ninety (60.7%) of patients had tumors 0–10 mm in size. Among these, 72.4% (n = 355) were observed, 9.6% (n = 47) underwent radiation, and 18.0% (n = 88) underwent microsurgery. Patients with small tumors who were managed by observation reported higher PANQOL (i.e., better quality of life) scores compared to those treated with radiotherapy and microsurgery. This was true for various subdomains, including hearing, where observation was more favorable than radiotherapy; balance, where observation was better than radiotherapy and microsurgery; face, where observation and radiotherapy were better than microsurgery; and energy, where observation was better than radiotherapy and microsurgery [124]. The negative correlation between self-reported symptoms and quality of life was largest for balance problems and vertigo.

Importantly, statistically significant differences between VS treatment groups may not necessarily bear clinical significance. In an attempt to account for this problem, Carlson et al. described the minimal clinically important difference (MCID)—that is, the smallest difference in quality of life scores that patients perceive as important and that could lead to a change in management—for the PANQOL and SF-36 Physical and Mental Health Component Summary Scores, two instruments commonly used in studies of quality of life in VS. The median MCID for total PANQOL score was found to be 11 points, and the MCIDs were 7 points and 8 points for the SF-36 Mental Health and Physical Health Component Summary scores [125]. These findings have important implications for interpreting VS-related quality of life literature. For example, if an 11-point MCID in total PANQOL score were used to interpret the aforementioned study by Soulier et al., then the reported statistical differences between observation, radiotherapy, and microsurgically treated patients with small VS would not be considered clinically significant [124]. Similarly, a host of other studies report long-term differences in SF-36 Mental Health and Physical Component Summary scores and PANQOL scores between treatment groups, but the reported differences generally do not exceed the respective MCIDs determined by Carlson et al. [7, 8, 10, 11, 126].

Microsurgery vs. Radiosurgery for Small VS: Vestibular Outcomes

There are several shortcomings in the literature describing vestibular outcomes of treatment for VS, including the

heterogeneity of methods and outcome measures between studies and the essential difficulty of quantifying pre- and post-treatment vestibular dysfunction. Several studies have attempted to compare long-term balance outcomes between treatment modalities for patients with small- and medium-sized tumors, with inconsistent results. In a retrospective study comparing outcomes of microsurgery versus radiosurgery for treatment of small tumors with no hearing, microsurgery yielded superior long-term balance outcomes as measured by the University of California Los Angeles Dizziness Questionnaire [127]. By contrast, a prospective comparison of outcomes of microsurgery and radiosurgery for management of small- and medium-sized tumors showed that radiosurgical patients had lower mean Dizziness Handicap Inventory scores compared to patients who underwent resection [11]. In a recent meta-analysis of 34 references reporting long-term balance outcomes after microsurgery or radiotherapy for VS, perceived dizziness improvement rate was higher in microsurgical than radiosurgical patients (odds ratio 1.61, $p < 0.05$), but no differences were detected in validated dizziness questionnaire scores or dizziness/disequilibrium incidence rates [128].

Theoretically, it is possible that patients with particularly disabling vestibular symptoms, such as intractable vertigo, may stand to benefit most from microsurgery because it affords the opportunity to section the ipsilateral vestibular nerve at the time of tumor resection. Corroborating this supposition, in a small retrospective series of VS patients who underwent microsurgical resection for treatment of intracanalicular tumors and had disabling preoperative vestibular symptoms, complete or near-complete resolution of vertigo was accomplished in all patients at 1 year after surgery [129].

Conclusions

Optimal management of small VS is controversial, and treatment selection depends on many factors, including but not limited to individual or institutional bias, surgical experience, pre-treatment hearing quality, tumor growth characteristics, and patient preference. Radiosurgical and microsurgical tumor control rates are excellent. While long-term outcomes are uncommonly reported, emerging literature suggests that surgical hearing preservation tends to endure. In general, quality of life measures do not significantly differ between treatment modalities. Based on the available evidence, treatment of small VS should be determined on a case-by-case basis, and the value of intervention (whether radiotherapy and surgical resection) is contingent on one's ability to achieve tumor control and hearing preservation with minimal morbidity.

Declarations

Conflict of Interest Kareem O. Tawfik, Usman Khan, and Rick A. Friedman declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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