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Extent of resection and progression-free survival in vestibular schwannoma: a volumetric analysis

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OBJECTIVE To preserve facial nerve function in vestibular schwannoma (VS) microsurgery, some have advocated subtotal resection (STR) if the tumor is densely adherent to a thinned facial nerve. The objective of this study was to determine if residual volume is associated with progression and whether there is a threshold residual volume that should be pursued during STR to prevent recurrence. A secondary objective of this study was to determine whether facial nerve function at last follow-up was associated with extent of resection (EOR).

METHODS Clinical and radiographic data were retrospectively collected from the records of 164 patients with VS who underwent resection. Tumor volumes were measured using Visage, and standard statistical methods were used. The House-Brackmann scale was used to assess changes in facial nerve function before surgery and at last follow-up.

RESULTS Sixty-one patients (37%) received gross-total resection (GTR) and 103 (63%) received STR. The median clinical and radiographic follow-ups were 49 and 48 months, respectively. The median residual volume was 0.5 cm^3 after STR. Kaplan-Meier actuarial survival analysis revealed a 96.3% 5-year progression-free survival (PFS) rate after GTR, which was greater than that after STR (84.5%, p = 0.03). Recursive partitioning analysis of patients receiving STR revealed a residual volume of 0.60 cm^3 as the optimal threshold for recurrence. Patients with residual volume ≥ 0.60 cm^3 had a 76.0% 5-year PFS, regardless of adjuvant SRS, which was lower than that for patients undergoing GTR (96.3%) or STR (95.6%) with residual volumes < 0.60 cm^3 (p < 0.01). On Cox regression analysis, residual volume ≥ 0.60 cm^3 (HR 14.4, p = 0.01) was independently associated with progression, even when accounting for patient age, adjuvant radiosurgery, and preoperative tumor size. In 112 patients with at least 24 months of follow-up after their last treatment, tumor control was achieved in 111 (99.1%) patients at a median last follow-up of 71 months. Worse facial nerve function at the last follow-up was independently associated with prior treatment for VS (adjusted OR 3.7, p = 0.04), but not residual volume cohort or preoperative tumor volume.

CONCLUSIONS Residual volume > 0.60 cm^3 after VS resection was independently associated with tumor progression, even accounting for adjuvant SRS. These data support maximizing the EOR during VS surgery, even if GTR cannot be safely achieved.

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KEYWORDS acoustic neuroma; facial nerve; extent of resection; recurrence; vestibular schwannoma; volumetrics; tumor

Vestibular schwannomas (VSs) derive from myelinating Schwann cells of cranial nerve VIII, the vestibulocochlear nerve. VSs are the most common nerve sheath tumors and the third most common nonmalignant brain tumor.[1] Epidemiological studies suggest that the incidence may be as high as 1 in 2000 adults, and there is variability in the management of VS.[2]

In recent decades, VS management has trended toward a more conservative wait-and-scan approach for patients without large symptomatic tumors.[3] Treatment is indicated when there is a neurological deficit or documented growth of the tumor, although some have argued for upfront radiosurgery treatment at diagnosis.[4] Outside of neurofibromatosis type 2, where anti-VEGF antibodies or tyrosine kinase inhibitors may play a role,[5] treatment options for sporadic VS include microsurgery or radiosurgery. De-

ABBREVIATIONS aOR = adjusted OR; EOR = extent of resection; GTR = gross-total resection; HB = House-Brackmann; KM = Kaplan-Meier; PFS = progression-free survival; p_{perm} = p value from log-rank permutation tests; RPA = recursive partitioning analysis; SRS = stereotactic radiosurgery; STR = subtotal resection; VS = vestibular schwannoma.

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spite both being established treatments, the optimal extent of resection (EOR) and role of radiosurgery remain controversial.[6,7] For small tumors, radiosurgery alone is often an excellent option.[8] Resection is necessary for large tumors with mass effect, hydrocephalus, and associated neurological symptoms or for select small tumors, especially those with vestibular symptoms.[9,10] Many intermediate-sized VSs fall into a gray zone where both radiosurgery and microsurgery are reasonable options for treatment.

To minimize risk to the facial nerve and optimize quality of life, some have advocated for subtotal resection (STR) of intermediate or large tumors with adjuvant radiosurgery to the residual tumor. However, while intentional STR can be protective of the facial nerve,[6] it may be associated with inferior tumor control.[7] The primary goal of this study was to retrospectively review cases of VSs that underwent resection and investigate the relationship between volumetric EOR and freedom from progression. A secondary goal of this study was to evaluate the role of EOR and other clinical predictors on long-term facial nerve outcome.

Methods

Study Design, Setting, and Participants

This was a retrospective study conducted at a major academic medical center following approval by the institutional review board. Informed consent was not required for this study. Chart reviews were conducted for adult patients who underwent resection for VSs between 2003 and 2023 and whose data were available in the institutional electronic data warehouse and brain tumor bank. Inclusion criteria for this study were patients who were 1) older than 18 years; 2) underwent resection of a VS at our institution; 3) had an electronic medical record with documentation of preoperative and postoperative symptomology and MRI; and 4) had at least 6 months of follow-up via MRI. One patient enrolled in a clinical trial for bevacizumab, 2 patients with insufficient documentation, and 18 patients with less than 6 months of follow-up were excluded.

Variables collected included demographic characteristics (age and sex) and pre- and postoperative tumor volumes. Outcomes of interest were time to tumor progression and change in facial nerve function classified as either same/improved or worse. Information on history of prior microsurgical resection or radiosurgery for VS was collected. History of adjuvant radiosurgery and postoperative hearing outcome at last follow-up were also collected. Tumors were classified by Koos grade and cystic versus mixed or solid consistency. Location of the residual was classified as internal auditory canal only, cistern only, brainstem only, or multiple locations. Peritumoral edema was collected based on review of T2-weighted MRI FLAIR sequences. Surgical approach was recorded from operative notes. EOR was recorded based on pre- and postoperative tumor volumes calculated from T1-weighted postcontrast MRI. Postoperative tumor volumes were calculated from MRI performed at 3 or 6 months of follow-up (whichever was first available) to allow for collapse of any residual tumor that consolidated in the initial postoperative period. Based on prior studies, failure after resection was defined as ≥ 20% increase in postoperative tumor volume in patients receiving STR or new contrast enhancement in patients receiving gross-total resection (GTR) on at least a 6-month interval of postoperative serial MRI.[11–13] Undergoing postresection salvage therapy (e.g., subsequent resection or stereotactic radiosurgery [SRS]) was also considered failure. Failure after SRS was defined as continued tumor growth for at least 36 months on post-SRS serial imaging or additional salvage therapy, based on prior volumetric analyses of post-SRS pseudoprogression.[14] Time to progression was calculated based on the date of last treatment (resection or adjuvant radiosurgery) and date of the first MRI session when tumor growth was noted. For patients receiving additional intervention after initial treatment failure, subsequent tumor control was defined as not needing further surgical or radiosurgical intervention. For patients who experienced posttreatment tumor progression with at least 12 months of follow-up before loss of follow-up or further treatment, tumor volumes were calculated for all available postoperative MR images to characterize volumetric trajectories. Adjuvant SRS was defined as within 12 months postoperatively and prior to documented treatment failure. To evaluate facial nerve function, House-Brackmann (HB) grades at presentation and last follow-up were collected from the charts of patients with at least 12 months of follow-up. HB grades were categorized as good (grade I or II), fair (grade III or IV), or poor (grade V or VI). Facial nerve function was considered to have worsened if the HB grade at last follow-up changed from good to fair or fair to poor. Postoperative hearing outcome was compared with the preoperative hearing as same, improved, or worse from the last clinical follow-up note based on subjective patient reports, physical examinations, and results of audiograms when available.

Statistical Analysis

For categorical data, Fisher's exact tests were performed. Unpaired Kruskal-Wallis rank-sum tests were used to compare medians between subgroups classified based on EOR. Univariate and multivariable logistic regression analyses were used to identify variables associated with tumor progression, and Kaplan-Meier (KM) time-to-event analysis was used to report time to progression based on EOR (GTR vs STR). Recursive partitioning analysis (RPA) was used to identify the optimal split for tumor size and progression. The optimal split defined by RPA was used to stratify patients by tumor residual size—into GTR, small residual, and large residual cohorts—for additional KM analyses. Log-rank tests were used for both KM analyses to determine statistical significance between cohorts. As optimal cutpoints derived from a sample can lead to falsely low p values in subsequent analyses,[15] p values from log-rank permutation tests (p_{perm}) with 2000 random permutations were also reported for analyses comparing subgroups based on the RPA-derived threshold. Multivariable Cox regression analyses were used to identify independent predictors of time to progression. Univariate and multivariate logistic regression analyses were also conducted to identify variables associated with worse facial nerve function at last follow-up. Variables with a predetermined p value threshold of < 0.10 were

TABLE 1. Univariate logistic regression of patient and tumor characteristics as predictors of VS progression

Variable	All Patients, n = 164	No Progression, n = 151	Progression, n = 13	OR (95% CI)	p Value
Age, yrs	50 (38–61)	50 (39–61)	47 (35–53)	1.0 (0.9–1.0)	0.93
Female sex, n (%)	98 (60)	90 (60)	8 (62)	0.9 (0.22–3.4)	>0.99
Previously treated VS, n (%)	21 (13)	19 (13)	2 (15)	1.3 (0.1–6.5)	0.67
STR*	103 (63)	91 (60)	12 (92)	7.8 (1.1–343.2)	**0.02**
IAC residual	91/103 (88)	79/91 (87)	12/12 (100)	NA	0.76
Brainstem residual	43/103 (42)	38/91 (42)	5/12 (42)	1.0 (0.2–4.0)	>0.99
Cistern residual	50/103 (49)	43/91 (47)	7/12 (58)	1.6 (0.4–6.7)	0.54
Multiple sites w/ residual	52/103 (50)	47/91 (52)	5/12 (42)	0.7 (0.2–2.7)	0.55
STR w/ residual ≥0.60 cm^3*	51 (31)	41 (27)	10 (77)	14.6 (1.8–118.7)	**0.01**
EOR, %	98 (93–100)	98 (93–100)	97 (87–97)	0.98 (0.94–1.02)	0.34
Preop size, cm^3	7.5 (3.5–16.3)	7.4 (3.4–14.4)	18.4 (5.8–33.8)	1.05 (1.01–1.10)	**0.03**
Residual size, cm^3	0.5 (0.3–1.1)	0.5 (0.3–1.1)	0.9 (0.6–2.0)	1.2 (0.9–1.5)	0.24
Adjuvant radiosurgery, n (%)	19 (12)	18 (12)	1 (8)	0.6 (0–4.7)	>0.99
Koos grade, n (%)					0.74
I	9 (5)	8 (5)	1 (8)	Reference	
II	9 (5)	9 (6)	0	0	
III	22 (13)	20 (13)	2 (15)	0.8 (0–10.1)	
IV	124 (76)	114 (75)	10 (77)	0.6 (0.1–5.7)	
Cystic, n (%)	59 (36)	56 (37)	3 (23)	0.6 (0.1–2.4)	0.54
Peritumoral edema, n (%)	15 (9)	12 (8)	3 (23)	3.8 (0.6–18.1)	0.09

IAC = internal auditory canal; NA = not available.
Continuous variables are presented as median (IQR) and odds ratios are per unit increase in predictor. Boldface type indicates statistical significance.
* Compared with patients who received GTR.

used for multivariable logistic regression and Cox regression analyses. JMP (version 16.1, SAS Institute Inc.), R (version 4.2.0, The R Project for Statistical Computing), and Prism (version 10.0.2, GraphPad Software) were used for statistical analyses. A p value ≤ 0.05 was considered statistically significant for all analyses.

Results

We identified 164 patients who underwent VS resection and had the necessary information to meet the inclusion criteria. The median radiographic and clinical follow-ups were 49 (IQR 21–87) months and 48 (IQR 20–84) months, respectively. All tumors were WHO grade 1. Three patients had neurofibromatosis type 2. Patient characteristics are reported in Table 1. The median patient age was 50 (IQR 38–61) years, and 98 (60%) patients were female. Surgical indications were large symptomatic tumors or those that had been observed with documented growth not amenable to radiosurgery, as reflected by 89% of tumors in the cohort being Koos grade III or IV. Small tumors, even if growing, are typically treated with radiosurgery at our institution unless the patient's symptoms include significant vestibulopathy. The most common surgical approach was retrosigmoid (143 patients, 87%) followed by translabyrinthine (17, 10%) and other (4, 2%) approaches. Sixty-one patients (37%) received GTR and 103 (63%) received STR. The median preoperative tumor volume was 7.5 (IQR 3.5–16.3) cm^3. The median residual volume after STR was 0.5 (IQR 0.3–1.1) cm^3. The median EOR for the entire cohort was 98% (IQR 93%–100%). Example preoperative, postoperative, and recurrent tumors in patients receiving GTR and STR are shown in Fig. 1. Nineteen patients (12%) received adjuvant radiosurgery following STR. The majority of patients undergoing adjuvant radiosurgery were treated with single-fraction Gamma Knife radiosurgery to 11.5–13 Gy at the 50% isodose line. Three patients underwent hypofractionated Gamma Knife radiosurgery with 25 Gy in 5 fractions. At last follow-up, 94 (57.3%) patients had worse ipsilateral hearing compared with preoperatively.

VS Progression

Thirteen (8%) patients experienced postoperative tumor progression at a median of 27 (IQR 7–53) months. On univariate analyses (Table 1), patients with VS progression after treatment were more likely to have received STR (OR 7.8 [95% CI 1.1–343.2], p = 0.02) than GTR, and to have larger preoperative tumors (OR 1.05 [95% CI 1.01–1.10] per cm^3, p = 0.03). There were no differences in age, sex, history of prior treatment for VS, tumor consistency, location of residual tumor, peritumoral edema, residual tumor volume, EOR, or use of adjuvant SRS.

The 5-year progression-free survival (PFS) rate was 96.3% for patients who received GTR and 84.5% for patients who received STR (p = 0.03) (Fig. 2A). On bivariate comparisons, there were no differences in patient age, sex, prior treatment for VS, preoperative tumor size, or follow-up time between patients with GTR and STR (Table 2).

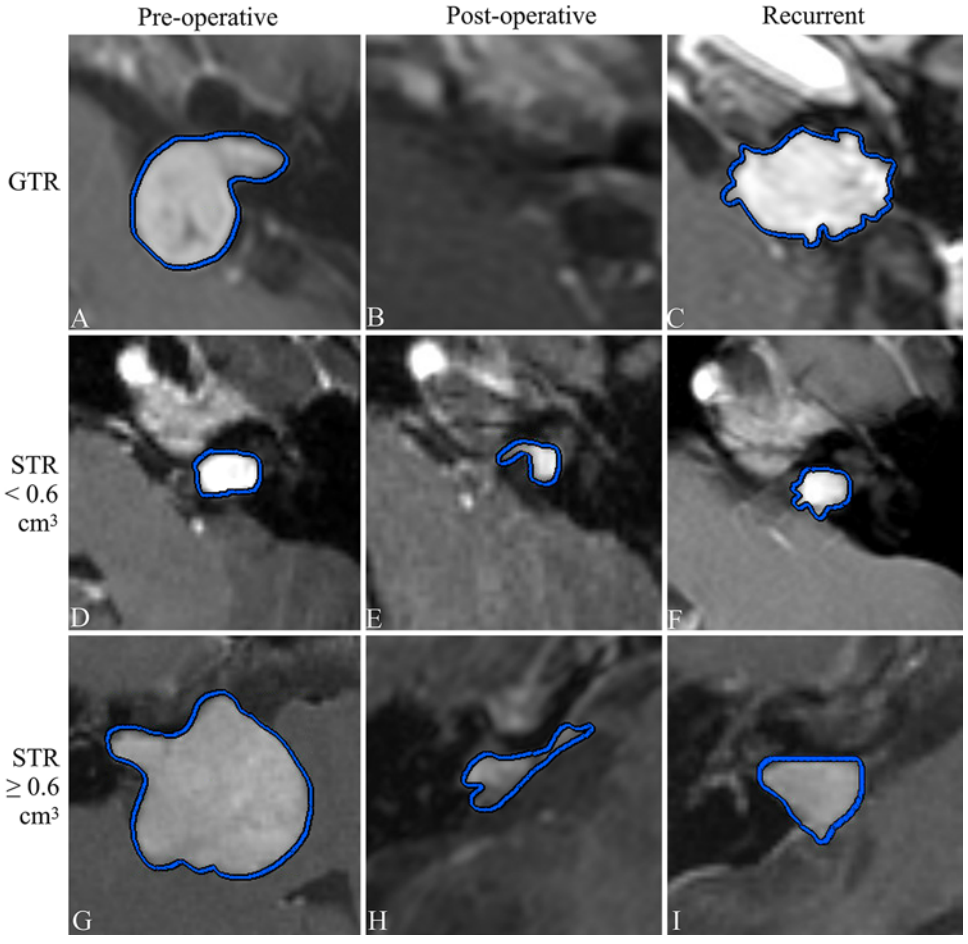

FIG. 1. T1-weighted postcontrast MR images showing preoperative (**A**), postoperative (**B**), and recurrent tumor (**C**) in a patient receiving GTR. Preoperative (**D**), postoperative (**E**), and recurrent tumor (**F**) in a patient receiving STR with residual < 0.60 cm^3. Preoperative (**G**), postoperative (**H**), and recurrent tumor (**I**) in a patient receiving STR with residual > 0.60 cm^3. Figure is available in color online only.

Further investigation with RPA revealed a residual volume of 0.60 cm^3 as the optimal volumetric split for recurrence (Fig. 2B). On univariate logistic regression, STR with residual ≥ 0.60 cm^3 was associated with greater odds of progression than GTR (OR 14.6 [95% CI 1.8–118.7], p = 0.01). Accordingly, patients with residual volume ≥ 0.60 cm^3 had a 5-year PFS rate of 76.0% (Fig. 2C), which was lower than that for patients undergoing GTR (96.3%) or STR (95.6%) with residual volumes < 0.60 cm^3 (p_{perm} < 0.01). Patients with residual volume ≥ 0.60 cm^3 who did not receive adjuvant radiosurgery had a 5-year PFS rate of 66.0% compared with patients with residuals ≥ 0.60 cm^3 who did receive adjuvant radiosurgery (100%) and those with residuals < 0.60 cm^3 (95.6%, p_{perm} = 0.04) (Fig. 2D). In the overall cohort, 5-year PFS after SRS was higher for patients who received adjuvant SRS than after salvage SRS (100% vs 76.2%, p = 0.01) (Fig. 2E). Lastly, there were no significant differences in patients who had worse ipsilateral hearing at last follow-up between patients with residual ≥ 0.60 cm^3 (49.0%), residual < 0.60 cm^3 (65.4%), and GTR (57.4%) (p = 0.25).

The results of multivariate analyses for predictors of tumor progression are summarized in Table 3. On multivariate logistic regression analysis controlling for residual subgroup and peritumoral edema, residual volume ≥ 0.60 cm^3 (adjusted OR [aOR] 11.1 [95% CI 1.3–93.1], p = 0.03) was associated with higher odds of progression. On multivariate Cox regression analysis controlling for patient age, adjuvant radiosurgery, residual volume ≥ 0.60 cm^3 (HR 14.4 [95% CI 2.7–266.9], p = 0.01) was associated with shorter PFS compared with GTR, but age, residual < 0.60 cm^3, and adjuvant radiosurgery were not associated with PFS.

Salvage Treatment and Outcomes After VS Progression

Following failure of primary microsurgical resection in 13 patients, 11 (85%) patients underwent salvage SRS, 1 patient chose not to receive further treatment, and 1 patient had not decided on further treatment at the time of data collection. Volumetric trajectories of patients with at least 24 months of postoperative radiographic follow-up whose tumors progressed after surgery are presented in Supplementary Fig. 1A and B. Of the patients who received salvage SRS, 8 (73%) had stable tumors at last

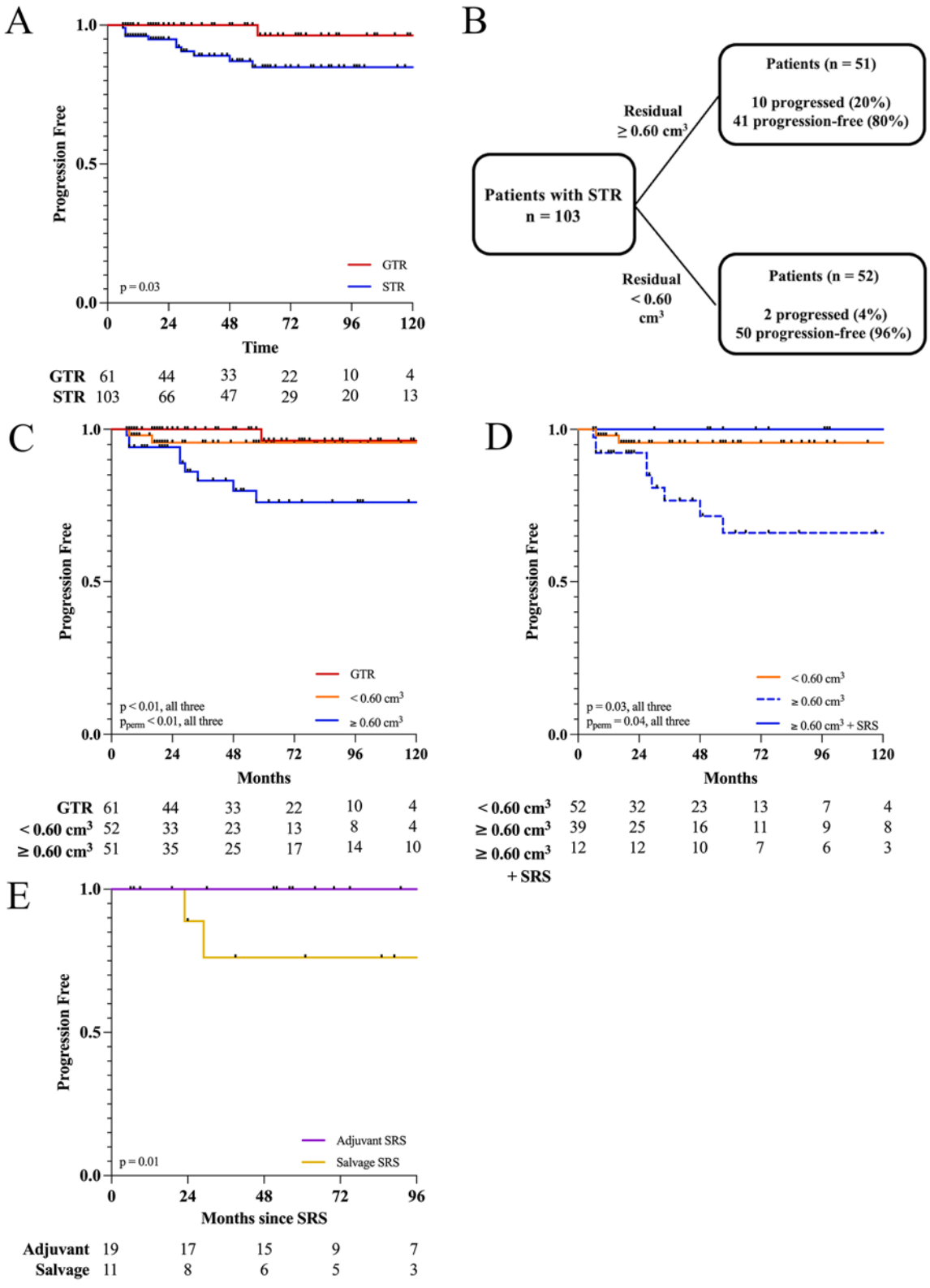

FIG. 2. A: VS patients receiving GTR had significantly longer PFS than patients receiving STR. **B:** RPA of 103 patients who received STR, demonstrating that residual tumor volume ≥ 0.60 cm³ is associated with binary tumor progression. **C:** On KM analysis, a residual tumor volume ≥ 0.60 cm³ is associated with faster time to progression than a residual tumor volume < 0.60 cm³ or GTR. **D:** In 103 patients receiving STR, patients with residual tumor volume ≥ 0.60 cm³ who did not receive adjuvant radiosurgery had shorter PFS than patients with a residual tumor volume ≥ 0.60 cm³ who did receive adjuvant radiosurgery and those with residuals < 0.60 cm³. **E:** In 30 cases in which SRS was administered, adjuvant SRS was associated with longer post-SRS PFS than salvage SRS. For patients who received SRS, follow-up and PFS were calculated from date of SRS completion. On KM curves, the *black dots* represent points at which individual patients were censored due to end of follow-up. Figure is available in color online only.

TABLE 2. Differences between patients receiving GTR versus STR

	GTR, n = 61	STR, n = 103	p Value
Age, yrs	49 (39–61)	50 (38–61)	0.93
Female sex, n (%)	38 (62)	60 (58)	0.63
Previously treated VS, n (%)	6 (10)	15 (15)	0.47
Prior resection	3 (5)	7 (7)	0.75
Prior SRS	3 (5)	12 (12)	0.17
Preop tumor size, cm^3	5.2 (1.7–8.9)	9.2 (5.1–19.0)	0.30
Postop tumor size, cm^3		0.5 (0.3–1.1)	
Radiographic follow-up, mos	49 (21–83)	48 (21–89)	0.44
Clinical follow-up, mos	48 (18–81)	48 (21–87)	0.65

Continuous variables are presented as median (IQR).

follow-up, and 3 patients experienced a second failure. Post-SRS volumetric trajectories of patients who received salvage SRS with at least 24 months of post-SRS follow-up are presented in Fig. 1C and D. Treatments and outcomes of patients who experienced VS progression are summarized in Supplementary Table 1, and Fig. 3 summarizes outcomes in the entire cohort with a focus on tumor control by last follow-up. In 112 patients with at least 24 months of follow-up after their last treatment, tumor control was achieved in 111 (99.1%) at a median last follow-up of 71 (IQR 43–100) months.

Facial Nerve Outcomes

Pre- and postoperative HB scores for 142 patients with at least 12 months of follow-up are reported in Table 4. At a median follow-up of 58 (IQR 29–89) months, 25 (18%) had facial nerve worsening. Eleven percent of patients receiving GTR and 21% of patients receiving STR had worse facial nerve function at the last follow-up ($p = 0.1717$). When analyzed by residual volume subgroup, 11% of patients receiving GTR, 14% of patients receiving STR with residual < 0.60 cm^3, and 28% of patients with residual ≥ 0.60 cm^3 had worse facial nerve function at last follow-up ($p = 0.0710$).

TABLE 3. Multivariate logistic regression for predictors of tumor progression

Multivariate Logistic Regression		
Variable	aOR (95% CI)	p Value
Peritumoral edema	2.5 (0.5–11.2)	0.24
Residual <0.6 cm^3*	2.1 (0.2–24.1)	0.56
Residual ≥0.6 cm^3*	11.1 (1.3–93.1)	**0.03**
Multivariate Cox Regression		
Variable	HR (95% CI)	p Value
Residual <0.6 cm^3*	2.8 (0.3–59.5)	0.41
Residual ≥0.6 cm^3*	14.4 (2.7–266.9)	**0.01**
Adjuvant radiosurgery	0.2 (0.01–1.3)	0.18
Age	0.98 (0.94–1.02)	0.27

Boldface type indicates statistical significance.
* Compared with GTR.

On univariate logistic regression analyses (Table 5), worse facial nerve function at the last follow-up was not significantly associated with patient age, sex, STR, STR with smaller residuals, EOR, residual volume, or adjuvant radiosurgery. Prior treatment of VS (OR 3.0 [95% CI 0.99–9.1], $p = 0.0516$) and preoperative tumor size (OR 1.04 [95% CI 1.00–1.08] per cm^3, $p = 0.0730$) approached but did not reach statistical significance. On multivariable logistic regression modeling, only prior treatment of VS (aOR 3.7 [95% CI 1.0–12.9], $p = 0.0433$) was independently associated with worse facial nerve function at last follow-up.

Discussion

Key Results

We found that patients with STR had a shorter PFS than patients who received GTR, and more specifically, patients who received STR with tumor residual ≥ 0.60 cm^3 had shorter PFS than patients with smaller residuals or GTR. Furthermore, tumor residual ≥ 0.60 cm^3 was an independent predictor of time to progression regardless of adjuvant radiosurgery, but in the overall cohort, adjuvant SRS was associated with longer PFS than salvage SRS. Lastly, worse facial nerve outcomes at the last follow-up trended toward being associated with larger preoperative tumor size and prior treatment for VS but not residual volume subgroup. Only prior treatment for VS was an independent predictor of worse facial nerve outcomes.

Interpretation

Despite a trend toward more conservative management of VSs to maximize patient quality of life, a consensus treatment plan remains elusive and is often subject to surgeon and patient bias/preferences. Whether it is better to maximize resection at the risk of damaging the facial nerve, or to intentionally leave a larger residual and treat it with radiosurgery to protect the facial nerve, remains controversial.

An overall tumor progression rate of 15%–20% following VS resection has previously been reported in the literature.[16,17] This is relatively consistent with our cohort, in which 7% of patients saw tumor progression following resection. Facial nerve outcomes, with 82% of patients having good (HB grade I or II) facial nerve function at the last follow-up, are also consistent with those reported by Samii et al. (75%)[18] and Anderson et al. (73%–90%).[19] In a large cohort of 624 patients with a median follow-up of 37 months, Bloch et al. reported that 59% of patients had good facial nerve function at 6 months postoperatively.[20]

In our cohort, a larger preoperative tumor volume was associated with STR, highlighting the technical difficulty in safely achieving GTR in patients with larger tumors. STR, and more specifically STR with residual volume ≥ 0.60 cm^3, was associated with shorter PFS. These data build on earlier studies that have found postoperative tumor volume or EOR to be significant independent predictors for tumor regrowth.[17,21,22] The reason patients with residual tumor < 0.60 cm^3 are less likely to have tumor progression remains unknown. Multiple reasons can be postulated; for instance, one could imagine that disruption

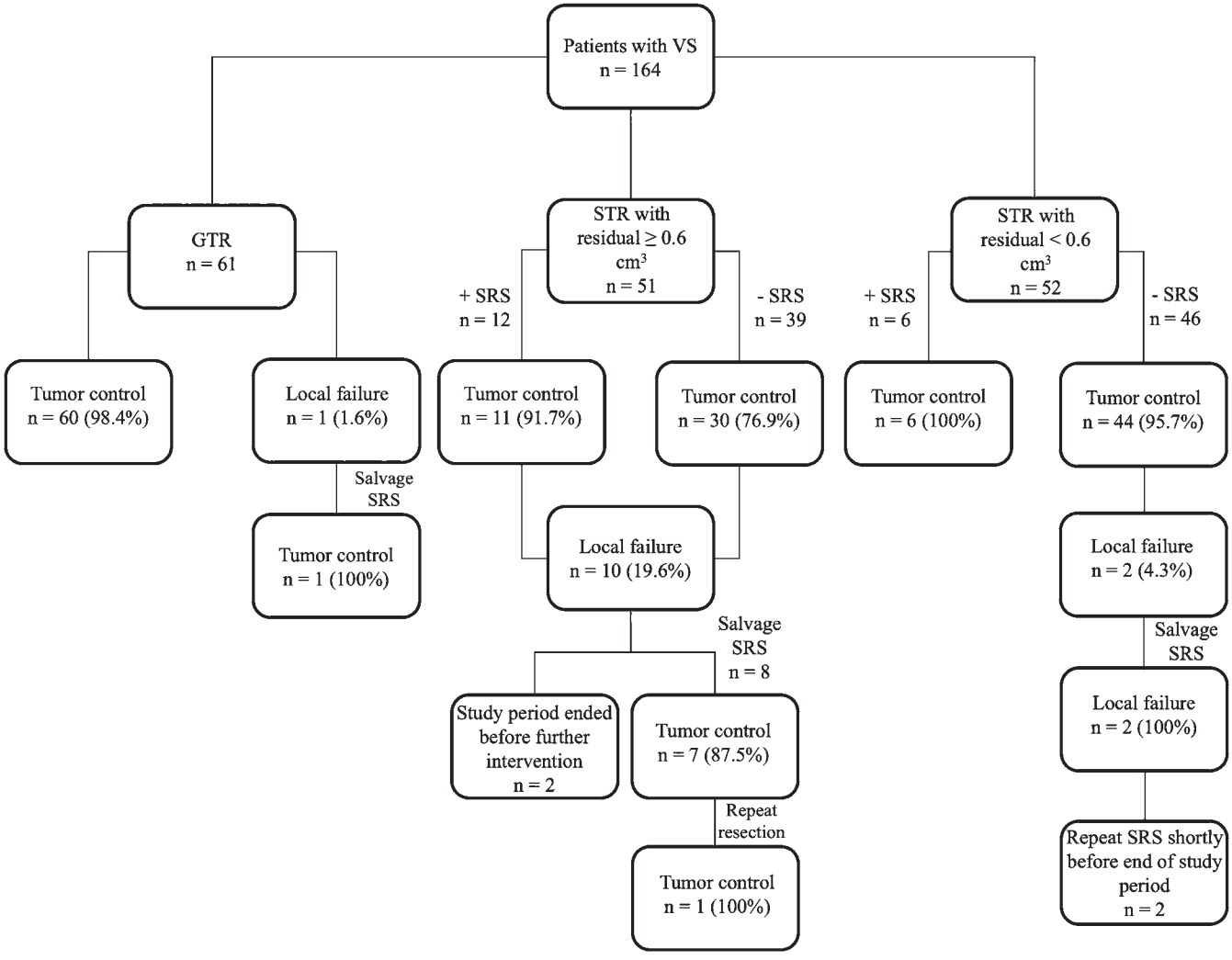

FIG. 3. Flowchart summarizing treatments and outcomes in the overall cohort of 164 VS patients with a median follow-up of 49 months.

of tumor vascular supply could play a role, or that tumor heterogeneity plays a role, where the regions with more proliferative cells are removed with the bulk of the tumor, or simply a volumetric explanation where so few dividing cells remain, that the growth rate of the tumor is so far to the left on an exponential curve that it appears not to grow

TABLE 4. Pre- and postoperative HB scores at a median last clinical follow-up of 58 months in 142 patients with ≥ 12 months of follow-up classified by EOR

	All	GTR	STR	p Value*	<0.60 cm³	≥0.60 cm³	p Value†
Total patients, n	142	53	89		43	46	
Preop HB, n (%)				0.88			0.67
Good (I or II)	138 (97)	51 (96)	87 (98)		41 (95)	45 (98)	
Fair (III or IV)	3 (2)	2 (4)	1 (1)		0	1 (2)	
Poor (V or VI)	1 (1)	0	1 (1)		2 (5)	0	
Postop HB, n (%)				0.27			0.16
Good (I or II)	113 (80)	46 (87)	67 (75)		35 (81)	33 (72)	
Fair (III or IV)	22 (15)	7 (13)	15 (17)		3 (7)	11 (24)	
Poor (V or VI)	7 (5)	0	7 (8)		5 (12)	2 (4)	
Facial nerve worse postop, n (%)	25 (18)	6 (11)	19 (21)	0.17	6 (14)	13 (28)	0.07

* Comparing GTR versus STR.
† Comparing GTR, residual volume < 0.60 cm³, and residual volume ≥ 0.60 cm³.

TABLE 5. Univariate logistic regression of patient and tumor characteristics as predictors of worse facial nerve function at last clinical follow-up in 142 patients with ≥ 12 months of follow-up

Variable	Facial Nerve Stable, n = 117	Facial Nerve Worse, n = 25	OR (95% CI)	Univariate p Value	aOR (95% CI)	Multivariable p Value
Age, yrs	51 (37–61)	51 (37–63)	1.01 (0.98–1.04)	0.51		
Female sex, n (%)	65 (56)	17 (68)	1.8 (0.7–4.7)	0.24		
Previously treated VS, n (%)	12 (10)	6 (24)	3.0 (1.0–9.1)	0.05	3.7 (1.0–12.9)	**0.04**
STR, n (%)*	68 (58)	17 (68)	1.9 (0.7–5.2)	0.20		
STR w/ residual <0.60 cm^3†	36 (53)	11 (65)	0.5 (0.2–1.5)	0.20	0.6 (0.2–2.1)	0.45
EOR, %	97 (91–100)	95 (90–100)	0.99 (0.96–1.04)	0.97		
Preop size, cm^3	5.8 (2.2–11.9)	7.8 (4–19.1)	1.04 (1.00–1.08)	0.07	1.05 (0.99–1.10)	0.10
Residual size, cm^3	0.2 (0–0.7)	0.5 (0–1.1)	1.01 (0.7–1.36)	0.96		
Adjuvant radiosurgery, n (%)	15 (13)	1 (4)	0.3 (0.04–2.4)	0.26		

Continuous variables are presented as median (IQR). Boldface type indicates statistical significance.
* Compared with GTR.
† Compared with STR with residual volume ≥ 0.60 cm^3.

for many years. In patients with residuals ≥ 0.60 cm^3, adjuvant radiosurgery was effective in prolonging PFS. However, adjuvant radiosurgery was not associated with PFS on multivariable Cox regression analysis, while residual volume > 0.60 cm^3 was an independent risk factor for tumor progression. Nevertheless, in the overall cohort, receiving adjuvant SRS rather than adopting a wait-and-scan approach to residual tumors was associated with longer post-SRS PFS compared with salvage SRS administered following treatment failure. Together, these data suggest that while minimizing residual volume is the most important factor in effective tumor control, adjuvant SRS may be more effective than salvage SRS in situations in which significant residual tumor remains. Larger, prospective, and multi-institutional studies with longer follow-up remain necessary to achieve consensus on the optimal timing of postoperative SRS.

Although patients with tumor residual ≥ 0.60 cm^3 did not have statistically significantly worse facial nerve outcomes at a median last follow-up of almost 5 years than patients with smaller residuals, they tended to have worse facial nerve outcomes ($p = 0.07$), and we believe that statistical significance would have been reached with a larger sample size. In a study of 60 patients undergoing VS resection, Strickland et al. reported that patients who underwent near-total resection had a higher likelihood of facial nerve recovery than those who underwent GTR and STR.[7] Similarly, in a larger cohort of 385 patients, Perkins et al. found that although propensity score–matched patients with STR were less likely to have poor facial nerve function at 2–3 weeks postoperatively, there was no significant difference between STR and facial nerve function at the 1-year follow-up.[6] Combined with our data, these studies suggest that a greater extent of VS resection and facial nerve preservation are not mutually exclusive, and they highlight the importance of long follow-ups to determine facial nerve outcomes. Interestingly, on multivariable analyses, prior microsurgical or radiosurgical treatment of the index VS was an independent predictor of worse facial nerve outcomes. This finding agrees with a 2019 review of 145 VS patients who found prior surgical treatment to be associated with long-term facial nerve impairment.[23] Together, these data suggest that patients and surgeons can aim for more aggressive resections without significant long-term impairment of the facial nerve, although the risk of long-term facial nerve impairment may be greater for patients with larger and previously treated VS.

Limitations

Limitations of this study include a relatively small sample size and retrospective design, with all the limitations of any retrospective study. Data on socioeconomic status of our patients, which often plays a role in frequency and quality of primary care and follow-up visits and thus may be an important factor in preoperative tumor volume or access to facial nerve rehabilitation, could not be reliably extrapolated from the electronic medical record and poses an interesting possibility for future studies. Furthermore, given the relatively slow rate of tumor growth of VSs, it would be ideal to only include patients with a minimum of 2 years of follow-up, which was not done in this study due to sample size considerations. The sample size of the present study is limited by underrepresentation in our institutional data warehouse, particularly of patients treated prior to 2009, as the data warehouse generally overrepresents patients who were treated after our institution switched to electronic medical records. As a result, it is likely that the effect sizes of statistically significant findings are overestimated.[24] Future studies should develop multi-institutional cohorts to ensure sufficient statistical power when excluding patients with short follow-up times. Lastly, the accuracy of volumetric calculations may be impacted by differences in imaging protocols such as slice thickness.

Conclusions

After VS resection, residual volume > 0.60 cm^3 was independently associated with progression in our cohort, even when adjuvant radiosurgery was considered. Prior treatment was an independent predictor of worse facial nerve outcomes at last follow-up, but not residual volume < 0.60 cm^3. These data suggest that maximizing EOR dur-

ing VS surgery maximizes freedom from progression. If tumor residual < 0.60 cm^3 cannot be safely achieved, adjuvant radiosurgery can provide excellent tumor long-term control after maximal safe resection.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Magill, Nandoliya. Acquisition of data: Nandoliya, Khazanchi, Winterhalter, Youngblood, Jain, Chandler. Analysis and interpretation of data: Magill, Nandoliya, Winterhalter, Karras, Jain. Drafting the article: Magill, Nandoliya, Khazanchi. Critically revising the article: Magill, Nandoliya, Khazanchi, Winterhalter, Youngblood, Karras, Chandler. Reviewed submitted version of manuscript: Magill, Nandoliya, Youngblood, Sonabend, Chandler. Approved the final version of the manuscript on behalf of all authors: Magill. Statistical analysis: Nandoliya. Administrative/technical/material support: Magill. Study supervision: Magill. Patient care: Sonabend.

Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

Supplementary Figure and Table. https://thejns.org/doi/suppl/10.3171/2024.4.JNS24157.

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