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Salvage Microsurgery Following Failed Primary Radiosurgery in Sporadic Vestibular Schwannoma

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IMPORTANCE Management of sporadic vestibular schwannoma with radiosurgery is becoming increasingly common globally; however, limited data currently characterize patient outcomes in the setting of microsurgical salvage for radiosurgical failure.

OBJECTIVE To describe the clinical outcomes of salvage microsurgery following failed primary stereotactic radiosurgery (SRS) or fractionated stereotactic radiotherapy (FSRT) among patients with sporadic vestibular schwannoma.

DESIGN, SETTING, AND PARTICIPANTS This was a cohort study of adults (≥18 years old) with sporadic vestibular schwannoma who underwent salvage microsurgery following failed primary SRS/FSRT in 7 vestibular schwannoma treatment centers across the US and Norway. Data collection was performed between July 2022 and January 2023, with data analysis performed between January and July 2023.

EXPOSURE Salvage microsurgical tumor resection.

MAIN OUTCOMES AND MEASURES Composite outcome of undergoing less than gross total resection (GTR) or experiencing long-term facial paresis.

RESULTS Among 126 patients, the median (IQR) age at time of salvage microsurgery was 62 (53-70) years, 69 (55%) were female, and 113 of 117 (97%) had tumors that extended into the cerebellopontine angle at time of salvage. Of 125 patients, 96 (76%) underwent primary gamma knife SRS, while 24 (19%) underwent linear accelerator-based SRS; the remaining patients underwent FSRT using other modalities. Postoperative cerebrospinal fluid leak was seen in 15 of 126 patients (12%), hydrocephalus in 8 (6%), symptomatic stroke in 7 (6%), and meningitis in 2 (2%). Each 1-mm increase in cerebellopontine angle tumor size was associated with a 13% increased likelihood of foregoing GTR (64 of 102 patients [63%]) or long-term postoperative House-Brackmann grade higher than I (48 of 102 patients [47%]) (odds ratio, 1.13; 95% CI, 1.04-1.23). Following salvage microsurgery, tumor growth–free survival rates at 1, 3, and 5 years were 97% (95% CI, 94%-100%), 93% (95% CI, 87%-99%), and 91% (95% CI, 84%-98%), respectively.

CONCLUSIONS In this cohort study, more than half of patients who received salvage microsurgery following primary SRS/FSRT underwent less than GTR or experienced some degree of facial paresis long term. These data suggest that the cumulative risk of developing facial paresis following primary SRS/FSRT by the end of the patient's journey with treatment approximates 2.5% to 7.5% when using published primary SRS/FSRT long-term tumor control rates.

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Supplemental content

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A substantial evolution in the management of sporadic vestibular schwannoma has transpired over the past century.[1,2] Driven by improved understanding of disease natural history as well as heightened detection in the post–magnetic resonance imaging era, initial management of newly diagnosed sporadic vestibular schwannoma has undergone a gradual shift toward increasingly conservative management.[3] International population-based studies indicate that most newly diagnosed patients undergo at least an initial period of observation with serial imaging, and among those undergoing definitive treatment, the incidence of cases treated by stereotactic radiosurgery (SRS) has steadily increased over the past 50 years.[4,5]

Durable tumor control is achieved in the majority of patients who undergo primary SRS.[6] Approximately 85% to 95% of patients demonstrate sustained tumor control at 10 years following treatment, although various factors such as radiation modality or tumor growth rate may affect long-term tumor control.[7-10] Importantly, a subset of patients undergoing primary SRS will experience persistent tumor growth beyond expected post-SRS pseudoprogression, and these patients often require salvage with microsurgery,[6] although repeat SRS in select patients has been reported.[11] Secondary to durable long-term tumor control, there exists limited published research on patient outcomes with salvage microsurgery following primary SRS. A recent review identified 17 reports published since 1995, and all except 3 included 20 cases or fewer.[12]

From understanding the aggregate risk of primary SRS to controversial aspects such as whether microsurgery following SRS is more technically challenging, several salient questions surrounding this subset of patients remain. Given the rarity of these cases, an international multi-institutional collaboration was initiated with the primary objective of characterizing postoperative outcomes among patients with sporadic vestibular schwannoma who underwent salvage microsurgery following failed primary SRS or fractionated stereotactic radiotherapy (FSRT).

Key Points

Question What are the long-term risks associated with microsurgical salvage following failed primary radiosurgery in sporadic vestibular schwannoma?

Findings In this cohort study of 126 patients with sporadic vestibular schwannoma who underwent salvage microsurgery following failed primary stereotactic radiosurgery or fractionated stereotactic radiotherapy, more than half underwent less than gross total resection or experienced facial paresis long term. Perioperative complications and tumor growth–free survival rates were also worse than published primary microsurgical resection rates.

Meaning The aggregate risk of facial paresis following primary radiosurgery was higher than the typically quoted 1% or less risk when considering potential tumor control failure and salvage microsurgery, despite only a minority of all treated patients receiving salvage surgery.

Methods

Clinical Data

After obtaining institutional review board approval from each participating center, clinical records were reviewed among adult patients (≥18 years old) with sporadic vestibular schwannoma who underwent SRS or FSRT as initial, primary treatment (with any radiation modality) and subsequently underwent salvage microsurgery for sustained tumor growth and/or advanced refractory symptoms of mass effect. Patient informed consent was not required because this study was classified as secondary use of information (record review only) with an authorization waiver and an assurance that all patient research data would be treated in a confidential manner with the same precautions used to protect patient clinical data. Patients with neurofibromatosis type 2–related schwannomatosis were excluded. Records were reviewed for clinical data surrounding the time of primary and salvage treatment. Audiometric data included word recognition scores (WRSs) and pure-tone averages (PTAs), defined as a PTA in the affected ear at 0.5, 1, 2, and 3 kHz.[13] An average decibel of 2 kHz and 4 kHz was used when 3 kHz testing was not performed.[14] Extent of resection was defined as follows: (1) gross total resection (GTR) was defined as all microscopic disease removed at surgery; (2) near-total resection (NTR) was defined as a 5 × 5 × 2-mm or smaller pad of adherent tumor intentionally left on the facial nerve, brain stem, or vasculature to preserve neurological integrity; and (3) subtotal resection (STR) was defined as anything less than NTR.[15] Hearing class was determined according to the American Academy of Otolaryngology–Head and Neck Surgery hearing class, and tumor size was measured in accordance with the 1995 American Academy of Otolaryngology–Head and Neck Surgery Foundation consensus guidelines.[16] Facial nerve function was graded in accordance with the House-Brackmann (HB) grading system.[17]

Statistical Analysis

Continuous features were summarized with medians and IQRs; categorical features were summarized with frequencies and percentages. Factors associated with NTR/STR, most recent postoperative HB grade I or higher, and the primary combined outcome of NTR/STR or most recent postoperative HB grade I or higher were evaluated using logistic regression models and summarized with odds ratios (ORs) and 95% CIs. Assessments of the functional form of the associations of the continuous features of years from primary SRS/FSRT to surgery, age, cerebellopontine angle (CPA) tumor size, PTA, and WRS with the outcomes studied suggested that years from primary SRS/FSRT to surgery, age, and tumor size could be modeled as continuous, but PTA and WRS could not; as such, PTA was categorized as normal hearing or mild, moderate, severe, or profound hearing loss as 25 or lower, 26 to 39, 40 to 69, 70 to 89, and 90 and higher dB hearing loss, respectively, and WRS was categorized as less than 0% and 0%. Tumor growth–free survival rates following salvage surgery were estimated using the Kaplan-Meier method. Statistical analyses were performed using SAS, version 9.4 (SAS Institute), and R, version 4.2.2 (R Foundation for Statistical Computing). All tests were 2-sided, and $P < .05$ was considered statistically significant.

Results

Among 126 patients who underwent salvage microsurgery following primary SRS/FSRT, median (IQR) age at time of salvage microsurgery was 62 (53-70) years, 69 (55%) were female, and 113 of 117 (97%) had tumors that extended into the CPA (**Table 1**). Of 125 patients, 96 (76%) underwent primary gamma knife SRS, while 24 (19%) underwent linear accelerator–based SRS; the remaining patients underwent FSRT using other modalities. A total of 113 of 125 patients (90%) underwent salvage microsurgery following detection of persistent tumor growth at a median (IQR) of 3.4 (2.6-5.1) years following primary SRS/FSRT. Twelve of 125 patients (10%) had intractable trigeminal neuralgia secondary to mass effect and underwent salvage microsurgery in the absence of tumor growth at a median (IQR) of 4.4 (2.4-8.3) years following primary SRS/FSRT. No patients underwent salvage microsurgery for isolated symptoms of dizziness, tinnitus, or generalized headache. Among 91 patients with available primary SRS/FSRT data who had CPA extension, the median (IQR) increase in CPA tumor size from primary SRS/FSRT to salvage microsurgery was 5.0 (2.7-7.0) mm. The median (IQR) WRS and PTA at time of salvage microsurgery was 0% (0%-10%) and 76 (59-120) dB hearing loss, respectively.

Postoperative complications among the 126 patients included cerebrospinal fluid leak in 15 (12%), development of new hydrocephalus in 8 (6%), symptomatic stroke in 7 (6%), and meningitis in 2 (2%). After a median (IQR) of 2.3 (0.9-6.7) years of follow-up after salvage microsurgery, 113 of the 126 patients studied were alive, 1 had died of complications related to vestibular schwannoma resection (secondary to postoperative intracranial hemorrhage), 9 had died of unrelated causes, and 3 had died of unknown causes.

Facial nerve function at salvage microsurgery and most recent follow-up are summarized in **Table 2**. Of the 104 patients with tumors that extended into the CPA at salvage microsurgery and who had normal facial nerve function prior to salvage, 3 were missing data regarding most recent HB grade. HB grades for the remaining 101 patients were I for 53, II for 24, III for 14, IV for 5, V for 2, and VI for 3 at a median (IQR) duration from salvage surgery to most recent facial nerve assessment of 2.0 (0.4-4.9) years. Of note, 23 of the 35 patients (66%) with less than 1 year of follow-up had HB grade I facial nerve function. In a univariable setting, no feature was found to be associated with HB grade higher than I at last follow-up (eTable 1 in Supplement 1). Among the 4 patients with tumors confined to the internal auditory canal at time of salvage microsurgery, 3 had normal preoperative facial nerve function and demonstrated HB grade I function at last follow-up; the fourth patient had HB grade III function preoperatively but recovered to grade I by last follow-up.

Of the 113 patients with tumors that extended into the CPA at salvage microsurgery, 2 were missing data regarding extent of resection. Extent of resection for the remaining 111 patients included GTR for 41 (37%), NTR for 28 (25%), and STR for 42 (38%). Associations of collected features with NTR/STR can be found in eTable 2 in Supplement 1. The 4 patients with tumors confined to the internal auditory canal at time of salvage microsurgery all underwent GTR.

The primary combined outcome of NTR/STR or most recent postoperative HB grade higher than I could be defined for 102 patients (eTable 3 in Supplement 1), with 33 experiencing NTR/STR, 17 having a most recent postoperative HB grade higher than I, and 31 with both NTR/STR and a most recent postoperative HB grade higher than I. Univariable associations with this combined outcome (81 of 102 [79%]) are summarized in **Table 3**. Each 1-mm increase in CPA tumor size was associated with a 13% increased likelihood of either NTR/STR or most recent postoperative HB grade higher than I (OR, 1.13; 95% CI, 1.04-1.23). As shown in the **Figure**, median (IQR) tumor size at time of salvage was larger for patients experiencing NTR/STR or HB grade higher than I compared with patients with GTR or HB grade I (20.0 [15.0-25.1] mm vs 12.1 [10.2-19.0] mm; difference in medians, 7.9 mm [95% CI, 3.2-12.6 mm]). An association with NTR/STR or HB grade higher than I at last follow-up was observed among female patients (OR, 2.49; 95% CI, 0.93-6.68), patients with macrocystic tumors at time of salvage (OR, 2.76; 95% CI, 0.45-17.04), those with profound hearing loss on PTA (OR, 2.23; 95% CI, 0.43-11.68), patients with preoperative facial numbness (OR, 2.78; 95% CI, 0.86-9.00), and those who underwent retrosigmoid resection for salvage (OR, 2.39; 95% CI, 0.87-6.56). The confidence intervals around the effect sizes for these associations were wide; thus, the estimates are imprecise and no definitive conclusion about the direction or strength of the associations can be made. This last association is confounded by the fact that tumors approached via the retrosigmoid approach were larger than the translabyrinthine group (median [IQR] size, 23 [15-27] mm vs 16 [12-21] mm). After adjusting for CPA tumor size, no other feature under study, including radiation modality used, age, sex, preoperative symptomatology, hearing status, or surgical approach, was independently associated with this combined outcome. Of note, the finding of the positive association between CPA tumor size and the combined outcome of NTR/STR or HB grade higher than I was not changed in a clinically meaningful way if patients with less than 1 year of clinical surveillance postoperatively were excluded (OR for each 1-mm increase in CPA tumor size, 1.13; 95% CI, 1.04-1.24).

Among all 126 patients under study, 117 had information regarding tumor growth following salvage microsurgery. Seven had tumors that demonstrated growth at a median (IQR) of 2.0 (0.4-2.8) years, 3 of whom underwent repeat gamma knife SRS following salvage microsurgery and 2 of whom underwent a second surgery (eTable 4 in Supplement 1). Estimated tumor growth–free survival rates at 1, 3, and 5 years following salvage microsurgery were 97% (95% CI, 94%-100%; 88 patients still at risk), 93% (95% CI, 87%-99%; 56 patients still at risk), and 91% (95% CI, 84%-98%; 40 patients still at risk), respectively.

Table 1. Summary of Study Cohort (N = 126)

Characteristic	No. (%)
Sex	
Female	69 (55)
Male	57 (45)
Age at diagnosis, median (IQR), y (n = 125)	56 (49-63)
Primary SRS/FSRT (n = 125)	
Age at primary SRS/FSRT, median (IQR), y	56 (50-65)
Primary SRS/FSRT modality	
Unfractionated gamma knife	96 (77)
Linear accelerator based	24 (19)
External beam radiation	2 (2)
Other	3 (2)
Salvage microsurgery	
Years from primary SRS/FSRT to surgery, median (IQR)	3.4 (2.6-5.1)
Age at surgery, median (IQR), y	62 (53-70)
Tumor size, mm	
Confined to the IAC (n = 4)[a]	8.5; 11.4; 12.5; 16.0
Extension into CPA (n = 113), median (IQR)	19.0 (13.9-25.0)
Macrocystic tumor (n = 112)	15 (13)
Fundal fluid cap (n = 112)	
Absent	67 (60)
Present	45 (40)
Fundal fluid cap length, median (IQR), mm (n = 45)	4.4 (3.1-6.2)
PTA in decibel hearing loss, median (IQR) (n = 99)	76 (59-120)
≤25	2 (2)
26-39	8 (8)
40-69	29 (29)
70-89	20 (20)
≥90	40 (40)
WRS in %, median (IQR) (n = 102)	0 (0-10)
WRS >0% (n = 102)	28 (27)
Hearing class (n = 100)	
A	5 (5)
B	5 (5)
C	6 (6)
D	84 (84)
Presurgery House-Brackmann grade	
I	115 (91)
II	6 (5)
III	3 (2)
IV	2 (2)
Presurgery complications	
Facial numbness	41 (33)
Facial spasms	27 (21)
Hydrocephalus	9 (7)
Reason for surgery (n = 125)	
Tumor growth	58 (46)
Symptoms	12 (10)
Tumor growth and symptoms	55 (44)
Surgical approach (n = 124)	
Translabyrinthine	66 (53)
Retrosigmoid	56 (45)
Retrolabyrinthine presigmoid	1 (1)
Transcochlear	1 (1)
Extent of surgical resection (n = 123)	
Gross total resection	48 (39)
Near-total resection	30 (24)
Subtotal resection	45 (37)
Salvage microsurgery follow-up complications within 30 d (n = 125)	
Cerebrospinal fluid leak	15 (12)
Other cranial nerve deficit	17 (14)
Hydrocephalus	8 (6)
Stroke	7 (6)
Meningitis	2 (2)
Most recent House-Brackmann grade (n = 123)	
I	62 (50)
II	25 (20)
III	19 (15)
IV	7 (6)
V	4 (3)
VI	6 (5)
Years from surgery to most recent House-Brackmann grade (n = 123)	1.5 (0.4-4.8)

Abbreviations: CPA, cerebellopontine angle; FSRT, fractionated stereotactic radiotherapy; IAC, internal auditory canal; PTA, pure-tone average; SRS, stereotactic radiosurgery; WRS, word recognition score.

[a] All reported because sample size was less than 5.

Discussion

In this multi-institutional international study of salvage microsurgery following failed primary SRS, more than half of patients who received salvage microsurgery following primary SRS/FSRT underwent less than GTR or experienced some degree of facial paresis long term. These data illustrate the reality that salvage microsurgery following failed primary SRS/FSRT is associated with greater morbidity than primary microsurgery, harboring an increased risk of foregoing GTR, long-term facial paresis, further tumor growth, hydrocephalus, and stroke compared with previous studies surrounding primary microsurgery (**Table 4**).[6,18,19] Patients presented for salvage microsurgery at a median of 3.4 years following primary SRS/FSRT, and most had lost functional hearing capacity by time of salvage. Patients consistently exhibited sustained interval tumor growth following primary SRS, with a median of 5 mm of additional tumor growth within the CPA prior to salvage microsurgery.

One of the most clinically salient implications of the current work surrounds the understanding of aggregate risk when undergoing primary SRS. Typically, patients are counseled that long-term facial paresis following primary SRS is rare, occurring in approximately 1% or less of cases when using conventional dose planning.[6,20] Counseling often also includes the notion that, should a patient have unsuccessful SRS, there is likely greater risk associated with surgery. The current study helps to quantify that risk.

For instance, when using published long-term tumor control rates of 85% to 95% following primary SRS,[7-10] the current data illustrate that the aggregate risk of long-term facial

Table 2. Comparison of Presurgery and Most Recent House-Brackmann Grades (N = 126)

	Most recent grade, No.							
Presurgery grade	NA	I	II	III	IV	V	VI	Total
I	3	59	25	18	5	2	3	115
II	0	1	0	1	2	2	1	6
III	0	2	0	0	0	1	1	3
IV	0	0	0	0	0	0	1	2
V	0	0	0	0	0	1	0	0
VI	0	0	0	0	0	0	0	0
Total	3	62	25	19	7	4	6	126

Abbreviation: NA, not available.

Table 3. Univariable Associations for Patients With Cerebellopontine Angle (CPA) Tumors and Normal Preoperative Facial Nerve Function (N = 102)

	Outcome, No. (%)		
Variable	GTR and HB I (n = 21)	NTR/STR or HB >I (n = 81)	Odds ratio (95% CI)
Primary SRS/FSRT modality			
All others	3 (14)	20 (25)	1 [Reference]
Unfractionated gamma knife	18 (86)	61 (75)	0.51 (0.14-1.91)
Years from primary SRS/FSRT to surgery, median (IQR)	3.5 (2.7-5.2)	3.4 (2.6-5.1)	1.03 (0.85-1.24)[a]
Age at surgery, median (IQR), y	58 (55-63)	61 (52-70)	1.23 (0.84-1.78)[b]
Female sex	8 (38)	49 (60)	2.49 (0.93-6.68)
CPA tumor size, mm, median (IQR)	12.1 (10.2-19.0)	20.0 (15.0-25.1)	1.13 (1.04-1.23)[a]
Macrocystic tumor (n = 96)	1 (5)	13 (17)	2.76 (0.45-17.04)
Fundal fluid cap (n = 95)			
Absent	13 (65)	40 (53)	0.62 (0.22-1.72)
Present	7 (35)	35 (47)	1 [Reference]
PTA in decibel hearing loss (n = 84)[c]			
≤39	3 (16)	7 (11)	1 [Reference]
40-69	6 (32)	19 (29)	1.36 (0.27-6.96)
70-89	5 (26)	13 (20)	1.11 (0.20-6.11)
≥90	5 (26)	26 (40)	2.23 (0.43-11.68)
WRS >0% (n = 85)	7 (37)	17 (26)	0.60 (0.20-1.76)
Hearing class (n = 84)			
A/B	2 (11)	8 (12)	1 [Reference]
C/D	17 (89)	57 (88)	0.84 (0.16-4.33)
Presurgery complications			
Facial numbness	4 (19)	32 (40)	2.78 (0.86-9.00)
Facial spasms	6 (29)	14 (17)	0.52 (0.17-1.58)
Hydrocephalus	1 (5)	7 (9)	1.89 (0.22-16.29)
Reason for surgery			
Tumor growth	11 (52)	38 (47)	1 [Reference]
Symptoms	4 (19)	7 (9)	0.51 (0.13-2.05)
Tumor growth and symptoms	6 (29)	36 (44)	1.74 (0.58-5.19)
Surgical approach (n = 100)[d]			
Translabyrinthine	14 (67)	36 (56)	1 [Reference]
Retrosigmoid	7 (33)	43 (54)	2.39 (0.87-6.56)

Abbreviations: FSRT, fractionated stereotactic radiotherapy; GTR, gross total resection; HB, House-Brackmann; NTR, near-total resection; PTA, pure-tone average; SRS, stereotactic radiosurgery; STR, subtotal resection; WRS, word recognition score.

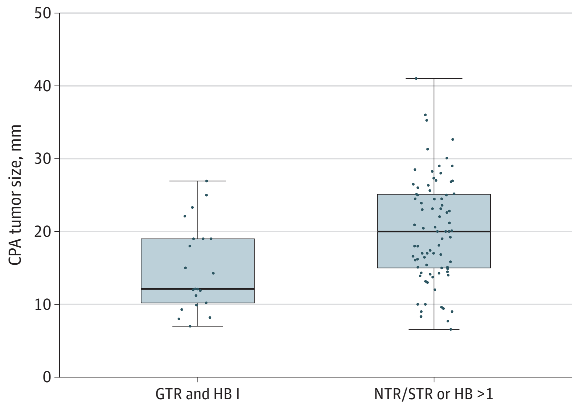
[a] Represents a 1-unit increase in the variable listed.

[b] Represents a 10-unit increase in the variable listed.

[c] PTA groups of 25 dB or lower and 26 to 39 dB were combined for analysis because only 2 patients (both NTR/STR or HB >I) had PTA of 25 dB or lower hearing loss.

[d] Transcochlear was combined with translabyrinthine and retrolabyrinthine presigmoid was excluded for analysis.

Figure. Comparison of Tumor Size Among Patients at Time of Salvage



Box plot comparing tumor size within the cerebellopontine angle (CPA) for patients who underwent gross total resection (GTR) and achieved most recent postoperative House-Brackmann (HB) grade I facial function compared with those who underwent near-total resection (NTR) or subtotal resection (STR) or experienced long-term HB grade higher than I facial function. The 25th and 75th percentiles of tumor size are depicted as the borders of the box surrounding the solid black line indicating the median tumor size, with the whiskers on either end of the box demarcating the range observed. Each dot represents tumor size for an individual patient.

Table 4. Comparison Between Postoperative Outcomes Among Patients Undergoing Primary Microsurgery and Salvage Microsurgery

Outcome	%, Primary microsurgery[a]	%, Salvage microsurgery
Gross total resection	94-98	39
Cerebrospinal fluid leak	9-12	12
Postoperative hydrocephalus	2-4	6
Stroke	2	6
Meningitis	2	2
Long-term facial paresis (HB grade >I)	10	50
Tumor growth ≤5 y after treatment	0-2	9

Abbreviation: HB, House-Brackmann.

[a] Based on estimates from previous publications, including ranges where appropriate.[6,18,19]

paresis when embarking on primary SRS is ultimately closer to 2.5% to 7.5%, as the current study demonstrates that half of patients who underwent salvage microsurgery displayed some degree of facial paresis long term. Stated otherwise, if approximately 10% of patients who undergo primary SRS ultimately have unsuccessful treatment and require salvage microsurgery, the current study demonstrates that half of these patients will harbor some degree of facial weakness long term, rendering the cumulative percentage of patients who end up with facial paresis at the conclusion of their treatment journey following primary SRS approximately 5%. It should be emphasized that this aggregate risk is within the context of conservative surgical resection at time of salvage, with more than 60% of patients in the current study undergoing less than GTR primarily in an effort to preserve neurologic function.

Stemming from these aggregate risk estimates following primary SRS, it is apparent that the long-term risk of facial paresis following primary SRS more closely approximates primary microsurgery than traditionally considered. For instance, when failure occurs following primary microsurgery, salvage SRS likely only increases long-term risk of facial paresis by published estimates of 1% or less.[20,21] Taken together, the aggregate risk of 2.5% to 7.5% long-term facial paresis following primary SRS inclusive of the need for salvage microsurgery more closely resembles the long-term risk of primary microsurgery.[6] With primary microsurgery, the risk of facial paresis is up front, with little added risk in the salvage setting where SRS is most commonly used, whereas the risk associated with primary SRS is long term in the setting where microsurgery is most commonly pursued for salvage. This is furthered by the small subset of patients whose salvage microsurgery may fail and who need a third treatment attempt (5 such cases reported in the current study). Notwithstanding, it is worth emphasizing that these estimates of risk occur on a population-based level, and high-volume gamma knife centers may harbor lower rates of failure following primary SRS, which would decrease the aggregate risk of facial paresis.[7,8,22] For example, assuming a 95% tumor control rate, then 2.5% of patients undergoing primary SRS would ultimately display some degree of facial paresis based on the current study.

One of the most controversial aspects surrounding primary SRS failure is tumor pseudoprogression. Transient tumor enlargement following primary SRS is common within the first 2 to 3 years following treatment.[6] However, when sustained growth persists beyond this duration, patients are typically considered to have experienced a radiosurgical failure, particularly when coinciding with symptomatic mass effect. The expected occurrence of post-SRS tumor swelling creates the opportunity for substantial tumor growth before salvage microsurgery is recommended. The current study illustrates this ramification of expected postradiosurgical tumor pseudoprogression, with the median interval tumor growth following primary SRS/FSRT of 5 mm within the CPA. The current work and prior studies illustrate that tumor size within the CPA constitutes the strongest association with poorer postoperative outcomes,[23,24] with the current study suggesting that every 1-mm increase in CPA tumor size is associated with a 13% increased risk of NTR/STR or long-term facial paresis. When considering continued observation in the setting of growing vestibular schwannoma during wait-and-scan management,[25,26] this finding suggests earlier intervention for a tumor with CPA extension may be preferable, rather than waiting until the upper limit of SRS of 2.5 to 3.0 cm of CPA extension.

Tumor growth following salvage microsurgery exceeds published rates of growth following primary microsurgery.[18,19] The current work demonstrates that 9% of patients exhibited further tumor growth within 5 years of salvage microsurgery. It is likely that the increased rate of NTR/STR in an effort to preserve neurologic function explains this difference between salvage and primary microsurgery. For instance, using a previously published calculator to predict the likelihood of GTR during primary microsurgery,[27] the current cohort—

based on age, CPA size, and presence or absence of a fundal fluid cap—would have an expected likelihood of NTR/STR of 47%, yet the current study harbors 63% with NTR/STR. In this way, additional tumor growth requiring further treatment after salvage expectedly occurs at a higher rate among tumors that have already shown resistance to treatment. Both repeat SRS and a second microsurgical salvage attempt have been successfully pursued to handle further growth following salvage microsurgery, although existing data remain preliminary. The combination of elevated risk of foregoing GTR, long-term facial paresis, hydrocephalus, stroke, and tumor growth collectively illustrate the intuitive assumption that salvage microsurgery following primary SRS is more technically difficult than primary microsurgery, oftentimes associated with dense tumor adherence to surrounding critical neurovascular structures.

Limitations

There are notable limitations of the current work. The study was retrospective in design, and, although describing more patients undergoing salvage microsurgery than prior studies, the current work remains limited in total number of included patients and outcomes. Given the relative rarity of the studied event, a prospective study may prove challenging. Controversy surrounding the potential for long-term differences in patient outcomes among the various SRS platforms remain, and the current work was predominantly composed of patients undergoing primary gamma knife SRS. Patient follow-up after salvage microsurgery was limited to a median of 2.3 years; consequently, only 40 patients had neuroimaging follow-up through 5 years following salvage microsurgery. For this reason, the estimated risk of tumor growth following salvage microsurgery of 9% within 5 years likely underestimates the true long-term risk beyond 5 years. Finally, HB grade was applied based on surgeon assessments preoperatively and postoperatively, which may inherently involve a degree of interpretation bias.

Conclusions

In this cohort study, more than 60% of patients who received salvage microsurgery following primary SRS/FSRT underwent less than GTR, and half ultimately displayed some degree of facial paresis long term. These data should be considered when contextualizing the aggregate risk of primary SRS. For instance, based on the current study, the cumulative risk of developing facial paresis following primary SRS/FSRT by the end of the patient's journey with treatment approximates 2.5% to 7.5% when using published primary SRS/FSRT long-term tumor control rates.

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