An Evidence-Based Vestibular Schwannoma Surgical Outcome Grading Scale for Large-to-Giant Vestibular Schwannomas

Nida Fatima (✉ fnida99@yahoo.com)

House Clinic Inc: House Institute <https://orcid.org/0000-0002-0976-888X>

Gregory P. Lekovic

House Ear Institute: House Institute

Research Article

Keywords: Acoustic Neuroma, Acoustic tumor Grading System, Facial Nerve, Extent of Resection, Vestibular Schwannomas

Posted Date: December 20th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-1167597/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Objectives: The objective of this study was to determine the relationship between facial nerve function and extent of resection (EOR) as outcomes in the surgical management of large vestibular schwannoma (VS) (≥ 2.5 cm maximal) and evaluate use of a new grading system that incorporates both outcomes.

Methods: We conducted a systematic review of the electronic databases using different MeSH terms from 1990 to 2021. 5,623 patients from 56 studies were found appropriate for inclusion in the study. Surgical approach was reported in 5,144 patients, including translabyrinthine approach (TL) in 43.3% (n=2,225), retrosigmoid (RS) approach in 56.3% (n=2,899), retrolabyrinthine (RL) approach in 0.3% (n=16), and extended translabyrinthine (EX) approach in 0.1% (n=4). The proposed VS Grading System defines outcomes of gross total resection (GTR), near total resection (NTR) and subtotal resection (STR) with good facial nerve function [House-Brackmann (HB) Grade I-II] as Classes A, B and C respectively. Those with poor facial nerve outcome (HB III-VI) are graded as Classes D, E and F, respectively.

Results: As expected, patients with STR had a higher likelihood of better facial nerve outcomes (HB I-II) compared to NTR [Odds Ratio (OR): 7.30, 95%CI: 2.45-12.1, $p=0.004$] and GTR (OR: 9.61, 95%CI: 3.61-15.6, $p=0.002$), while NTR had better facial nerve outcome than GTR (OR: 1.5, 95%CI: 1.14-4.6, $p<0.0001$). A Class A result, representing the best possible outcome, was obtained in 55.8% of TL vs. 49.4% undergoing RS approach.

Conclusion: Complete surgical resection with preservation of facial nerve function is the gold standard for large VS.

Introduction

Recently, the paradigm for vestibular schwannoma (VS) surgical treatment has been shifting towards what is sometimes referred to as a “nerve-centered” approach, in which preservation of facial nerve function (and, if possible, hearing) is the most important determinant of good versus poor outcome after surgery.[1–7] With the advancement in microsurgical techniques and neurophysiological monitoring, surgical mortality has been reduced to as low as 0.4% ,with anatomical preservation of facial nerve approaching 100%. [8–10]

Although gross total resection (GTR) is the treatment of choice, near total resection (NTR) or subtotal resection (STR) is warranted in situations where facial nerve function is jeopardized by aggressive resection.[11] Therefore, there is a need to weigh the risk of future tumor growth against the benefit of facial nerve function in terms of extent of resection (EOR). The ideal EOR was historically controversial as Walter Dandy [12] opted for total resection of VS while Harvey Cushing [13] advocated partial resection to reduce morbidity. Further, William House reported in 1968 [14] that partial tumor removal was a

reasonable alternative to total removal among patients who are elderly, have unstable vital signs, or are a poor surgical risk.

We aimed to address how to best evaluate surgical outcomes following resection of large to giant VS in particular. We believe, as do most other authors, that minimizing the risk of injury to facial nerve function is the paramount concern for the VS surgeon, and a post-operative facial nerve palsy is, generally speaking, incompatible with a good outcome overall. It follows that factors that expose the nerve to elevated risk should be avoided when possible. Studies have shown that EOR (usually categorized as GTR, NTR, and STR) is an independent risk factor for facial nerve injury, with the lowest risks of injury associated with STR in most studies [15–17].

What concerns us here is that EOR is most often treated as an independent risk factor for facial nerve outcome but not as a clinically relevant outcome in and of itself. In addition to the risk of facial nerve injury at the time of initial treatment, there is a risk of tumor recurrence with less than total removal, and, if severe enough, requirement for re-treatment with the consequent additional risk of facial or other nerve injury. Hence, the ideal surgical outcome is defined as that in which both risk of injury to facial nerve and tumor recurrence are minimized. Previous studies note that while STR is associated with good facial nerve outcome, it is also associated with higher tumor recurrence rates.[11],[18] Other studies have also shown that EOR is an independent risk factor for tumor recurrence.[11, 15–17] We contend that because EOR is an important proxy for the risk of recurrence, it should be considered as a surgical outcome, albeit secondary in importance to risk of facial nerve injury at the time of treatment.

We performed a systematic review and meta-analysis incorporating large, pooled data sets using double evaluation methods (coupling facial nerve outcome and EOR). The main determinant for good outcomes remains facial nerve function, but our proposed outcome scale distinguishes good surgical outcomes (good facial nerve function and STR) from better and best outcomes (good facial nerve function and NTR, vs GTR, respectively), as well as bad outcomes (GTR with poor facial nerve function) from “worse” and “worst” (NTR and STR with poor facial nerve function, respectively). Based on available data, this meta-analysis demonstrates that a surgical outcome grading scale using both facial nerve function and EOR as one integrated outcome may be useful for setting standard outcome reporting for patients undergoing VS surgery.

Methods

Data search strategy:

We followed the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines for literature search.[19] A detailed systematic review was performed of electronic databases using PubMed, Google Scholar, EMBASE, Medline, The Cochrane library, Scopus, CINAHL, Primary studies and FDA reports, bibliographies of the key articles, and ClinicalTrials.gov for articles published in the English

language between January 1st, 1990 and August 1st, 2021. MeSH terms (using the Boolean operators “and” and “or”) were used.

Inclusion and Exclusion Criteria:

The inclusion and exclusion criterion were based upon the PICOS framework which included, (i) Types of participants: Adult patients who underwent VS surgery for large to giant tumor $\geq 2.5\text{cm}$, (ii) Interventions: Surgical treatment of VS using a variety of surgical approaches, (iii) Control: Not Applicable, (iv) Outcome measures: (a) Facial nerve function graded by the House-Brackmann (HB) scale at 1-year follow-up, (b) EOR (GTR, NTR and STR). Randomized controlled trials (RCTs), prospective cohort studies (PCS), retrospective comparative studies (RCS) and retrospective series were included in our analysis. Case reports and studies without a facial nerve outcome according to extent of resection were excluded. The study components along with inclusion and exclusion criterion are detailed in Table 1.

Data Extraction and Outcome measures:

The data were extracted using a structured template form based on the Cochrane Consumers and Communication Group. The meta-analysis was conducted in accordance with the criteria set by the Cochrane Consumers and Communication Group reviews: Meta-analysis. Both authors reviewed each article, and any disagreement among the authors was resolved by discussion. The following data were extracted from each article: (i) demographic characteristics, (ii) type of surgery (translabrynthine, retrosigmoid, and others), (iii) extent of resection, and (iv) HB grade facial nerve outcome..

Statistical analysis:

Logistic regression analysis was used to measure the odds ratio (OR) and 95% confidence interval (CI) using random effect model. All tests were 2-tailed, and p value < 0.05 was considered statistically significant. SPSS 23 was used to conduct independent sample t-tests and Spearman's coefficient correlation. For the establishment and validation of new grading system, z-test for the difference between two proportions was carried out.

Risk of bias across studies:

The Cochrane Collaboration's tool was used to assess the risk of bias across the included studies, including symmetry of the funnel plots and the Egger test to evaluate publication bias. A non-parametric trim-and-fill procedure identified and corrected for funnel plot asymmetry and re-estimated the aggregate results. The high heterogeneity among studies was further analyzed using funnel plots, which showed asymmetrical distribution. This bias can be attributable to sample size as the removal of smaller-sized cohorts significantly decreased heterogeneity.

Study Selection:

A total of 335 articles were retrieved from the various electronic databases (see Search Strategy in Methods) and reviewed according to PRISMA guidelines. After screening the abstracts, 256 articles were excluded as the data were not related to surgical treatment of large VS or did not present quantitative

results. A total of 79 full text articles were assessed for eligibility, of which 23 were excluded based upon the inclusion and exclusion criteria. The remaining 56 articles were included in this review, including non-RCTs [20][8, 15–17, 21–52, 52–71].

Overall characteristics of the study:

The 56 studies provided a total of 5,623 patients for analysis, of which complete data for surgical approach was available for 5,144 (91.4%) patients. Baseline characteristics of the included studies are presented in Table 2. Surgical approaches included translabyrinthine in 43.3% (n=2,225/5,144), retrosigmoid in 56.3% (n=2,899/5,144), retrolabyrinthine in 0.3% (n=16/5,144), and extended translabyrinthine in 0.1% (n=4/5,144).

Results

Overall, the studies reported EOR in 4,533 (80.6%) patients which included GTR in 83.2% of the patients (n=3,775/4,533), NTR in 3.8% (n=167/4,533) and STR in 13.0% (n=591/4,533).. Good HB facial nerve function was reported among 56.8% (n=2,145/3,775) undergoing GTR, 85.3% (n=111/130, data missing for 37 patients) undergoing NTR, and 84.5% (n=469/555, data missing for 36 patients) undergoing STR .

Facial Nerve Outcome and Extent of Resection as Independent Variables:

There is a higher likelihood of better facial nerve outcomes (HB I-II) compared to near total resection (OR: 7.30, 95%CI: 2.45-12.1, p=0.004) and gross total resection (OR: 9.61, 95%CI: 3.61-15.6, p=0.002), while NTR had better facial nerve outcome than GTR (OR: 1.5, 95%CI: 1.14-4.6, p<0.0001).

Use of the Grading System to compare surgical approaches:

We used the Vestibular Schwannoma Surgical Outcome Grading Scale to perform a non-weighted pooling of cases across those 40 of the 56 studies that included only one surgical approach or the other and used a simple statistical test of the difference between proportions. Overall, TL resulted in good HB function in 64.4% and RS in 57.1% (Z=4.12, $p \leq .0001$). GTR was performed slightly more often by surgeons using RS than TL (91.9% vs 89.6%; Z=2.23, $p \leq .026$). Table 3 presents the results using the grading system that combines EOR and HB facial nerve grade. For all six Grade outcomes, there was a significant difference between TL and RS. TL cases showed a higher rate of Grade A and Grade B results, the two best outcomes, while RS had a higher rate of Grade C outcomes as well as Grade D outcomes. Although percent of cases with Grades E or F were quite small, RS showed slightly lower rates for these two poorest results categories. That is, when a combination of extent of resection and facial nerve function is considered, TL outperformed RS in providing a good facial nerve function outcome with the greatest extent of resection. A further look showed that when GTR was performed, TL had a rate of good HB of 62.2% compared to RS with a rate of 53.7% (Z=4.52, $p \leq .0001$). Although GTR was reported more

often when using RS than TL, good facial nerve results with GTR were more likely with the TL surgical approach. When STR was performed, RS outperformed for good HB result (94.5% vs 74.5%, respectively; $Z=4.11$, $p \leq .0001$). The difference for NTR was not significant.

Table 1
Inclusion and Exclusion criteria's for our study

Study Component	Inclusion	Exclusion
Participants	<ul style="list-style-type: none"> • Adult patients (18 – 80 years old) • Patients with Vestibular Schwannoma • Tumor size ≥ 2.5 cm 	<ul style="list-style-type: none"> • History of previous Tumor resection • Infection • Trauma/Fracture
Intervention	All Vestibular Schwannoma surgeries with good clinical outcome	• Stereotactic radiosurgery and/or radiation therapy alone
Comparators	All Vestibular Schwannoma surgeries with poor clinical outcome	Studies that do not include any patients in whom surgical approaches were not mentioned
Outcomes	<ul style="list-style-type: none"> -Facial Nerve Outcome at 1-year according to House-Brackmann Scale -Extent of resection (Gross Total Resection, Subtotal Resection, and Near Total Resection) 	Studies that did not facial nerve and extent of resection as a potential outcome
Study Design	RCTs, cohort studies, prospective or retrospective studies with ≥ 10 patients per group	<ul style="list-style-type: none"> • In vitro studies, animal studies • Case reports • Comparative studies with <10 patients per treatment group
Publication	<p>Studies published in English in peer reviewed journals, publicly published HTAs or available FDA reports.</p> <p>(Each publication with a full review should be indicated whether or not it is an industry supported study.)</p> <p>Databases to be searched: PubMed, EMBASE, Cochrane, clinical trial.gov</p>	<ul style="list-style-type: none"> • Abstracts, editorials, letters • Duplicate publications of the same study which do not report on different outcomes • Single reports from multicentre trials • Studies reporting on the technical aspects of biologics use in fusion surgery • White papers • Narrative and systematic reviews • Articles identified as preliminary reports when results are published in later versions
Timing	Published in 1990 or later	

Table 2: Baseline Characteristics of all included studies

Author's Name and Year	No. of Pts	Surgical Approach	Degree of Resection	House-Brackman Scale	
				Good Poor	
				I-II	III-VI
Kirkpatrick et al 1993 [20]	16	TL: NA RS: NA EX: NA	GTR: 16 STR: 0 NTR: 0	GTR: 4	GTR: 12
Wu et al. 2000 [75]	40	TL: 40 RS: 0 RL: 0	GTR: 39	GTR: 26	GTR: 13
Jung et al 2000 [22]	30	TL: 0 RS: 30 RL: 0	GTR: 22	GTR: 8	GTR: 14
Sluyter et al 2001 [23]	99	TL: 99 RS: 0 RL: 0	GTR: 91	GTR: 46	GTR: 45
Mamikoglu et al 2002 [24]	81	TL: 81 RS: 0 RL: 0	GTR: 77	GTR: 35	GTR: 42
Lee et al 2002 [25]	36	TL: 0 RS: 36 RL: 0	GTR: 11	GTR: 7	GTR: 4
Iwai et al 2003 [26]	14	TL: 1 RS: 13 EX: 0	STR: 14	STR: 10	STR: 4
Yamakami et al 2004 [27]	50	TL: 0 RS: 50 RL: 0	GTR: 43	GTR: 36	GTR: 7
Roland JT et al 2004 [28]	56	TL: 46 RS: 10	GTR: 35 STR: 6	GTR: 34 STR: 6	GTR: 4 STR: 0

		EX: 0	NTR: 5	NTR: 2	NTR: 3
Sanna et al 2004 [29]	175	TL: 175 RS: 0 RL: 0	GTR: 150	GTR: 52	GTR: 98
Gerganov et al 2005 [30]	18	TL: 0 RS: 18 RL: 0	GTR: 11	GTR: 4	GTR: 7
Darwish et al 2005 [31]	35	TL: 0 RS: 35 RL: 0	GTR: 35	GTR: 7	GTR: 28
Raftopoulos et al 2005 [32]	16	TL: 1 RS: 15 RL: 0	GTR: 11	GTR: 11	GTR: 0
Anderson et al 2005 [33]	71	TL: 50 RS: 21 RL: 0	GTR: 68	GTR: 50	GTR: 18
Zhang X et al 2005 [16]	105	TL: 0 RS: 105 RL: 0	GTR: 91	GTR: 51	GTR: 40
Jain et al 2005 [34]	145	TL: 0 RS: 145 RL: 0	GTR: 142	GTR: 43	GTR: 99
Samii et al 2006 [35]	92	TL: 0 RS: 92 RL: 0	GTR: 88	GTR: 46	GTR: 42
Park et al 2006 [36]	50	TL: 6 RS: 43 RL: 1	GTR: 9 STR: 31 NTR: 8	GTR: 5 STR: 27 NTR: 5	GTR: 4 STR: 4 NTR: 3
Liu et al 2007 [37]	19	TL: 0 RS: 19	GTR: 12	GTR: 8	GTR: 4

		RL: 0			
Yang et al 2008 [38]	110	TL: 0 RS: 110 RL: 0	STR: 61	STR: 58	STR: 3
Fuentes et al 2008 [39]	8	TL: 0 RS: 8 RL: 0	STR: 8	STR: 7	STR: 1
Strauss et al 2008 [40]	10	TL: 0 RS: 10 RL: 0	GTR: 7	GTR: 4	GTR: 3
Chen et al 2009 [8]	39	TL: 0 RS: 39 RL: 0	NR	GTR: 27	GTR: 12
Godefroy WP et al 2009 [41]	50	TL: 50 RS: 0 EX: 0	GTR: 13 STR: 8 NTR: 29	GTR: 9 STR: 8 NTR: 22	GTR: 4 STR: 0 NTR: 7
Samii M et al 2010 [42]	36	TL: 0 RS: 36 EX: 0	GTR: 36 STR: 0 NTR: 0	GTR: 16	GTR: 20
Zhao et al 2010 [43]	89	TL: 0 RS: 89 RL: 0	GTR: 38	GTR: 20	GTR: 18
Talfer et al 2010 [44]	51	TL: 51 RS: 0 RL: 0	GTR: NR	GTR: 25	GTR: 26
Bloch et al 2011 [45]	100	TL: NR RS: NR RL: NR	GTR: NR	GTR: 44	GTR: 56
Di Maio et al 2011 [46]	47	TL: 0 RS: 47	GTR: 41	GTR: 38	GTR: 3

		RL: 0			
Haque et al 2011 [47]	151	TL: NR RS: NR RL: NR	GTR: 55 STR: 96 NTR: 0	GTR: 53 STR: 93 NTR: 0	GTR: 2 STR: 3 NTR: 0
Langenberg RV et al 2011 [48]	42	TL: NR RS: NR EX: 0	GTR: 0 STR: 42 NTR: 0	STR: 34	STR: 16
Nuseir A et al 2011 [49]	232	TL: 226 RS: 2 EX: 4	GTR: 163 STR: 69 NTR: 0	STR: 40	STR: 15
Silva J et al 2012 [50]	29	TL: 0 RS: 29 RL: 0	GTR: 29 STR: 0 NTR: 0	GTR: 13	GTR: 16
Pan et al 2012 [51]	35	TL: NR RS: NR RL: NR	GTR: NR STR: 18 NTR: NR	STR: 16	STR: 2
Zhang Zh. et al 2012 [52]	115	TL: 115 RS: 0 RL: 0	GTR: 103	GTR: 37	GTR: 66
Schwartz M et al 2013 [53]	400	TL: 400 RS: 0 RL: 0	GTR: 325 STR: 31 NTR: 44	GTR: 250 STR: 30 NTR: 43	GTR: 75 STR: 1 NTR: 1
Nonaka et al 2013 [54]	62	TL: NR RS: NR RL: NR	GTR: 28	GTR: 19	GTR: 9
Porter et al 2013 [55]	153	TL: 153 RS: 0 RL: 0	GTR: 55	GTR: 43	GTR: 12
Lim et al 2013 [56]	27	TL: 0 RS: 27	GTR: NR	GTR: 20	GTR: 7

		RL: 0			
Anaizi AN et al 2014 [57]	52	TL: 34 RS: 18 RL: 0	GTR: 17 STR: 23 NTR: 12	GTR: 16 STR: 21 NTR: 11	GTR: 1 STR: 2 NTR: 1
Daming et al 2014 [58]	37	TL: 0 RS: 37 RL: 0	GTR: 35	GTR: 28	GTR: 7
Moffat et al 2014 [59]	145	TL: 137 RS: 8 RL: 0	GTR: NR	GTR: 64	GTR: 81
Iwai et al 2015 [60]	40	TL: 0 RS: 40 RL: 0	STR: 40	STR: 38	STR: 2
Radwan et al 2015 [61]	22	TL: 0 RS: 22 RL: 0	STR: 22	STR: 19	STR: 3
Liu S et al 2015 [62]	106	TL: 0 RS: 106 RL: 0	GTR: 87	GTR: 68	GTR: 19
Turel et al 2016 [63]	179	TL: 0 RS: 179 RL: 0	GTR: 154	GTR: 54	GTR: 100
Monfared et al 2016 [17]	73	TL: NR RS: NR RL: NR	GTR: 12 STR: 39 NTR: 22	GTR: 10 STE: 30 NTR: 18	GTR: 2 STR: 9 NTR: 4
Zhang S et al 2016 [64]	218	TL: 0 RS: 218 RL: 0	GTR: 58	GTR: 34	GTR: 24
Zhang S et al 2016 [71]	186	TL: 186 RS: 0	GTR: 182	GTR: 145	GTR: 37

		RL: 0			
Daniel et al 2017 [15]	32	TL: 0 RS: 32 RL: 0	STR: 32	STR: 32	STR: 0
Huang et al 2017 [65]	657	TL: 0 RS: 657 RL: 0	GTR: 556	GTR: 183	GTR: 373
Boublata et al 2017 [66]	151	TL: 0 RS: 151 RL: 0	GTR: 126	GTR: 103	GTR: 23
Hoshide et al 2018 [67]	45	TL: 0 RS: 45 RL: 0	GTR: 29	GTR: 25	GTR: 4
Breun et al 2019 [68]	320	TL: 0 RS: 320 RL: 0	GTR: 196	GTR: 187	GTR: 9
Grinblat G et al 2020 [69]	389	TL: 374 RS: 0 ET: 15	GTR: 301 STR: 51 NTR: 37	GTR: 102	GTR: 199
Schneider JR et al 2020 [70]	37	TL: 0 RS: 37 RL: 0	GTR: 27 STR: 0 NTR: 10	GTR: 21 STR: 0 NTR: 10	GTR: 6 STR: 0 NTR: 0

TL: Trans-labyrinthine, EX: Extended trans-labyrinthine, RS: Retro sigmoid, GTR: Gross Total Resection, NTR: Near Total Resection, STR: Sub-Total Resection

Table 3. Comparison of translabyrinthine (TL) and retrosigmoid (RS) surgical approaches using new grading system based on 40 studies in which only TL or only RS were used.

Acoustic Neuroma Grading System Outcome	TL N=1198	RS N=2127	Statistical Significance*
Class A (GTR+Good HB)	55.8%	49.4%	Z=3.54, p≤ .0004
Class B (NTR+Good HB)	5.4%	0.5%	Z=9.11, p≤ .0001
Class C (STR+Good HB)	3.2%	7.2%	Z= 4.75, p≤ .0001
Class D (GTR+Poor HB)	33.9%	42.5%	Z= 4.87, p≤ .0001
Class E (NTR+Poor HB)	0.7%	0.0%	Z=3.75, p≤ .0002
Class F (STR+Poor HB)	1.1%	0.4%	Z=2.41, p≤ .016
*Z-test for the difference between two proportions			
GTR=Gross total resection, NTR=Near total resection, STR=Subtotal resection			
Good HB=House-Brackmann facial nerve grade I or II, Poor HB=HB grades III-VI			

Publication Bias:

We found some evidence of publication bias, as suggested by slight asymmetry of the funnel plot

(Egger test, $z=-2.48$; $p = 0.009$) and association between effect sizes and corresponding sampling variances (Begg test, $z=-1.49$; $p = 0.04$). According to the trim-and-fill method to correct for publication bias, the association in terms of clinical outcome was still significant after imputing 2 possible missing studies (adjusted OR: 6.18; 95% CI, 3.46-11.9; $p < 0.0001$), suggesting no potential role for small-study effects or publication bias on the meta-analysis results.

Discussion

The ideal treatment for large VS is complete surgical removal with preservation of facial nerve function. However, these large tumors pose challenges and increase postoperative complication rates compared to smaller VS because patients may present with intracranial hypertension, multiple cranial nerve deficits, and/or signs of brainstem/cerebellum compression. Therefore, the choice of EOR for large VS remains unsettled. Most published studies use facial nerve function alone as the measure of outcome.[33, 41, 45, 53] However, the current study presents and shows the usefulness of a novel surgical outcome scoring system incorporating both EOR and facial nerve function for evaluating the functional outcome in VS surgery.

STR is usually adopted as a nerve-centered approach, hence mostly performed in patients having large tumors adherent to the facial nerve.[72] However, patients with STR have a higher likelihood of tumor regrowth compared to NTR or GTR.[73, 74] GTR is considered to be optimal to prevent tumor recurrence, while NTR also decreases recurrence rate due to the fact that it reduces blood supply or removes critical tumor mass to prevent regrowth. Therefore, the Vestibular Schwannoma Surgical Outcome Grading Scale

presented here takes this into account in defining outcome and may provide a standard method of evaluating surgical outcome among patients with VS worldwide. Hence, Grade A represents the ideal outcome and Grade F the worst outcome obtained from VS surgery for large to giant tumors.

Previous studies have shown that good facial nerve results can be obtained with GTR and NTR. For example, Strickland et al ⁷⁴ reported that patients with NTR achieved better tumor control and higher likelihood of facial nerve recovery compared with STR, while Samii et al [42] reported excellent facial nerve outcome in 75% of patients following GTR of large VS. Our results are consistent with these and other prior reports in that STR is associated with better facial nerve outcomes when looked at in isolation. If we consider, EOR and HB facial nerve grade as independent variables, patients undergoing STR had a higher rate of good facial nerve outcome (61.0%) (Grade C) than NTR (59.9%) (Grade B) and GTR (52.2%) (Grade A). This concurs with a previously conducted meta-analysis by Gurgel et al [11] which found that STR was better than NTR and NTR was significantly better than GTR with regard to facial nerve outcomes. These results, as well as those in the current study, may be confounded by pre-operative HB grade, tumor size, cranial nerve deficits, adherence to facial nerve and other factors for which data were not available by individual patient for the meta-analysis. However, use of a grading system that combines HB grade with EOR can provide a different perspective on overall outcome.

There also remains a question about whether choice of surgical approach makes a difference for optimal facial nerve outcome [11]. The current meta-analysis suggested that the two most common approaches, translabyrinthine and retrosigmoid, were not significantly different when assessing facial nerve outcome or EOR alone. However, a difference could be shown using the new grading system. A further non-weighted pooling of cases across those 40 studies that included only one surgical approach or the other and use of a simple statistical test of the difference between proportions also showed the usefulness of the grading system, with TL outperforming RS in obtaining the two best outcome grades. Results might also be interpreted to suggest that if the surgeon is planning to do a subtotal resection, which is inherently less likely to damage the facial nerve, RS should have a higher proportion of good facial nerve outcome, but if planning to attempt to remove the entire tumor TL will yield better facial nerve results. That is, surgeon intention regarding EOR is a confounder for facial nerve outcome as those not intending on trying to remove the whole tumor will generally be less inclined to go through the longer and more demanding translab approach. A significant caveat here is surgeon/inherent bias as these 40 studies included only surgeries performed by surgeons who preferred and used one surgical technique over the other, so that the differences between surgical approaches is confounded by possible differences between surgeons, their experience, and even possibly their patient populations.

A meta-analysis pools data from different studies and because of that there are a number of potential limitations: (i) inherent bias of the surgeons regarding EOR as well as surgical approach, (ii) variability in tumor size, (iii) degree of resection, (iv) length of follow-up, (v) varying surgical protocols among surgeons worldwide, and (vi) heterogenous populations. In addition, as noted above, it may not be possible in a meta-analysis to account for confounding factors such as pre-operative facial nerve grade, cranial nerve deficits, adherence of tumor to facial nerve or other individual patient risk factors. However,

these are issues that will likely always remain problematic in trying to compare results across different studies of very large VS. Our proposed Acoustic Tumor Grading System would lessen some of the variability in reporting results while taking into account the two most important measures of success.

Conclusion

Complete surgical resection with preservation of facial nerve is the gold standard for large VS. However, a nerve-centered approach using near total and subtotal extent of resection is gaining in prominence. This new proposed grading system may help reduce inconsistencies in reporting of outcomes and help when strategizing management of such patients.

Abbreviations

VS
Vestibular Schwannoma
STR
Subtotal resection
NTR
Near Total Resection
GTR
Gross Total Resection
TL
translabrynthine
RS
RetroSigmoid
RL
Retrolabyrinthine
EX
Extended translabrynthine.

Declarations

Submission Statement: This manuscript is original and has not been submitted elsewhere in part or in whole

Running Title: Vestibular Schwannoma Surgical Outcome Grading Scale

Declarations:

Acknowledgments: None

Funding: None.

Conflict of interest/Competing Interest: None

Ethics Approval: Not required

Availability of data and material: All data generated or analyzed during this study are included in this published article

Consent to Participate: Not Applicable

Consent to Publish: Not Applicable

Authors Contribution: Nida Fatima, Gregory P Lekovic: Manuscript Writing; Gregory P Lekovic, Nida Fatima: Data Collection, Nida Fatima and Gregory P Lekovic: Data/Statistical Analysis; Nida Fatima, Gregory P Lekovic: Editing and Final Revision; Supervision: Gregory P Lekovic

Previous Presentation: None

References

1. Luetje CM, Whittaker CK, Callaway LA, Veraga G, HISTOLOGICAL ACOUSTIC TUMOR INVOLVEMENT OF THE VIIth NERVE AND MULTICENTRIC ORIGIN IN THE VIIIth NERVE (1983) : The Laryngoscope 93:1133-1139. <https://doi.org/10.1288/00005537-198309000-00004>
2. Stangerup S-E, Caye-Thomasen P (2012) Epidemiology and Natural History of Vestibular Schwannomas. Otolaryngol Clin North Am 45:257–268. <https://doi.org/10.1016/j.otc.2011.12.008>
3. Khrais T, Romano G, Sanna M (2008) Nerve origin of vestibular schwannoma: a prospective study. J Laryngol Otol 122:128–131. <https://doi.org/10.1017/S0022215107001028>
4. Tripathi S, Zhang J, Xiong M (2016) Risk factors of microtia: A systematic review and meta-analysis. Eur J Plast Surg 39:335–344. <https://doi.org/10.1007/s00238-016-1196-4>
5. Elsmore AJ, Mendoza ND (2002) The operative learning curve for vestibular schwannoma excision via the retrosigmoid approach. Br J Neurosurg 16:448–455. <https://doi.org/10.1080/0268869021000030249>
6. Samii M, Matthies C (1997) Management of 1000 Vestibular Schwannomas (Acoustic Neuromas): The Facial Nerve-Preservation and Restitution of Function. Neurosurgery 40:684–695. <https://doi.org/10.1097/00006123-199704000-00006>
7. Misra B, Purandare H, Ved R et al (2009) Current treatment strategy in the management of vestibular schwannoma. Neurol India 57:257. <https://doi.org/10.4103/0028-3886.53263>
8. Cheng S, Naidoo Y, da Cruz M, Dexter M (2009) Quality of life in postoperative vestibular schwannoma patients. Laryngoscope 119:2252–2257. <https://doi.org/10.1002/lary.20217>
9. Arriaga MA, Chen DA (2001) Facial Function in Hearing Preservation Acoustic Neuroma Surgery. Arch Otolaryngol Head Neck Surg 127:543. <https://doi.org/10.1001/archotol.127.5.543>

10. Arts HA, Telian SA, El-Kashlan H, Thompson BG (2006) Hearing Preservation and Facial Nerve Outcomes in Vestibular Schwannoma Surgery: Results Using the Middle. Cranial Fossa Approach: *Otology & Neurotology* 27:234–241. <https://doi.org/10.1097/01.mao.0000185153.54457.16>
11. Gurgel RK, Dogru S, Amdur RL, Monfared A (2012) Facial nerve outcomes after surgery for large vestibular schwannomas: do surgical approach and extent of resection matter? *FOC* 33:E16. <https://doi.org/10.3171/2012.7.FOCUS12199>
12. Dandy WE, RESULTS OF REMOVAL OF ACOUSTIC TUMORS BY THE UNILATERAL APPROACH (1941) *Arch Surg* 42:1026. <https://doi.org/10.1001/archsurg.1941.01210120061006>
13. Cushing H (1932) Intracranial Tumor. In: Springfield
14. House WF (1968) Partial tumor removal and recurrence in acoustic tumor surgery. *Arch Otolaryngol* 88:644–654. <https://doi.org/10.1001/archotol.1968.00770010646013>
15. Daniel RT, Tuleasca C, George M et al (2017) Preserving normal facial nerve function and improving hearing outcome in large vestibular schwannomas with a combined approach: planned subtotal resection followed by gamma knife radiosurgery. *Acta Neurochir* 159:1197–1211. <https://doi.org/10.1007/s00701-017-3194-0>
16. Zhang X, Fei Z, Chen Y-J et al (2005) Facial nerve function after excision of large acoustic neuromas via the suboccipital retrosigmoid approach. *Journal of Clinical Neuroscience* 12:405–408. <https://doi.org/10.1016/j.jocn.2004.03.042>
17. Monfared A, Corrales CE, Theodosopoulos PV et al (2016) Facial Nerve Outcome and Tumor Control Rate as a Function of Degree of Resection in Treatment of Large Acoustic Neuromas. *Neurosurgery* 79:194–203. <https://doi.org/10.1227/NEU.0000000000001162>
18. Nakatomi H, Jacob JT, Carlson ML et al (2020) Long-term risk of recurrence and regrowth after gross-total and subtotal resection of sporadic vestibular schwannoma. *J Neurosurg* 133:1052–1058. <https://doi.org/10.3171/2016.11.JNS16498>
19. Moher D, Liberati A, Tetzlaff J, Altman DG (2009) Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *J Clin Epidemiol* 62:1006–1012. <https://doi.org/10.1016/j.jclinepi.2009.06.005>
20. Kirkpatrick PJ, Tierney P, Gleeson MJ, Strong AJ (1993) Acoustic tumour volume and the prediction of facial nerve functional outcome from intraoperative monitoring. *Br J Neurosurg* 7:657–664. <https://doi.org/10.3109/02688699308995095>
21. Wu ZB, Yu CJ, Guan SS (2005) Posterior petrous meningiomas: 82 cases. *J Neurosurg* 102:284–289. <https://doi.org/10.3171/jns.2005.102.2.0284>
22. Jung S, Kang S-S, Kim T-S et al (2000) Current surgical results of retrosigmoid approach in extralarge vestibular schwannomas. *Surg Neurol* 53:370–378. [https://doi.org/10.1016/S0090-3019\(00\)00196-8](https://doi.org/10.1016/S0090-3019(00)00196-8)
23. Sluyter S, Graamans K, Tulleken CAF, Van Veelen CWM (2001) Analysis of the results obtained in 120 patients with large acoustic neuromas surgically treated via the translabyrinthine—transtentorial approach. *J Neurosurg* 94:61–66. <https://doi.org/10.3171/jns.2001.94.1.0061>

24. Mamikoglu B, Wiet RJ, Esquivel CR (2002) Translabyrinthine Approach for the Management of Large and Giant Vestibular Schwannomas. *Otology & Neurotology* 23:224–227. <https://doi.org/10.1097/00129492-200203000-00020>
25. Lee SH, Willcox TO Jr, Buchheit WA (2002) Current Results of the Surgical Management of Acoustic Neuroma. *Skull Base* 12:189–196. <https://doi.org/10.1055/s-2002-35750-1>
26. Iwai Y, Yamanaka K, Ishiguro T (2003) Surgery combined with radiosurgery of large acoustic neuromas. *Surg Neurol* 59:283–289. [https://doi.org/10.1016/S0090-3019\(03\)00025-9](https://doi.org/10.1016/S0090-3019(03)00025-9)
27. Yamakami I (2004) Removal of large acoustic neurinomas (vestibular schwannomas) by the retrosigmoid approach with no mortality and minimal morbidity. *Journal of Neurology, Neurosurgery & Psychiatry* 75:453–458. <https://doi.org/10.1136/jnnp.2003.010827>
28. Roland JT, Fishman AJ, Golfinos JG et al (2004) Cranial Nerve Preservation in Surgery for Large Acoustic Neuromas. *Skull Base* 14:85–90. <https://doi.org/10.1055/s-2004-828699>
29. Sanna M, Russo A, Falcioni M et al (2004) Enlarged Translabyrinthine Approach for the Management of Large and Giant Acoustic Neuromas: A Report of 175 Consecutive Cases. *Ann Otol Rhinol Laryngol* 113:319–328. <https://doi.org/10.1177/000348940411300412>
30. Gerganov VM, Romansky KV, Bussarsky VA et al (2005) Endoscope-Assisted Microsurgery of Large Vestibular Schwannomas. *Minim Invasive Neurosurg* 48:39–43. <https://doi.org/10.1055/s-2004-830171>
31. Darwish BS, Bird PA, Goodisson DW et al ORIGINAL ARTICLE FACIAL NERVE FUNCTION AND HEARING PRESERVATION AFTER. 4
32. Raftopoulos C, Abu Serieh B, Duprez T et al (2005) Microsurgical results with large vestibular schwannomas with preservation of facial and cochlear nerve function as the primary aim. *Acta Neurochir (Wien)* 147:697–706. <https://doi.org/10.1007/s00701-005-0544-0>
33. Anderson DE, Leonetti J, Wind JJ et al (2005) Resection of large vestibular schwannomas: facial nerve preservation in the context of surgical approach and patient-assessed outcome. *J Neurosurg* 102:643–649. <https://doi.org/10.3171/jns.2005.102.4.0643>
34. Jain V, Mehrotra N, Sahu R et al (2005) Surgery of vestibular schwannomas: An institutional experience. *Neurol India* 53:41. <https://doi.org/10.4103/0028-3886.15052>
35. Samii M, Gerganov V, Samii A (2006) Improved preservation of hearing and facial nerve function in vestibular schwannoma surgery via the retrosigmoid approach in a series of 200 patients. *JNS* 105:527–535. <https://doi.org/10.3171/jns.2006.105.4.527>
36. Park C-K, Kim D-C, Park S-H et al (2006) Microhemorrhage, a possible mechanism for cyst formation in vestibular schwannomas. *JNS* 105:576–580. <https://doi.org/10.3171/jns.2006.105.4.576>
37. Liu B, Tian Y, Liu W et al (2007) Intraoperative facial motor evoked potentials monitoring with transcranial electrical stimulation for preservation of facial nerve function in patients with large acoustic neuroma. *Chin Med J (Engl)* 120:323–325
38. Yang I, Sughrue ME, Han SJ et al (2009) Facial nerve preservation after vestibular schwannoma Gamma Knife radiosurgery. *J Neurooncol* 93:41–48. <https://doi.org/10.1007/s11060-009-9842-3>

39. Fuentes S, Arkha Y, Pech-Gourg G et al (2008) Management of Large Vestibular Schwannomas by Combined Surgical Resection and Gamma Knife Radiosurgery.. In: In: Régis J, Roche P-H (eds) Progress in Neurological Surgery. KARGER, Basel, pp 79–82
40. Strauss C, Bischoff B, Romstöck J et al (2008) Hearing preservation in medial vestibular schwannomas. JNS 109:70–76. <https://doi.org/10.3171/JNS/2008/109/7/0070>
41. Godefroy WP, Hoekstra ER, Malessy MJA (2009) Surgery for Large Vestibular Schwannoma: Residual Tumor and Outcome. 30:6
42. Samii M, Gerganov VM, Samii A (2010) Functional outcome after complete surgical removal of giant vestibular schwannomas: Clinical article. JNS 112:860–867. <https://doi.org/10.3171/2009.7.JNS0989>
43. Zhao X, Wang Z, Ji Y et al (2010) Long-term facial nerve function evaluation following surgery for large acoustic neuromas via retrosigmoid transmeatal approach. Acta Neurochir 152:1647–1652. <https://doi.org/10.1007/s00701-010-0705-7>
44. Talfer S, Dutertre G, Conessa C et al (2010) Surgical treatment of large vestibular schwannomas (stages III and IV). European Annals of Otorhinolaryngology, Head and Neck Diseases 127:63–69. <https://doi.org/10.1016/j.anorl.2010.03.003>
45. Bloch O, Sughrue ME, Kaur R et al (2011) Factors associated with preservation of facial nerve function after surgical resection of vestibular schwannoma. J Neurooncol 102:281–286. <https://doi.org/10.1007/s11060-010-0315-5>
46. Di Maio S, Malebranche AD, Westerberg B, Akagami R (2011) Hearing Preservation After Microsurgical Resection of Large Vestibular Schwannomas. Neurosurgery 68:632–640. <https://doi.org/10.1227/NEU.0b013e31820777b1>
47. Haque R, Wojtasiewicz TJ, Gigante PR et al (2011) Efficacy of facial nerve–sparing approach in patients with vestibular schwannomas: Clinical article. JNS 115:917–923. <https://doi.org/10.3171/2011.7.JNS101921>
48. van de Langenberg R, Hanssens PEJ, van Overbeeke JJ et al (2011) Management of large vestibular schwannoma. Part I. Planned subtotal resection followed by Gamma Knife surgery: radiological and clinical aspects: Clinical article. JNS 115:875–884. <https://doi.org/10.3171/2011.6.JNS101958>
49. Nuseir A, Sequino G, De Donato G et al (2012) Surgical management of vestibular schwannoma in elderly patients. Eur Arch Otorhinolaryngol 269:17–23. <https://doi.org/10.1007/s00405-011-1566-2>
50. Silva J, Cerejo A, Duarte F et al (2012) Surgical Removal of Giant Acoustic Neuromas. World Neurosurgery 77:731–735. <https://doi.org/10.1016/j.wneu.2011.08.019>
51. Pan H-C, Sheehan J, Sheu M-L et al (2012) Intracapsular decompression or radical resection followed by Gamma Knife surgery for patients harboring a large vestibular schwannoma: Clinical article. JNS 117:69–77. <https://doi.org/10.3171/2012.6.GKS12697>
52. Zhang Z, Wang Z, Huang Q et al (2012) Removal of Large or Giant Sporadic Vestibular Schwannomas via Translabyrinthine Approach: A Report of 115 Cases. ORL 74:271–277. <https://doi.org/10.1159/000343791>

53. Schwartz MS, Kari E, Strickland BM et al (2013) Evaluation of the Increased Use of Partial Resection of Large Vestibular Schwannomas: Facial Nerve Outcomes and Recurrence/Regrowth Rates. *Otology & Neurotology* 34:1456–1464. <https://doi.org/10.1097/MAO.0b013e3182976552>
54. Nonaka Y, Fukushima T, Watanabe K et al (2013) Contemporary Surgical Management of Vestibular Schwannomas: Analysis of Complications and Lessons Learned Over the Past Decade. *Operative Neurosurgery* 72:ons103–ons115. <https://doi.org/10.1227/NEU.0b013e3182752b05>
55. Porter RG, LaRouere MJ, Kartush JM et al (2013) Improved Facial Nerve Outcomes Using an Evolving Treatment Method for Large Acoustic Neuromas. *Otology & Neurotology* 34:304–310. <https://doi.org/10.1097/MAO.0b013e31827d07d4>
56. Lim SL, Hieng AWS (2013) Review of an 11-year Experience in Retrosigmoid Approach for Treatment of Acoustic Neuromas. 68:6
57. Anaizi AN, Gantwerker EA, Pensak ML, Theodosopoulos PV (2014) Facial Nerve Preservation Surgery for Koos Grade 3 and 4 Vestibular Schwannomas. *Neurosurgery* 75:671–677. <https://doi.org/10.1227/NEU.0000000000000547>
58. Daming C, Yiwen S, Bin Z et al (2014) Large Vestibular Schwannoma Resection Through the Suboccipital Retrosigmoid Keyhole Approach. *Journal of Craniofacial Surgery* 25:463–468. <https://doi.org/10.1097/SCS.0000000000000528>
59. Moffat DA, Parker RA, Hardy DG, Macfarlane R (2014) Factors affecting final facial nerve outcome following vestibular schwannoma surgery. *J Laryngol Otol* 128:406–415. <https://doi.org/10.1017/S0022215114000541>
60. Iwai Y, Ishibashi K, Watanabe Y et al (2015) Functional Preservation After Planned Partial Resection Followed by Gamma Knife Radiosurgery for Large Vestibular Schwannomas. *World Neurosurgery* 84:292–300. <https://doi.org/10.1016/j.wneu.2015.03.012>
61. Radwan H, Eisenberg MB, Sandberg Knisely JP et al (2016) Outcomes in Patients with Vestibular Schwannoma after Subtotal Resection and Adjuvant Radiosurgery. *Stereotact Funct Neurosurg* 94:216–224. <https://doi.org/10.1159/000447520>
62. Liu S, Jiang W, Zhang H et al (2015) Intraoperative neuromonitoring for removal of large vestibular schwannoma: Facial nerve outcome and predictive factors. *Clin Neurol Neurosurg* 133:83–89. <https://doi.org/10.1016/j.clineuro.2015.03.016>
63. Turel M, D'Souza W, Chacko A, Rajshekhar V (2016) Giant vestibular schwannomas: Surgical nuances influencing outcome in 179 patients. *Neurol India* 64:478. <https://doi.org/10.4103/0028-3886.181558>
64. Zhang S, Liu W, Hui X, You C (2016) Surgical Treatment of Giant Vestibular Schwannomas: Facial Nerve Outcome and Tumor Control. *World Neurosurgery* 94:137–144. <https://doi.org/10.1016/j.wneu.2016.06.119>
65. Huang MJ, Kano H, Mousavi SH et al (2017) Stereotactic radiosurgery for recurrent vestibular schwannoma after previous resection. *J Neurosurg* 126:1506–1513. <https://doi.org/10.3171/2016.5.JNS1645>

66. Boublata L, Belahreche M, Ouchtati R et al (2017) Facial Nerve Function and Quality of Resection in Large and Giant Vestibular Schwannomas Surgery Operated By Retrosigmoid Transmeatal Approach in Semi-sitting Position with Intraoperative Facial Nerve Monitoring. *World Neurosurgery* 103:231–240. <https://doi.org/10.1016/j.wneu.2017.02.053>
67. Hoshide R, Faulkner H, Teo M, Teo C (2018) Keyhole retrosigmoid approach for large vestibular schwannomas: strategies to improve outcomes. *NeuroSurg Focus* 44:E2. <https://doi.org/10.3171/2017.11.FOCUS17607>
68. Breun M, Nickl R, Perez J et al (2019) Vestibular Schwannoma Resection in a Consecutive Series of 502 Cases via the Retrosigmoid Approach: Technical Aspects, Complications, and Functional Outcome. *World Neurosurgery* 129:e114–e127. <https://doi.org/10.1016/j.wneu.2019.05.056>
69. Grinblat G, Dandinarasaiah M, Braverman I et al (2021)) “Large and giant vestibular schwannomas: overall outcomes and the factors influencing facial nerve function.. ” *Neurosurg Rev* 44:2119–2131. <https://doi.org/10.1007/s10143-020-01380-6>
70. Schneider JR, Chiluwal AK, Arapi O et al (2020) Near Total Versus Gross Total Resection of Large Vestibular Schwannomas: Facial Nerve Outcome. *Operative Neurosurgery* 19:414–421. <https://doi.org/10.1093/ons/opaa056>
71. Zhang Z, Nguyen Y, Seta DD et al Surgical treatment of sporadic vestibular schwannoma in a series of 1006 patients. 7
72. Starnoni D, Daniel RT, Tuleasca C et al (2018) Systematic review and meta-analysis of the technique of subtotal resection and stereotactic radiosurgery for large vestibular schwannomas: a “nerve-centered” approach. *NeuroSurg Focus* 44:E4. <https://doi.org/10.3171/2017.12.FOCUS17669>
73. Carlson ML, Van Abel KM, Driscoll CL et al (2012) Magnetic resonance imaging surveillance following vestibular schwannoma resection. *Laryngoscope* 122:378–388. <https://doi.org/10.1002/lary.22411>
74. El Kashlan H, Zeitoun H, Arts H et al (2000) Recurrence of acoustic neuroma after incomplete resection. *Am J Otolaryngol* 21:389–392. [https://doi.org/10.1016/S0196-0709\(00\)80049-6](https://doi.org/10.1016/S0196-0709(00)80049-6)
75. Wu H, Sterkers J-M (2000) Translabyrinthine removal of large acoustic neuromas in young adults. *Auris Nasus Larynx* 27:201–205. [https://doi.org/10.1016/S0385-8146\(00\)00057-2](https://doi.org/10.1016/S0385-8146(00)00057-2)

Figures

Figure 1

Electronic Database Search Strategy using PRISMA Guideline