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Neurosurgical Review

ISSN 0344-5607

Neurosurg Rev
DOI 10.1007/s10143-020-01380-6

ONLINE FIRST

Springer

Neurosurgical Review
https://doi.org/10.1007/s10143-020-01380-6

ORIGINAL ARTICLE

"Large and giant vestibular schwannomas: overall outcomes and the factors influencing facial nerve function"

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Received: 29 April 2020 / Revised: 2 August 2020 / Accepted: 24 August 2020

Abstract

(1) To study the overall outcomes of patients surgically treated for large/giant vestibular schwannomas (VSs) and (2) to identify and analyze preoperative and intraoperative prognostic factors influencing facial nerve (FN) outcome. A retrospective clinical study was conducted at a quaternary referral otology and skull-base center. A total of 389 cases were enrolled. The inclusion criteria were patients with tumor > 30 mm undergoing surgery with a minimum follow-up of 12 months. Neurofibromatosis-II, previous radiotherapy, revision surgeries, preoperative FN House-Brackmann (HB) grade > I, partial resections, incomplete records, or those lost to follow-up for a minimum period of 1 year were excluded. In addition, partial resections and cases where FN was sacrificed intraoperatively were also excluded and were analyzed separately. The mean duration of symptoms was 35.4 months, pronounced more in elderly (58.3 months) than in younger individuals (28.4 months). Mean tumor diameter was 36 mm and 52.7% was cystic. Total resection (TR), near total resection (NTR), and subtotal resections (STR) were achieved in 77.4%, 9.5%, and 13.2% of cases, respectively. Regrowth was observed only after STR (19.6%). Good (HB I-II), moderate (HB III), and poor (HB IV-VI) FN functions were observed in 36.8%, 51.7%, and 11.6% cases, respectively. Younger individuals underwent TR in 259 (86.9%) cases against 42 (46.2%) in elderly individuals. Non-total resections (NTR/STR) were performed in 49 (53.8%) cases in elderly as against 39(13.1%) in younger individuals. Good FN outcome was observed in 28 (57.1%) cases of non-total resections in elderly as against 13 (33.3%) cases in younger individuals. On multiple logistic regression analysis, size of the tumor, preoperatively prolonged duration of symptoms, profound deafness, and antero-superiorly located FN with respect to the tumor played a detrimental role in the final facial nerve outcome postoperatively. On the contrary, in large tumors (3–3.9 cm), presence of vertigo/disequilibrium had a relatively better impact on final FN outcome. Partial resections accounted for 41(7.8%) cases and FN was interrupted in 71(13.6%) cases in total. Factors detrimental to better FN outcome were giant VSs (> 4 cm), antero-superiorly located FN intratumorally, preoperatively prolonged duration of symptoms, and profound deafness. In large tumors (3–3.9 cm), presence of vertigo/disequilibrium had a better impact on FN outcome. Understandably, cases with TR in comparison with NTR/STR had worse FN outcomes. In comparison with younger patients, elderly patients underwent higher NTR/STR resulting in better FN outcomes. The above factors can be used as prognosticators for patient counseling and surgical decision making.

Keywords Giant vestibular schwannoma · Facial nerve outcome · Predictive factors

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Introduction

The treatment of vestibular schwannoma (VS) has been a challenge for a century since the days of Cushing and Dandy [12, 15]. Dramatic changes occurred at early 1960s, when by a use of the surgical microscope, a resurrection of the translabyrinthine approach (TLA) occurred, establishing the pathway to the modern neuro-otology [19].

Further progress in neuro-anesthesia, microsurgical refinements, use of intraoperative neurophysiological monitoring

Published online: 29 August 2020

and immense cumulative surgical experience within specialized centers led to shifting from life-savior surgery to the ultimate goals of total tumor resection with functional preservation [16].

The scenario is even more challenging when dealing with tumors measuring > 3 cm, as their outcomes are less optimal [2, 24, 25, 33, 39]. Patients with large/giant VSs are generally symptomatic due to brainstem/cerebellar compression and distension, with their tumor contacting/distorting both trigeminal and lower cranial nerves (LCN) resulting in incoordination, ataxia, trigeminal, or swallowing deficits [2, 25, 39]. In many instances, the plane of cleavage becomes unrecognizable, leaving no option for total tumor removal and strategies adopted are near-total, subtotal, or partial resections with consequent wait-and-scan, revision surgeries, or radiotherapy [7, 22, 34, 39].

Preservation of the FN function during large/giant tumor removal represents a major concern owing to extreme nerve splay and every effort should be made to maintain its proper functionality. Apart from delicate nerve preservation, intraoperative factors such as size, FN positioning, tumoral adherence, cysticity, and type of resection influence the FN outcomes [5, 17, 18, 38, 39, 43, 45, 46]. There are number of studies reporting on possible predictive factors on the FN outcomes, focus being largely directed towards general VSs, irrespective of the tumor size [9, 30].

Hence, the current study was aimed at investigating pre and intraoperative factors influencing the final FN outcome in addition to the analysis of demographics, clinical features, surgical strategies, intraoperative findings, and post-surgical complications and outcomes. An elaborate review of the literature was conducted and its comparison with the current results undertaken.

Materials and methods

A retrospective chart analyzing the review of patients who have been operated for large/giant VSs at a quaternary referral center for otology and lateral skull-base surgery in Italy from February (1989) to March (2017) was conducted.

To analyze the influence of age, two age-dependent categories were defined: younger patients ≤ 65 years and the elderly (> 65 years). The data regarding demographics, laterality, clinical presentation, tumoral characteristics, intraoperative findings, postoperative FN Function (FNF), complications, tumoral growth, revision surgeries, and follow-ups were analyzed and compared between the two age groups categorically.

All patients underwent complete preoperative otoneurologic evaluation. FNF was graded pre- and postoperatively by the House-Brackmann (HB) grading system [20] and was classified into 3 categories: good (HB I-II), moderate (HB III), and poor (HB IV-VI). Results were adherent to the "Consensus Meeting in systems for reporting results in VS" [25].

Surgeries adopted in this series included the following: enlarged TLA with/without transapical extension, transcochlear (TCA), and transotic approach (TOA). Enlarged TLA and the transapical extensions are technical refinements introduced for the treatment of LVS/GVS tumors and include a broad mastoidectomy where bone anterior and posterior to the sigmoid sinus and around the middle fossa is completely removed. The internal auditory canal is exposed 270° (Enlarged TLA) or 300°–360° (transapical extensions). The superior ampullary nerve presents the main anatomic landmark in identification of the FN, which is discovered at the level of superior semicircular canal's ampulla and detached from its bony canal. Tumor debulking is gradually done until the small layer of tumor and capsule is attached to neurovascular structures which lie anteriorly. Once the cleavage plain is found, removal is completed. The incus is disarticulated and removed. The content of the middle ear and eustachian tube is plugged with periosteum.

In the final step, obliteration of the surgical cavity is accomplished by long strips of abdominal fat. The transotic approach represents an anterior prolongation of the enlarged TLA at the expenses of the cochlea. The FN is maintained in place. In the transcochlear approach, posterior re-routing of the FN along with the removal of cochlea is done. In last two approaches, the middle ear is removed and the external auditory canal is closed in two layered blind sac [4].

Intraoperative electromyographic FN neuromonitoring was employed in every case [32]. Until 1990, a pneumatic system called Myo-Alarm (Otolab, Italy) was used and subsequently this system was replaced with an electromyographic system [37, 48]. A pair of subdermal needle electrodes were placed 5 mm apart in the orbicularis oculi and orbicularis oris muscles to allow continuous EMG monitoring of the FNF. Another needle electrode was applied at forehead which acted as a ground electrode. FNF monitoring is useful for mapping of the nerve inside the tumoral mass, thus avoiding surgical trauma on the nerve. It is performed through monopolar and/or bipolar stimulators to determine the function and position of nerve in relation to the tumor.

All patients underwent preoperative gadolinium-enhanced MRI (1.5 T). The preoperative tumor size and postoperative residual size were evaluated by measuring their diameters in two perpendicular directions (in mm). Growth of the residual tumor was determined by the increase in its greatest dimension on follow-up MRI scans [10].

Resections were defined as total removal (TR) when 100% of the tumor was removed. Near-total removal (NTR), subtotal removal (STR), and partial removal (PR) designate the tumoral remnant of < 2%, 2–5%, and > 5%, respectively. This was noted by the surgeon intraoperatively and confirmed at 1-week postoperative MRI.

The inclusion criteria were patients with tumor > 30 mm, according to the largest extra meatal diameter seen in last preoperative MRI, with a minimum follow-up of 12 months. Nineteen cases with preoperative FN grade > HB I including five cases of neurofibromatosis-II, two cases of previous radiotherapy, and twelve cases of revision surgeries along with three cases with incomplete records/lost to follow-up for a minimum period of 1 year were excluded. In addition, partial resections ($n = 41$) and cases where FN was sacrificed intraoperatively ($n = 71$) were also excluded as extremes of the FN results spectrum, however, were included in separate analysis of FNF.

Postoperative MRI was performed at 1 week, 3 months, 12 months, and subsequently once a year or as indicated clinically which has been the protocol followed at our center. Postoperative FN status was assessed at 3 months and again at last follow-up (minimum 1 year).

Review of the literature A review of the last decade literature was performed by a PubMed search using relevant keywords. The demographics, presentation, tumor dimension, approaches, extent of resection, residue, last postoperative FN examination, complication, tumoral regrowth\growth rate, and recurrence/revision rates with follow-up have been tabulated for comparison and analysis. The present study was approved by the institutional review board of the hospital for ethical research and the consent from the patients taken at the time of surgery which includes using patient data for publication as well.

Statistical analysis Data analysis was done using SPSS 24 (IBM, New York) statistical package. Chi-square test was used to measure the significance of the non-parametric data. ANOVA was made useful to analyze the differences among means. Multiple logistic regression analysis was used to identify/locate the factors influencing the final FN outcome. A p value ≤ 0.05 was considered statistically significant (95% confidence interval).

Results

A total of 3252 patients were operated for VS between 1989 and 2017. Of these, 523 were large/giant VSs, constituting 16.1% of surgically managed VSs. A total of 134 patients who failed to meet the inclusion and exclusion criteria were excluded from the study yielding 389 patients for the analysis.

Patient and tumor characteristics ($n = 389$) with operative details (Table 1)

The mean age of the cohort was 48.5 years and ranged from 19 to 83 years. Profound deafness (47.3%) and disequilibrium/vertigo were more pronounced in elderly (83.5%), while younger patients suffered more from tinnitus (75.2%) and both these findings were statistically significant. The mean duration of symptoms was 35.4 months and in comparison with younger patients (28.4 months), elderly reported longer (58.3 months) symptomatology which was statistically significant. Mean tumor diameter was 36 mm, with increased tendency for fundus occupation (89%) and cysticity (68.1%) in elderly, comparing with younger cases with 66.1% and 47.9% respectively ($p < 0.05$). TLA was performed in 374 (96.1%) cases; TO and TC approaches were preferred in 15 (3.9%) cases for more anteriorly positioned tumors with/without cochlear involvement. While TR was achieved in 301 (77.4%) cases, NTR and STR were accomplished in 37 (9.5%) and 51 (13.2%) of cases, respectively.

Factors influencing the final facial nerve outcome ($n = 389$)

Age and the type of resection

Poor FN outcomes (HB IV-VI) among TRs, NTRs, and STRs were observed in 12.3%, 5.4%, and 11.8% respectively.

In comparison with total resections, non-total resections (Table 2) resulted in good (HB I–II) FN outcomes in 46.6% vs 33.9% in TRs. HB III–IV were observed in 66.1% and 53.4% respectively in TRs and non-total resections. This association was statistically significant.

Majority of the younger population i.e., 259 (86.9%) underwent TRs whereas it was only in 42 cases (46.2%) in the elderly population. In the elderly population, good FN outcome was observed in 28 (57.1%) cases of non-total resections as against 33.3% cases in younger population.

Preoperative and intraoperative factors influencing facial nerve function—multiple logistic regression analysis ($n = 389$)

Multiple logistic regression analysis was used on various preoperative and intraoperative parameters suspected to have a role in the final FN outcome (Table 3). Symptom duration of > 51 months, profound deafness, tumor size of ≥ 4 cm, and the antero-superior FN position were related to poor outcome, while the presence of vertigo/disequilibrium resulted in satisfying outcome.

At the last follow-up, mean facial nerve function was HB 2.6, range HB I–VI. Moderate outcomes were achieved in 201 (51.7%), followed by good in 143 (36.8%) and poor in 45

Table 1 Patient and tumor characteristics

	Features	Total, $n = 389$ n (%)	≤ 65 years	> 65 years	p value
Demographics	Mean age, (range 19–83), STDEV	48.5 (± 14.4)	298 (76.6)	91 (23.4)	
	Female	199 (51.2)	145 (48.7)	54 (59.3)	0.74
	Male	190 (48.8)	153 (51.3)	37 (40.7)	
Laterality	Right side	191 (49.1)	144 (48.3)	47 (51.6)	0.579
	Left side	198 (50.9)	154 (51.7)	44 (48.4)	
Signs and symptoms	Hearing loss	352 (90.5)	263 (88.3)	89 (97.8)	
	Progressive	310 (79.7)	228 (76.5)	82 (90.1)	0.02
	SSNHL	39 (10.0)	32 (10.7)	7 (7.7)	
	Fluctuant	3 (0.7)	3 (1.0)	0 (0)	
	Tinnitus	281 (72.2)	224 (75.2)	57 (62.6)	0.019
	Disequilibrium	270 (69.4)	194 (65.1)	76 (83.5)	0.001
CN deficit (other than CN7 and CN8)	LCN	35 (8.9)	28 (9.4)	7 (7.7)	0.639
	Trigeminal n.	301 (77.4)	232 (77.9)	69 (75.8)	
	Abducens n.	15 (3.9)	13 (4.4)	4 (4.4)	
	Headache	83 (21.3)	66 (22.1)	17 (18.7)	0.48
	Hydrocephalus	67 (17.2)	50 (16.7)	17 (18.7)	0.674
	V-P shunt	67 (17.2)	50 (16.7)	17 (18.7)	0.674
Audiometry	Profound HL	94 (24.2)	51 (17.1)	43 (47.3)	0.001
	Other HL**	295 (75.8)	247 (82.9)	48 (52.7)	
	AC-PTA (mean dB)	52.6	49.9	66.0	0.001
	BC-PTA (mean dB)	47.5	44.9	60.5	
	SDS (%) (mean)	68.1	71.2	52.3	
Symptom duration	≤ 1 year n (%)	164 (42.2)	151 (50.7)	17 (18.7)	0.001
	> 1 year n (%)	225 (57.8)	147 (49.3)	74 (81.3)	
	Mean in months, (range)	35.4 (1–240)	28.4 (1–204)	58.3 (1–180)	
Tumor diameter, mean mm, (range), STDEV.		36 (3.1–5.6), (± 0.6)	36 (3.1–5.1)	35 (3.1–5.6)	0.446
< 4 cm, n (%)		278 (71.5)	207 (69.5)	71 (78.0)	0.114
≥ 4 cm, n (%)		111 (28.5)	91 (30.5)	20 (22.0)	
Cysticity n (%)		205 (52.7)	143 (47.9)	62 (68.1)	0.001
Fundus occupied n (%)		278 (71.5)	197 (66.1)	81 (89.0)	0.001
FN position n (%)					
Antero-inferiorly		234 (60.2)	172 (57.7)	62 (68.1)	0.091
Antero-superiorly		147 (37.8)	118 (39.6)	29 (31.9)	
Posterior		8 (2.1)	8 (2.7)	0	
Follow-up (months) mean, (range)		51 (12–248)	51(12–248)	53 (12–203)	0.56

****NS* non-significant, *STDEV* standard deviation; radiologically observed hydrocephalus, PTA-AC, PTA-BC, and SDS were calculated in cases of measurable hearing ($n = 295$). For ≤ 65 years ($n = 247$), > 65 years ($n = 48$)

(11.6%) cases. To sum-up, satisfying FN outcome (HB I-III) was observed in 88.5% of cases.

Facial nerve outcome in partial resections and nerve interruptions (*n* = 523)

Partial resections

Out of the total cohort, 41 (7.8%) cases underwent partial resection. The mean patient age was 62.1 years. The mean tumor diameter was 40 mm; cysticity and fundus occupation were observed in 27 (65.9%) and 33 (80.5%) respectively. Antero-inferior FN position was most found in 27 (65.9%) cases. Intraoperatively, tumor adhered firmly, with no plain of cleavage over the FN in all these 41 cases. Facial nerve was anatomically preserved in all PR cases with the mean HB of 1.7, range HB I–III. Twelve younger patients that underwent the second stage revision surgery after a mean 7.3 months managed to anatomically preserve the FN with the mean final FNF of HB III after a mean follow-up of 14.2 months.

Table 2 Association between type of resection and facial nerve outcome

Type of resection	FN function		p value	95% (CI)	Odds ratio
	Good (HB I-II)	Moderate/poor (HB III-VI)			
Total 301 (77.4%)	102 (33.9)	199 (66.1)	0.035	1.00–1.52	1.238
Non-total* 88 (22.6%)	41 (46.6)	47 (53.4)			
Elderly (> 65 years), ($n = 91$), n (%)			0.036	1.02–5.60	2.400
Total 42 (46.2%)	15 (35.7)	27 (64.3)			
Non-total* 49 (53.8%)	28 (57.1)	21 (42.9)			
Younger (≤ 65 years), ($n = 298$), n (%)			0.565	0.48–2.01	0.989
Total 259 (86.9%)	87 (33.6)	172 (66.4)			
Non-total* 39(13.1%)	13 (33.3)	26 (66.6)			

*Non-total resections here correspond to near-total and sub-total resections. *FN* facial nerve, *HB* House-Brackmann

Facial nerve interruption cases

FN was interrupted in 71 (13.6%) patients of the entire cohort. Among these, the FN was found embedded within tumor in 81.7% and the nerve was atrophic at the root-entry-zone in 16.9%. In the remaining 1.4% cases, the nerve was found to be either posteriorly positioned or the cause could not be ascertained due to the retrospective nature of the study. Depending on proximal-distal stump distance, immediate reconstruction by tension free end to end anastomoses was performed in 9/71 (12.7%) cases or sural nerve cable graft interpositions in 39/71 (54.9%) cases. In 22 cases where the proximal-stump was lacking, the hypoglossal-facial and masseter-nerve-facial anastomosis were subsequently employed in 19/71 (26.7%) and 3/71 (4.2%) of cases within mean time of 4.9 and 6 months, respectively. The 81-year-old patient which FN was involved within tumoral tissue refused subsequent reconstruction. Both end-to-end anastomosis and sural nerve interposition resulted in HB III after 12.9 and 18.4 months respectively. Similarly, hypoglossal-facial and masseter nerve-facial anastomosis recovered to a mean HB 3.3 and HB 2.6, respectively, 14.5 and 12 months after the anastomosis. Overall, a final FNF after FN interruption ($n = 71$) recovered to HB III after a mean of 16.5 months.

Complications ($n = 389$)

Intracranial hematoma was observed in eight (2.0%) cases. In six of them, cerebro-pontine angle (CPA) hematoma with severe tumoral adherence resulted in transient ataxia, with additional transient abducens-palsy in one and consequent hemiplegia in other two cases which were partially rehabilitated. In yet another patient, tumor was surrounded by a huge arachnoid-cyst and subarachnoid hemorrhage at the level of foramen magnum with consequent loss-of-consciousness on the second postoperative-day requiring revision and insertion of a V-P shunt. His transient abducens-palsy resolved within 6 months. Subdural parietal hematoma resulted in transient aphasia for 7 months in yet another case.

Postoperative ataxia was observed in nine (2.3%) cases. In eight cases, it was transient, with a complete resolution in about 7 months. A 72-year-old patient developed permanent ataxia. He underwent STR via transotic approach for a giant (4.5 cm) tumor due to loss of cleavage plane in the brainstem/cerebellum.

CSF leak was observed in fourteen (3.5%) patients. Postoperative CSF rhinorrhea occurred between 2 and 40 days in three, successfully treated by 48-h lumbar drainage in one and middle-ear-obliteration (MEO) in another two cases. CSF wound fistula that appeared within 2–30 days in ten patients was conservatively treated by compressive bandage in half the cases, while the other half had CSF collections in the hypercellular hypotympanum/peri-carotid areas and was managed by MEO. In one case, combined rhinorrhea/wound fistula was resolved by adding more fat in the attic area.

Apart from abovementioned two cases of abducens palsy, nine patients presented with transient diplopia accounting for a total of eleven (2.9%) cases of diplopia, which ultimately resulted in complete resolution within 6 months.

Lower cranial nerve palsy occurred in seven (1.8%) cases. Temporary palsy with complete resolution within 3–7 months was observed in five of them. In one case, a good spontaneous compensation was achieved within a year, while the other case required thyroplasty with satisfactory glottic compensation.

Permanent trigeminal palsy occurred in two (0.5%) patients. In first case, ipsilateral hypoesthesia with anesthesia for warmth developed. In second case, V2 branch neuralgia occurred 8 months postoperatively. MRI revealed mild dysmorphia of V2 which was placed more laterally probably due to the surgically induced fibrosis. Retrosigmoid approach was attempted for its relief but without much success.

One patient of 59-year-old male with giant tumor died after the surgery and intraoperatively abundant arterio-venous malformations were detected which started to bleed profusely. Although hemostasis was achieved, surgery had to be

Table 3 Multiple logistic regression analysis of preoperative and intraoperative prognostic indicators for facial nerve outcome ($n = 389$)

	Factors	HB I–III *n* (%)	HB IV–VI *n* (%)	Odds ratio	*p* value
Age groups (years)	20–29	29 (85.3)	5 (14.7)		
	30–39	77 (88.5)	10 (11.5)	0.35	0.0940
	40–49	87 (90.6)	9 (9.4)	0.61	0.4210
	50–59	68 (89.5)	8 (10.5)	0.98	0.9690
	60–69	59 (85.5)	10 (14.5)	2.61	0.2010
	>= 70	24 (88.9)	3 (11.1)	0.74	0.7600
Side	Left	176 (88.9)	22 (11.1)		
	Right	168 (87.9)	23 (12.0)	0.71	0.3750
Tinnitus	No	92 (85.2)	16 (14.8)		
	Yes	252 (89.7)	29 (10.3)	0.76	0.4880
Vertigo/disequilibrium	No	101 (84.8)	18 (15.2)		
	Yes	243 (90.0)	27 (10.0)	0.26	0.0010*
Symptom duration (mo)	1–10	68 (90.7)	7 (9.3)		
	11–20	73 (82.9)	15 (17.1)	1.29	0.6290
	21–30	53 (91.4)	5 (8.6)	0.65	0.5290
	31–40	40 (86.9)	6 (13.0)	0.52	0.3190
	41–50	28 (96.5)	1 (3.5)	0.10	0.0880
	≥51	82 (88.2)	11 (11.8)	0.28	0.0500*
AC (WHO)	Normal	38 (92.7)	3 (7.3)		
	Mild	51 (92.7)	4 (7.3)	1.02	0.9830
	Moderate	84 (88.4)	11 (11.6)	1.66	0.4290
	Severe	75 (94.9)	4 (5.1)	0.49	0.3960
	Profound	96 (80.7)	23 (19.3)	9.28	0.0060*
Tumor size (cm)	3–3.9	254 (94.4)	15 (5.6)		
	> 4	90 (75)	30 (25)	5.6	0.0001*
Cysticity	Yes	156 (84.8)	28 (15.2)		
	No	188 (91.7)	17 (8.3)	0.49	0.0650
Tumor origin	IVN	323 (88.3)	43 (11.8)		
	IVN + SVN	4 (100)	0	–	–
	SVN	17 (89.5)	2 (10.5)	4.23	0.1470
FN position intra-tumoral	Antero-inferior	218 (93.2)	16 (6.8)		
	Antero-superior	126 (85.7)	21 (14.3)	2.20	0.0168*
	Posterior	7 (87.5)	1 (12.5)	1.94	0.5378

**mo* months, *WHO AC* World Health Organization classification, air-conduction, *IVN* inferior vestibular nerve, *SVN* superior vestibular nerve. $p \leq 0.05$ (statistically significant)

terminated. Postoperative CT scan revealed CPA hematoma, which on exploration was evacuated. He further developed cerebellar edema and died on day seven following surgery.

Abdominal hematoma occurred in ten (2.5%) cases from the site of harvesting fat for obliteration of cavity following enlarged TLA. This resolved within first postoperative week.

Re-growth/recurrence

No recurrences were observed in cases of GTR and NTR after a mean follow-up of 51 and 59 months, respectively. Out of fifty-one cases of STR, forty-one (80.4%) maintained same dimension, while ten (19.6%) cases exhibited varying levels of growth between 2.5 and 6 years postoperatively (mean 3.4 years). Among them, four underwent Gamma knife therapy at 3.5, 4, 2.5, and 3 years which did not show further growth at a follow-up period 10, 4, 1.5, and 0.5 years, respectively; two patients underwent revision surgery, first TO at 2.5 years and second TLA at 4 years after primary surgery. A growth of up to 2 mm was observed in remaining four elderly patients with annual wait-and-scan management with a mean follow-up of 72 months.

On the contrary, regrowth was observed in 23/41 (56.1%) of cases after partial-resections, after a mean of 3.7 years. For the eleven elderly patients, this was a preoperative decision due to age and concomitant comorbidities. Among them, five underwent Gamma knife therapy after a mean of 3 years with tumoral stabilization, and the remaining six cases were managed by annual wait-and-scan policy with a mean follow-up of 3.7 years due to a slight regrowth of about 2 mm. Out of the reminder twelve patients (mean age 53.8, range 27–64 years), whether PR was intraoperatively decided or was a priori planned staged-surgery, ten underwent revision TLA and two TOA after a mean of 7.3 months.

Discussion

Currently, large/giant VSs constituted 16.1% of all operated VSs. However, in some parts of the world like China/India they comprise the majority [24–26].

Although their removal still presents a surgical challenge, the advancements in neuroradiology, neuro-anesthesia, and microsurgical techniques along with carefully selected resection types have significantly led to advanced improvements not only in tumor control rates but also its functional outcomes.

In the literature, the mean tumor re/growth in TR, NTR, and STR rates were 1.4%, 7.5%, and 11.4%, respectively, which were surgically revised in 1.5%, and underwent stereotactic radiosurgery in 4.5% of cases.

Currently, whenever NTR/STRs have been performed, tumors were more adherent to neurovascular structures compared with total resections. We believe it is prudent and logical to leave small piece of tumor behind in NTR/STRs which ultimately will yield excellent long-term result in relation to tumor growth/regrowth rate especially in NTR. To substantiate this fact, in 27.9% cases of NTR, follow-up MRI showed no residual tumor in 4.9 year follow-up period. In STR, however, every fifth tumor remnant exhibited growth after a mean of 3.4 years, seemingly higher rate compared with the literature. Furthermore, non-total resections yielded a significantly higher probability rate for a good FN outcome compared with total resections (Table 2).

On the contrary, when dealing with partial resections, regrowth will occur in more than a half of current cases after a mean of 3.7 years; however, rendering overall optimal FNF results with the mean HB of 1.7, range HB I–III, compared with other resection types (mean HB 2.6, range HB I–VI).

In view of the considerable ambiguity in the reports regarding both extension of resections and terminology of residual as well as non-standardized measurement of tumors, despite having worldwide agreed consensus, the comparison between the studies was unfeasible (Table 4).

In elderly, duration of symptoms was much longer in comparison with younger population (58.3 vs 28.4 months). This fact could presumably be explained by tumor having more time and possibility to grow and adhere to nearby structures, thus becoming more laborious to extirpate. Perhaps because of this, in 54% of elderly, non-total resections were employed in addition to its benign and slow growing nature. Furthermore, in STR, the remnant showed growth only in every fifth case and none in NTRs which only justified the approach adopted. Moreover, these remnant tumors were on wait-and-scan or stereotactic radiosurgery further strengthening the fact not to be too aggressive in elderly and yet achieving the desired results.

On the contrary, in younger patients, 87% achieved TR with only 13% undergoing non-total removals. This could possibly be due to a more pragmatic and aggressive approach adapted since they have many years of life ahead still in them. Again, even in younger individuals who underwent total resections, the facial nerve function did not alter significantly in comparison with non-total resections (Table 2).

Due to a lack of data of vast majority studies regarding the duration of symptoms and age-related differences, the comparison with other studies could not be performed (Table 4).

Multivariate analysis of factors influencing the final FN outcome

Tumor size has been described as a major factor wherein, the functional outcome is inversely proportional to the tumor diameter. Tumors measuring ≥ 4 cm are always more difficult to manage in terms of surgical challenge and complications involved. Predictably, the size of the tumor had an adverse outcome on the facial nerve outcome which is also supported by numerous studies [14, 28, 39].

The type of intra-tumoral FN displacement might be theoretically explained by the nerve of origin of tumor. Tumors growing superiorly from the SVN could displace FN inferiorly. Jacob et al. [23] found that the nerve of origin did not impact FN outcomes while examining the general VS population. In milieu of LVS/GVSs, the situation is even more complex, and it is more likely that the FN position is rather influenced by the direction of ongoing tumoral growth. Therefore, it always seems reasonable to identify the FN at the fundus as the tumor at this level exerts enough pressure and can give some clue to the change of FN direction. Furthermore, by employing the translabyrinthine approach, we facilitate early FN identification not only at the fundus but also at root-entry-zone at the brainstem. It is well agreed that antero-superior displacement of the FN is found to be associated with adverse FN outcome as supported by other studies as well [30, 45, 46].

Prolonged duration of symptom too had an unfavorable impact on the final FN function. This phenomenon is obvious as the size of the tumor keeps increasing in size with increasing duration of the symptoms obviously resulting in worse facial nerve outcomes in these cases.

Table 4 Review of the literature of large and giant vestibular schwannomas

Author, year	No of patients, no of surgery	Age mean, (range)	Signs and symptoms at presentation (%), symptom duration mean (months)	Preop. FN function (%)	Mean tumor dimension (mm), (range), (classification) cysticity (%)	Surgical approach (%)
Mehrotra et al. [28], 2008	62, 62	38.3, (13–78)	Disequilibrium (100), headache (83.8), tinnitus (37.8), papilledema (66.1), trigeminal n. deficit (64.5), (23.6)	HB I + II (90.3), HB III + IV (9.7)	(46), NA, (unspecified) (16.1)	RS (100)
Samii et al. [39] 2010	50, 50	42.1, (19–73)	HL (100), tinnitus (34), trigeminal n. deficit (38), abducens palsy (4), LCN palsy (10), ataxia (64), ICH (26), papilledema (10), (NA)	HB I + II (90), HB III (4), HB IV + V (6)	(44), (41–65) (Tokyo) (NA)	RS (100)
Charpiot et al. [9], 2010	123, 123	46.4, (23–71)	HL (100), disequilibrium (75.9), tinnitus (38.5), headache (33.3), trigeminal n. deficit (4), (NA)	HB I + II (98.4), HB III–VI (1,6)	(> 40), (Koos 3 + 4) (NA)	TLA (100)
Pai et al. [33], 2011	45, 45	43, (16–84)	Ataxia (55,5), trigeminal n. deficit (51,1), (NA)	HB II (4.4), HB IV (2.2)	(41), (35–55), (unspecified) (NA)	RS (100)
Zhang et al. [46], 2012	115, 115	46.8, (11–74)	HL (100), tinnitus (77.4), disequilibrium (30.4), trigeminal n. deficit (64.3), LCN palsy (26.9), headache (72.2), papilledema (53.9), (31,2)	HB I + II (93.9), HB III/IV (4.3), HB V/VI (1.7)	(41.3) (31–70) (Tokyo) (31.3)	TLA (100)
Raslan et al. [36], 2012	47, 75	48.9 (27–89)	HL (100), disequilibrium (51), tinnitus (29.7), headache (25.5), trigeminal n. defi.it (17), hydrocephalus (17), (36)	FN weakness (not clear)	(39), (31–70) (max. transverse diameter) (NA)	RS (40), RS + TLA (60)
Silva et al. [41], 2012	29, 29	45, (14–72)	HL (100), tinnitus (100), trigeminal n. deficit (17), abducens palsy (4), ataxia (28), papilledema (7), LCN palsy (4), (NA)	NA	Mean NA, (40–61), (unspecified) (17.2)	RS (100)
Schwartz et al. [40], 2013	400, 400	45.7, (NA)	HL (91.8), disequilibrium (44.3), tinnitus (73.3), headache (32), trigeminal n. deficit (22.4) (NA)	NA	(32), (25- > 40) (maximum diameter) (NA)	TLA (100)
Anaizi et al. [1], 2014	52, 52	52, (NA)	NA	NA	NA (Koos 3 + 4) (NA)	RS (34,6), TLA (65.4)
Monfared et al. [31], 2015	73, 73	48.7, (19–79)	NA	NA	33 (25-larger) (Tokyo) (34)	RS (29), TLA (71)
Liu et al. [26], 2015	106, 106	48, (19–76)	NA	HB I + II (92.5), HB III (7.5)	38.6 (30–57.4) (Lalwani) (60.4)	RS (100)
Zhang et al. [47], 2016	218, 218	41.8, (15–69)	HL and tinnitus (94.9), ataxia (47.2), disequilibrium (40.8), trigeminal n. deficit (33.5), LCN palsy (12.4), hydrocephalus (39.4), (24.6)	HB I (100)	48.3 (40–65) (Tokyo) (59.6)	RS (100)

Table 4 (continued)

Boublata et al. [6], 2017	151, 151	48.2, (17–78)	HL (41.6), disequilibrium (48.6), tinnitus (34.7), trigeminal n. deficit (20), LCN palsy (2.6), hydrocephalus (33.1), (NA)	HB I (95.4), HB II-VI (4.6)	LVS (61), GVS (39), (31–60)ø, (Tokyo) (6.6)	RS (100)
Huang et al. [21], 2017	657, 657	46.8, (12–80)	HL (100), trigeminal n. deficit (68.9), tinnitus (45.1), disequilibrium (44.6), (NA)	HB I (68.9), HB III + IV (31.1)	(> 40), (NA), (Tokyo) (NA)	RS (100)
Present series	389, 389	48.5 (19–83)	HL (90.5), tinnitus (72.2), disequilibrium (69.4), LCN palsy (8.9), trigeminal n. deficit (77.4), abducens palsy (3.9), headache (21.3), hydrocephalus (17.2), (37.3)	HB I (100)¥	36 (31–56) (Tokyo) (52.7)	TLA (96.1), TCA (0.3), TOA (3.6)

Author, year	Extent of resection (%) definition of residua (mm/%/mm^3)	FN function (%), FN interruption (%)	Complications (%)	Tumor re/growth according extent of resection (%)	Further therapy (%)	FU (month)
Mehrotra et al. [28], 2008	GTR (90.3), NTR/STR (NA) (unspecified)	HB I + II (16), HB III + IV (58), HB V + VI (26), (*n* = 50) (12.9)	Mortality (11.3), I-C hemorrhage (3.2), cerebellar edema (4.8), air-embolism (1.6), MI (1.6), meningitis (6.5), LCN palsy (19.4), CSF leak (33.8), extradural hematoma (1.6)	0	0	NA
Samii et al. [39] 2010	GTR (100)	HB I–III (75), HB IV (19), HB V (6) (8)	LCN palsy (6), I-C hemorrhage (8), cerebellar edema (2), CSF leak (6), epilepsy (2)	0	0	34
Charpiot et al. [9], 2010	GTR (97), NTR (3) (unspecified)	HB I–III (68.5), HB IV–VI (31.5) (4)	Mortality (0.8), cerebellar disturbance (13.8), subdural/epidural hematoma (1.6), lateral sinus thrombosis (0.8), meningitis (1.6), LCN palsy (1.6), 6CN palsy (17.8), CSF leak (6.5), abdominal wound issues (7.3)	0	0	12
Pai et al. [33], 2011	GTR (31.1), NTR (<– 5%) (57.8), STR (> 5%) (11.1)	HB I + II (55.6), HB III + IV (35.6) HB V + VI (8.9) (NA)	Mortality (2.2), ataxia (6.6), CSF leak (2.2), trigeminal n. deficit (2.2)	GTR (0), NTR (42.3), STR (25) ‡	(8.8) revision surgery, (20) SRS	57.5
Zhang et al. [46], 2012	GTR (89.5), NTR (– < 2%) (7.8), STR (– < 5%) (2.6)	HB I + II (35.6), HB III + IV (58,3) HB V + VI (6.1) (12.2)	Mortality (0.9), CPA hematoma (1.7), hemiplegia (0.9), meningitis (0.9), CSF leak (7), LCN palsy (13), abdominal hematoma (1.7)	GTR (1.7), NTR (1.7), STR (0)	(1.7) revision surgery	(12–60) range
Raslan et al. [36], 2012	GTR (65.9), NTR (23.4), STR (10.6), (unspecified)	HB I + II (67.5), HB III–VI (32.5)(10.6)	Pseudo meningocele (8.5), meningitis (4.3), sinus thrombosis (2.1), headache (12.7), hydrocephalus (4.3), intestinal obstruction (2.1) DVT (4.3), wound infection (6.4)	GTR (0), NTR (0), STR (8.5)	(8.5) SRS	30
Silva et al. [41], 2012	GTR (100)	HB I + II (45), HB III (17), HB IV (10), (*n* = 21) (13.8)	CSF leak (13.7), meningitis (7), LCN palsy (3.5), pneumonia (3.5),	0	0	39

Table 4 (continued)

			pseudo meningocele (3.5), permanent visual loss (3.4)			
Schwartz et al. [40], 2013	GTR (81), NTR(< 10 mm) (11), STR (> 10 mm) (7.7)	HB I + II (80.3), HB III (7.2), HB IV-VI (12.6) ($n = 320$) (NA)§	CN neuropathy (2.5), ataxia (2.2), meningitis (0.3), CSF leak (8), wound infection (0.3)	GTR (2.8), NTR (20.8), STR (22.2) ($n = 155$)	(0. 7) SRS, (0.2) revision surgery	(36–60)†
Anaizi et al. [1], 2014	GTR (33), NTR(< 5 mm) (23), STR(> 5 mm) (44)	HB I + II (92.3), HB III (5.7), HB IV-VI (1.9) (0)	NA	GTR (0), NTR (8.3), STR (17.4)	0	33
Monfared et al. [31], 2015	GTR (16), NTR(<−5 mm^3) (30), STR(> 5 mm^3) (54)	HB I + II (81), HB III-VI (19) (NA)	NA	GTR (8.3), NTR (9.1), STR (28.2)	SRS (15), revision surgery (7.1)	38
Liu et al. [26], 2015	GTR (82.1), STR (< 10%) (14.2) PR (10–40%) (3.7)	HB I + II (78.3), HB III (20.7), HB IV (0.7) (0.9)	Transient headache (23.5), transient vertigo (50.9), tinnitus (15.1), unsteady gait (25.5), I-C hemorrhage (2.8), CSF leak (4.7)	GTR (0), STR/PR (100)	0	24
Zhang et al. [47], 2016	GTR (28.6), NTR(< 5 mm) (50.7), STR(5-10 mm) (20.7) ($n = 203$)	HB I + II (73.8)** (0)	Mortality (0.9), Intracranial infection (4.6), I-C hemorrhage (2.8), LCN palsy (1.8), pneumonia + tracheostomy (1.2), CSF leak (0.9), 6CN palsy (0.9), wound infection (0.4)	GTR (3.4), NTR (7.7), STR (23.8)	(9.2) SRS	39.7
Boublata et al. [6], 2017	GTR (82.8), STR (< 10%) (13.9), PR (10–40%)(3.3)	HB I + II (82), HB III (7), HB IV-VI (11) (1.3)	Mortality (1.3), CSF leak (2.6), LCN palsy (2.6), meningitis (1.3), I-C hemorrhage (2.6), trochlear palsy (0.6), 6CN palsy (1.3), cerebellar ataxia (4)	NA	NA	28
Huang et al. [21], 2017	GTR (84.6), NTR (15.1), PR (0.3)***	HB I + II (55.8), HB III (19.8), HB IV-VI (24.4), ($n = 566$) (10.4)	Mortality (0.6), intracranial hematoma (1.2), meningitis (7.6), CSF leak (2.7), LCN palsy (7.5), pneumonia (6.2)	NA	NA	59.6 ($n = 566$)
Present series	GTR (77.4), NTR (<2%) (9.5), STR (2–5%) (13.2) ···	HB I + II (36.8) HB III (51.7), HB IV-VI (11.6) (13.6) ($n = 523$)	Mortality (0.5), I-C hemorrhage/hematoma (2), hemiplegia (0.5), ataxia (2.3), CSF leak (3.5), LCN palsy (1.8) transient abducens palsy (2.9) Permanent trigeminal n. neuralgia (0.5), abdominal hematoma (2.5)	GTR (0), NTR (0), STR (19.6), ······	(0.5) Revision surgery, (1.0) SRS	51

*#‡§†**ø***¥Tokyo Consensus on Systems for Reporting Results 2003, symptom improvement related to hearing preservation only. *FN* facial nerve, *HB* House-Brackmann grading system, *LCN* lower cranial nerves, *NA* non-available, *RS* retrosigmoid, *TLA* trans-labyrinthine, *GTR* gross-total resection, *NTR* near-total resection, *STR* subtotal resection, *I-C* intracranial, *MI* myocardial infarction, *HL* hearing loss, *ICH* intracranial hypertension, *CSF* cerebro-spinal, SRS: stereotactic radiosurgery, *CPA* cerebro-pontine angle. One patient had better hearing postop. In STR out of 5 pts., one died from complications. In the remaining 4 pts., only 1 had tumor growth. 186/400 (46.5%) were 25–30 mm and 24/400 (6%) were > 40 mm; 3 to 5 year follow-up, :no other specified, HB I + II as presumed for favorable outcome, mean value not specified, definition of residual tumor not specified, :no included in the study per exclusion criteria, HB II (5.3), HB III (0.7), HB IV (0.2); *TCA* transcochlear approach, *TOA* transotic approach. ··· Partial resections were excluded per exclusion criteria. Out of 523 LVS/GVS, partial resections were (> 5%) (7.8%); ······ in 56.1% of partial resections, tumor regrowth occurred

Furthermore, preoperative profound deafness too had an adverse outcome as this suggests an advanced disease process affecting cochlear nerve and even cochlea in a considerable few patient. This again indirectly points to the larger tumor to have a role as this can exert pressure on the cochlear nerve resulting in profound deafness over a time.

Presence of preoperative vertigo\disequilibrium had a favorable impact on final FN outcome. This observation might be explained by the fact that vertigo\disequilibrium was encountered more in elderly, who substantially suffered longer and underwent non-total resections in much higher percentage than younger counterpart, contributing to higher rates of satisfying nerve function.

The influence of cysticity is still controversial; however, it is generally agreed that it positively correlates with the tumor diameter, resulting in degeneration/necrosis and cystic formation [8, 11, 13, 27, 42, 44]. The high rate of cysticity (52.7%) presently found does not appear to influence the FN outcome and is in concordance with our previously published study [35].

The employment of NTR/STR strategy in antero-medially positioned cysts by leaving parts of the peripheral, thin-walled cyst over the FN, lower-cranial-nerves, and vasculature is justified as it has not only preserved the nerve functionality but also reduced the morbidity and mortality.

As per variety of the functional FN categorization, only eight out of fourteen (57%) studies (Table 4) concerning satisfying FN outcome (HB I-III) were eligible for comparison with a reported rate of 85.6%, which is in concordance with the current rate of 88.5% [1, 6, 9, 21, 26, 39–41].

Intraoperative facial nerve interruption

FN interruption still presents a significant problem in patients with large/giant VSs. In the review of literature, interruption rate has been reported between 0 and 13.8% (Table 4). In 13.6% ($n = 523$) reported cases, the nerve was lost within the tumoral tissue in 82%. In addition, relatively high current interruption rate might be explained by high cysticity rate (53.2%). Similar findings have been highlighted by Zhang et al. [46], where the FN interruption rate was observed in 22.2% cases of cystic tumors as against 7.6% in non-cystic tumors. Furthermore, Mehrotra et al. [28] stressed that in cases in whom the cystic component was high, the anatomical continuity of the FN could not be preserved due to a lack of well-defined plane between the arachnoid membrane and the thin tumoral capsule.

Complications

Vascular complications can have devastating consequences, mainly caused by increased intracranial pressure leading to loss of consciousness and prompt neurological deficits [4]. The large/giant tumors create larger adhesive tumor-brain interfaces, both over the brainstem and cerebellum. Meticulous care in preserving the arachnoid plane with subpial vessels is crucial in prevention of vascular injuries. Prompt patient awakening ensures early recognition of any neurologic changes and immediate intervention. As a result, the current incidence of intracranial hemorrhage/hematomas was at 2.0%, which is comparable with the others with a mean rate of 2.7% (Table 4).

Among neurological complications, LCN palsy was observed in 1.8% of cases which was mostly transient. In two other patients with permanent palsy, good spontaneous glottic compensation occurred with no requirement for tracheotomy/gastrostomy. The incidence of reported LCN palsy varied greatly between 1.6 and 19.4%. A few series with higher incidence of LCN palsy utilized retrosigmoid approach. However, they dealt with larger tumors with a mean size of 43 mm [28, 39, 41]. On the other hand, two series (Table 4) employed TLA for the similar sized tumors, with extremely varying results (1.6% vs 13%).

Diplopia was reported in three out of fifteen series which varied from 0.9–17.8%. Currently, transient diplopia rate of 2.9% occurred, presumably due to abducent nerve stretching while removing far-anterior tumoral extension which fully recovered within 6 months.

CSF leakage occurred in 3.5% of cases, which is seemingly less, comparing with mean reported rate of 8% in eleven out of fourteen series. The reason for lower incidence could be attributed to meticulous sealing of the petrous bone during the enlarged TLA, as previously described [3–5, 29]. Aptly, there were no reported cases of meningitis in the present series (Table 4).

Drawback of the study As the study is retrospective in nature, the possibility of bias in decision making especially in different age groups is bound to be present unlike in an experimental study design. The present study highlights the experience and principles followed in approaching these tumors in one of the largest skull base centers.

Conclusion

When dealing with large/giant VS microsurgical removal, one must balance between a long-lasting tumor control and maximal retainment of the FN function. Following this philosophy, current results demonstrated zero recurrences in total or near-total resections. In addition, merely a 20% chance of residual re-growth after subtotal resections was achieved along with an overall satisfactory FN outcome of about 90% on a long-term follow-up. Preoperatively longer symptom duration, profound deafness, tumor diameter of ≥4 cm, and antero-superior FN displacement were found to have an adverse influence on the facial nerve outcome after surgery. On the contrary, preoperative vertigo/disequilibrium had a favorable influence on final FN outcome.

Acknowledgments We thank the team of Mrs. Sathi Chakraborty, Director, Tagore Institute, Bengaluru, for agreeing to review the paper for English corrections. We also thank Dr. Shivalingappa Javali, Associate Professor, USM-KLE, International Medical College, Belgaum and Professor, Michael Hopp, Medical statistician, Tel Aviv University, Israel, for performing all the statistical work involved in the paper.

Funding This study is funded by all the members of the Gruppo Otologico, Italy.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical statement The Gruppo Otologico -Institutional Review Board (IRB) has given ethical clearance for this retrospective analysis (GO IRB-182/2020).

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