The Natural History of Facial Schwannomas: A Meta-Analysis of Case Series

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Abstract

Objective This study is to establish predictors of facial paralysis and auditory morbidity secondary to facial schwannomas by assimilating individualized patient data from the literature.

Design A systematic review of the literature was conducted for studies regarding facial schwannomas. Studies were only included if they presented patient level data, House–Brackmann grades, and tumor location by facial nerve segment. Odds ratios (OR) were estimated using generalized linear mixed models.

Main Outcome Measures Facial weakness and hearing loss.

Results Data from 504 patients were collected from 32 studies. The geniculate ganglion was the most common facial nerve segment involved (39.3%). A greater number of facial nerve segments involved was positively associated with both facial weakness and hearing loss, whereas tumor diameter did not correlate with either morbidity. Intratemporal involvement was associated with higher odds of facial weakness (OR = 4.78, $p < 0.001$), intradural involvement was negatively associated with facial weakness (OR = 0.56, $p = 0.004$), and extratemporal involvement was not a predictor of facial weakness (OR = 0.68, $p = 0.27$). The odds of hearing loss increased with more proximal location of the tumor (intradural: OR = 3.26, $p < 0.001$; intratemporal: OR = 0.60, $p = 0.14$; extratemporal: OR = 0.27, $p = 0.01$).

Conclusion The most important factors associated with facial weakness and hearing loss are tumor location and the number of facial nerve segments involved. An understanding of the factors that contribute most heavily to the natural morbidity can help guide the appropriate timing and type of intervention in future cases of facial schwannoma.

Keywords
- facial schwannoma
- facial nerve
- facial palsy
- hearing loss
- parotid neoplasm
- temporal bone neoplasm
- cerebellopontine angle neoplasm

Introduction

Facial schwannomas are benign tumors originating from the myelin producing schwann cell sheath.[1] These tumors are so rare that determining their true incidence has been difficult; however, it is thought to be the most common primary neoplasm of the facial nerve.[2] Schwannomas can be found anywhere along the facial nerve and skip lesions have been described.[3] It can be difficult to distinguish a facial schwannoma from a vestibular schwannoma based on imaging alone, particularly when it involves only the internal auditory canal (IAC) or cerebellopontine angle (CPA). The distinction is primarily made

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based on clinical symptoms.[4] The clinical presentation of facial schwannoma is variable but usually consists of facial weakness, hearing loss, and/or a parotid mass.[2]

Facial schwannomas create a management dilemma because the morbidity of the treatment can be greater than the morbidity of the natural course of disease. Considerable controversy surrounds the treatment of these tumors. Fortunately, most facial schwannomas are slow growing, and many can be observed for years.[5] Growth rates have been reported between 0.4[6] and 2.0 mm/year.[7] This creates a delicate balance when considering the timing and type of treatment. The primary goal of treatment is to preserve facial nerve function for the longest duration possible, unless there are other factors making intervention absolutely necessary.[2]

Historically, the treatment options for facial schwannomas were observation with radiographic surveillance, facial schwannoma decompression, and total resection with nerve grafting. Decompression gives the tumor additional space to grow before the facial nerve becomes compressed. However, it is not a definitive treatment and a resection may eventually be required. Even following grafting, the best possible outcome with total resection is House–Brackmann (HB) grade III.[2] Most facial schwannomas were observed until facial nerve function deteriorated to HB grade IV or worse at which point intervention was considered. More recently, new treatment options and consideration of a new treatment paradigm have emerged. Subtotal resection, or nerve "stripping" surgery, with tumor debulking can be attempted to spare the facial nerve.[1,8–10] Radiation therapy, as with vestibular schwannomas, has also emerged as a treatment option in certain scenarios that avoids operative intervention.[11–13] Regardless of the type of treatment, the timing of the treatment is also controversial. The management discussion varies depending on the location of the tumor due to the variable morbidities of the approaches required.

Several factors make the research to determine a definitive treatment algorithm challenging. First, the rarity of the neoplasm limits the sample size in published case series. This rarity is exacerbated because of the wide variability in anatomic locations of facial schwannomas. For example, intraparotid facial schwannomas are managed completely differently than intradural facial schwannomas. The variability in clinical presentation also plays a part, particularly with regards to facial nerve function and hearing status. A patient with HB grade I will have different treatment options than a patient with HB grade VI.

Our objective in this study is to establish predictors of morbidity secondary to facial schwannomas.

Methods

This study was performed according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) guidelines.[14] The review protocol was registered on PROSPERO (International Prospective Register of Systematic Review) (CRD42016050204). An Institutional Review Board exemption was granted because human subjects were not involved in this study.

Eligibility Criteria

(1) The reference must have data on individual patients, not aggregated data; (2) each patient must have a preintervention HB grade reported; (3) each patient must have the schwannoma location reported by specific facial nerve segment(s) involved; (4) patients must not have had any prior interventions; (5) patients must not have neurofibromatosis type II; (6) the reference must have at least five eligible patients. References were still included if only a portion of patients were eligible; (7) the reference must contain primary data; (8) the same patient must not have been reported multiple times; (9) the reference must be in English.

Search Strategy

To identify relevant studies, searches were performed in PubMed–NCBI (National Center for Biotechnology Information) and Scopus by an academic librarian. The search strategies employed are included in the ►**Appendix A**. Only articles in English were included, and only papers after 1985 were used, as that is when the HB grading system was introduced.[15]

Study Selection and Validation

Two reviewers independently screened each abstract and then evaluated the remaining full articles for eligibility. Discrepancies were resolved by a third reviewer.

Data Abstraction

Information was extracted at two levels, a study level and a patient level. Information extracted from each study included author, year of publication, number of patients, whether the study was restricted to a specific population based on location or facial nerve status, whether it was retrospective or prospective, and the study's level of evidence based on the Oxford Centre for Evidence Based Medicine 2011 criteria.[16] Information extracted from individual patients when available, included gender, age, laterality, symptoms at presentation, tumor location by facial nerve segment(s) involved, tumor diameter, tumor volume, preintervention HB grade, and preintervention hearing status. The hearing status was documented as normal or abnormal because of the variability in reporting. Hearing was considered normal if it was American Academy of Otolaryngology–Head and Neck Surgery Class A.[17] The CPA and IAC segments of the facial nerve were considered intradural; the labyrinthine, geniculate ganglion, tympanic, and mastoid were considered intratemporal; and the parotid segment was considered extratemporal. When more than one paper that met criteria had the same author institution, they were cross referenced to ensure that the same patient was not reported more than once by examining years included and patient details. When a redundancy was seen, the data was omitted from the more recently published study for the applicable patients. The data were entered into an electronic research database (REDCap).[18]

Assessment of Quality and Bias of Individual Studies

The National Institutes of Health's (NIH) Quality Assessment of Case Series Studies[19] was used to evaluate quality and bias

1. Was the study question or objective clearly stated?
2. Was the study population clearly and fully described, including a case definition?
3. Were the cases consecutive?
4. Were the subjects comparable?
5. Was the intervention clearly described?
6. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?
7. Was the length of follow-up adequate?
8. Were the statistical methods well-described?
9. Were the results well-described?

Fig. 1 Criteria for the National Institutes of Health's Quality Assessment of case series studies.[17]

of individual studies. ►**Fig. 1** shows the criteria used in this assessment.

Statistical Methods

Generalized linear mixed effects models were used to examine associations between patient characteristics and HB grade accounting for patient clustering using random intercepts for each article. When proportional odds assumptions were met, univariable ordinal logistic mixed effects regression models were specified for each predictor and a cumulative logit link was used to estimate the odds ratios (OR) and 95% confidence intervals (CI). For those models for which the proportional odds assumption was violated, HB grade was collapsed into 1 to 2 versus 3 to 6 and a binomial distribution was specified for the outcome using a logit link. These HB grade groupings were chosen because of their implications for treatment since the best possible outcome following total resection with grafting is HB grade III.[2]

Separate generalized linear mixed effects models were used to estimate the odds of preoperative hearing loss as a function of univariable preoperative patient characteristics. As with facial weakness, to account for patient clustering, random intercepts were assigned to each article. A binomial distribution was specified for each model and a logit link was used to estimate the OR and its 95% CI. All analyses were performed using SAS Version 9.4 (Cary, NC, U.S.A).

Results

Study Selection

A total of 605 studies were identified from the PubMed and Scopus searches. After duplicates were removed, 458 abstracts were screened. After implementation of our selection criteria, 396 studies were excluded based on their abstracts. The remaining 62 full articles were reviewed and 32 studies fulfilled all criteria for inclusion. The reasons for exclusion of studies are listed in ►**Fig. 2**.

Study Characteristics

The studies that met inclusion criteria were published between 2000 and 2016. ►**Table 1** describes the characteristics of each study. A total of 504 patients were included. Preintervention hearing status was described in 18 references and 254 patients. There were 189 patients where the tumor diameter was recorded and 35 patients where the volume was recorded, but none of those studies had multiple preintervention time points to document growth rates. Age was reported for 378 patients, gender in 364 patients, and laterality in 119 patients. Per the inclusion criteria, all patients had documented HB grades and tumor location by facial nerve segment. The assessment of quality and bias for each study was recorded in ►**Table 2**.

Epidemiology

Demographic data, for the patients in which it was recorded, are listed in ►**Table 3**. ►**Fig. 3** shows the age distribution of patients by decade of life. The minimum age is 13 months and the maximum age is 87 years old. ►**Table 4** shows location characteristics of facial schwannomas by segment and site for all patients included in this study. ►**Table 5** shows the same location characteristics but it excludes studies that

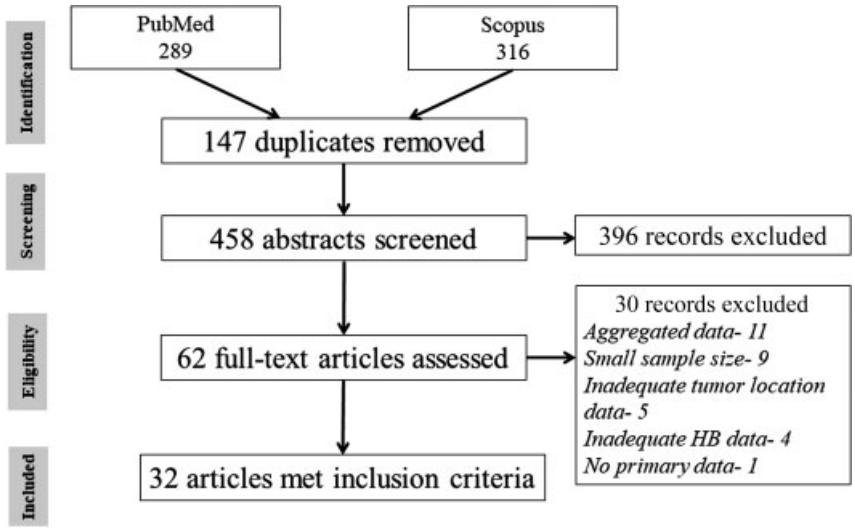


Fig. 2 Study selection process and reasons for exclusion.

Table 1 Study characteristics

Ref.	First author	PY	HL	SP	Type of SP	Pts in study	Pts used	Reason for pt removal
20	Zheng	2016	No	Yes	Parotid only	28	28	
8	Sun	2015	Yes	Yes	Favorable FN function	18	14	Redundant patients from other study
21	Xiang	2015	Yes	Yes	Favorable FN function	19	19	
9	Lu	2015	Yes	Yes	Poor FN function	17	17	
5	Yang	2015	Yes	Yes	Favorable FN function	21	21	
22	Doshi	2015	No	No		26	26	
11	Fezeu	2015	Yes	No		5	5	
12	Moon	2014	Yes	No		14	9	Prior treatment
1	Park	2014	Yes	No		28	28	
23	Bacciu	2014	Yes	Yes	CPA/IAC only	23	23	
24	Li	2014	Yes	No		15	15	
25	Lee	2013	No	Yes	Parotid only	15	15	
26	Bacciu	2013	Yes	Yes	Complex cases only with specific criteria	13	13	
27	Li	2012	No	Yes	Parotid only	7	7	
28	Gross	2012	No	Yes	Parotid only	15	15	
29	Mowry	2012	Yes	Yes	CPA/IAC only	16	11	Inadequate location data
30	Lee	2011	No	No		25	25	
31	Günther	2010	Yes	No		26	26	
32	Bäck	2010	No	No	Parotid only	10	5	Inadequate location data
33	Guzzo	2009	No	Yes	Parotid only	8	8	
34	McMonagle	2008	No	No		53	52	Inadequate location data
35	Kohmura	2007	Yes	Yes	CPA/IAC only	6	6	
36	Lee JD	2007	Yes	Yes	Favorable FN function	6	6	
37	Kida	2007	Yes	No		14	6	Prior treatment–7, NF2–1
38	Litre	2007	No	No		11	9	Prior treatment
6	Perez	2005	Yes	Yes	Intratemporal only	24	24	
39	Minovi	2004	No	No		11	11	
40	Chung	2004	Yes	No		8	8	
10	Nadeau	2003	No	Yes	CPA/IAC only	7	7	
41	Kim	2003	No	Yes	Intratemporal only	18	18	
42	Liu	2001	No	No		22	22	
43	Chong	2000	Yes	Yes	Parotid only	5	5	

Abbreviations: CPA, cerebellopontine angle; FN, facial nerve; HL, documented hearing loss; IAC, internal auditory canal; NF2, neurofibromatosis type 2; Pts, patients; PY, publication year; Ref., reference number; SP, specific populations.

selected patients from specific populations based on location or facial nerve function. Presenting symptoms were described in 401 patients and their frequencies are listed in ►**Table 6**. The most common presenting symptom for intradural facial schwannoma was hearing loss, for intratemporal tumor was facial weakness, and for extratemporal tumor was a parotid mass. Average tumor diameter was 21.3 +/− 12.0 mm ($n = 189$) and average tumor volume was 4,167 +/− 8,387 mm^3 ($n = 35$). An effort was made to collect data for tumor growth, but unfortunately there were not enough tumor sizes reported at multiple time points for meaningful results to be reported. The average number of facial nerve segments involved was 2.15 +/− 1.29 segments.

Facial Weakness

►**Table 7** shows the analysis of factors associated with facial weakness. Demographics, such as gender, age, and laterality were not predictors of facial weakness. Hearing status also

Table 2 Assessment of quality and individual bias for individual studies based on the Oxford Centre for Evidence Based Medicine 2011 criteria (OCEBM)[16] and the Standardized Risk Assessment of Individual Studies based on the NIH Quality Assessment Tool for case series studies.[19]

Ref.	First author	PY	P/R	OCEBM	1	2	3	4	5	6	7	8	9
[20]	Zheng	2016	R	4	Y	Y	Y	Y	Y	Y	Y	Y	Y
[8]	Sun	2015	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[21]	Xiang	2015	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[8]	Lu	2015	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[5]	Yang	2015	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[22]	Doshi	2015	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[11]	Fezeu	2015	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[12]	Moon	2014	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[1]	Park	2014	R	4	Y	Y	Y	Y	Y	Y	Y	Y	Y
[23]	Bacciu	2014	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[24]	Li	2014	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[25]	Lee	2013	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[26]	Bacciu	2013	R	4	Y	Y	N	Y	Y	Y	Y	NA	Y
[27]	Li	2012	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[28]	Gross	2012	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[29]	Mowry	2012	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[30]	Lee	2011	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[31]	Gunther	2010	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[32]	Back	2010	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[33]	Guzzo	2009	R	4	Y	Y	N	Y	Y	Y	Y	NA	Y
[34]	McMonagle	2008	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[35]	Kohmura	2007	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[36]	Lee	2007	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[37]	Kida	2007	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[38]	Liter	2007	P	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[6]	Perez	2005	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[39]	Minovi	2004	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[40]	Chung	2004	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[10]	Nadeau	2003	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[41]	Kim	2003	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y
[42]	Liu	2001	R	4	N	Y	Y	Y	Y	Y	Y	NA	Y
[43]	Chong	2000	R	4	Y	Y	Y	Y	Y	Y	Y	NA	Y

Abbreviations: N, no; NA, not applicable; NIH, National Institutes of Health; P, prospective; PY, publication year; R, retrospective; Ref., reference number; Y, yes.
Note: Numbers are based on questions from ►**Fig. 1**.

did not predict the development of facial weakness. Interestingly, tumor diameter was not a predictor, but the total number of facial nerve segments involved is positively associated with a higher HB grade.

Table 3 Patient demographics

Age ($n = 378$)	43.7 +/− 14.8 y old
Gender ($n = 364$)	44.8% male; 55.2% female
Laterality ($n = 119$)	46.2% left; 53.8% right

The location of the facial schwannoma had a major impact on the likelihood of facial weakness. Intradural and extratemporal facial schwannomas had a low incidence of facial weakness, whereas intratemporal tumors had a high incidence of facial weakness. ►**Fig. 4** shows[44] the likelihood of a higher HB grade by facial nerve segment.

Hearing Loss

►**Table 8** shows the analysis of factors associated with hearing loss. Gender and laterality were not predictors of hearing loss. Older age was correlated with hearing loss. As

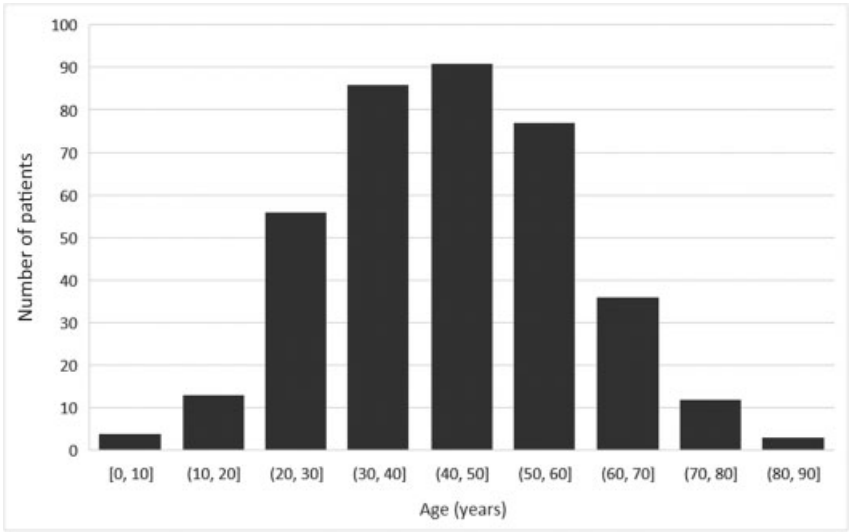


Fig. 3 Patient ages at presentation ($n = 378$).

Table 4 Tumor location by facial nerve segment involvement and sites with all studies included ($n = 504$)

Segments involved	*n*	%
CPA	119	23.6%
IAC	185	36.7%
Labyrinthine	127	25.2%
GG	198	39.3%
Tympanic	181	35.9%
Mastoid	147	29.2%
Parotid	127	25.2%
No. of segments involved	*n*	%
1	197	39.1%
2	161	31.9%
3	64	12.7%
4	52	10.3%
5	18	3.6%
6	9	1.8%
7	3	0.6%
Sites involved	*n*	%
Intradural	217	43.1%
Intratemporal	309	61.3%
Extratemporal	127	25.2%
No. of sites involved	*n*	%
1	361	71.6%
2	137	27.2%
3	6	1.2%

Abbreviations: CPA, cerebellopontine angle; GG, geniculate ganglion; IAC, internal auditory canal; No., number.

Table 5 Tumor location by facial nerve segment involvement and sites with studies focusing on specific populations excluded ($n = 247$)

Segments involved	*n*	%
CPA	68	27.5%
IAC	105	42.5%
Labyrinthine	81	32.8%
GG	121	49.0%
Tympanic	114	46.2%
Mastoid	80	32.4%
Parotid	34	13.8%
No. of segments involved	*n*	%
1	80	32.4%
2	69	27.9%
3	40	16.2%
4	37	15.0%
5	11	4.5%
6	8	3.2%
7	2	0.8%
Sites involved	*n*	%
Intradural	123	49.8%
Intratemporal	177	71.7%
Extratemporal	34	13.8%
No. of sites involved	*n*	%
1	165	66.8%
2	77	31.2%
3	5	2.0%

Abbreviations: CPA, cerebellopontine angle; GG, geniculate ganglion; IAC, internal auditory canal; No., number.

Table 6 Frequencies of presenting symptoms ($n = 401$).

Presenting symptom	Frequency
Facial palsy	51.2%
HB 1	48.8%
HB 2	15.1%
HB 3	15.3%
HB 4	5.8%
HB 5	7.3%
HB 6	7.7%
HL	43.1%
Sensorineural HL	53.3%
Conductive HL	42.7%
Mixed HL	4.0%
Tinnitus	21.7%
Vertigo/imbalance	20.2%
Parotid mass	18.7%
Facial spasm	5.2%
Facial pain	3.2%
Otalgia	3.0%
Aural fullness	1.7%
Otoscopic finding	1.2%
Dysgeusia	1.0%
Hypesthesia	1.0%
Otorrhea	0.5%
Headaches	0.5%
Incidental finding	0.5%
Hyperlacrimation	0.5%
Xerophthalmia	0.3%

Abbreviations: HB, House–Brackmann grade; HL, hearing loss.

Table 7 Predictors of a higher House–Brackmann grade

	n	Odds Ratio (95% CI)	*p*
Demographics			
Sex (female vs. male)	364	1.13 (0.73–1.75)	0.59
Age (y, older)	378	0.99 (0.97–1.00)	0.05
Laterality (left vs. right)	119	2.31 (0.99–5.37)	0.05
Hearing (abnormal vs. normal)[a]	254	0.97 (0.55–1.72)	0.92
Tumor extent			
Tumor diameter (mm)	93	0.95 (0.89–1.01)	0.10
Facial nerve segments involved	504	1.40 (1.20–1.63)	< 0.001
Sites			
Intradural	504	0.56 (0.37–0.83)	0.004
Intratemporal[a]	504	4.78 (2.66–8.58)	< 0.001
Extratemporal[a]	504	0.68 (0.34–1.34)	0.27

Abbreviation: CI, confidence interval.
[a]House–Brackmann grade collapsed into 1–2 and 3–6 because proportional odds assumption violated.

with facial weakness, tumor diameter was not a predictor but the number of facial nerve segments involved was a positive predictor for hearing loss.

Location was also important for predicting the likelihood of hearing loss. The more proximal the involvement of the facial nerve, the more likely there was to be hearing loss. ►**Fig. 5** shows[44] the OR for each facial nerve segment.

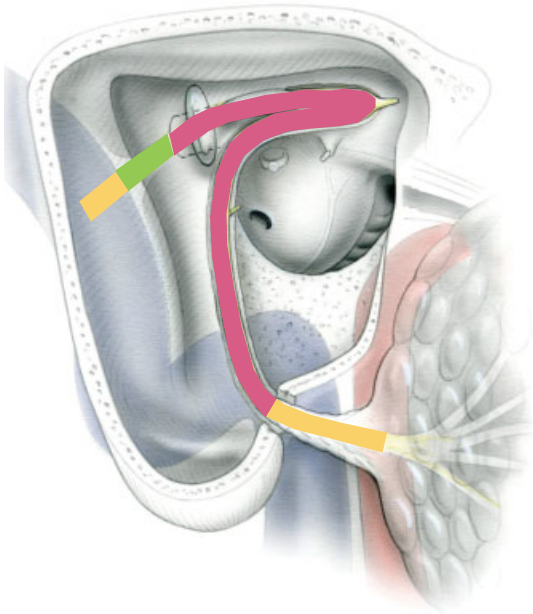
Among patients who had sensorineural and conductive hearing loss documented ($n = 75$), 53.3% were sensorineural, 42.7% were conductive, and 4.0% had a mixed loss. Each patient with documented sensorineural hearing loss had intradural involvement and every patient with conductive hearing loss had intratemporal involvement.

Discussion

Treatment for facial schwannomas is a delicate balancing act, so understanding the characteristics that are more closely correlated with morbidity will help the surgeon and patient decide the best course of treatment. Using a unique systematic review study design that only includes studies with detailed patient data, we were able to obtain a sample size unprecedented in the literature. This level of detail allowed meaningful conclusions relevant to the management of facial schwannomas. First, it provides epidemiologic data with regard to demographics, tumor location, and clinical presentation. Second, we found that the number of facial nerve segments involved by tumor is a better predictor than tumor diameter for both facial weakness and hearing loss. Third, we learned intratemporal tumor location is a predictor for facial weakness. Finally, the more proximal the schwannoma is located, the more likely there is to be hearing loss. The term predictor in this study refers to variables associated with morbidity at presentation, this is not examining future prognosis with observation.

The epidemiologic data accumulated in this study offers some value to the literature given the multi-institutional nature of a systematic review and the large sample size. The average age was 43.7 years old, with a slight preponderance toward females and right sided neoplasms. There is wide variability in the age at presentation and the distribution across that span follows a normal distribution. The largest clinical studies that have been performed[7,34,45] which largely were not used in this study because the data was understandably aggregated, also had average ages in the fifth decade of life.

We found that the most common facial nerve segment involved was the geniculate ganglion which was closely followed by the tympanic segment and the IAC. When



Location	Odds Ratio (95% CI)	p
CPA*	0.64 (0.37–1.09)	0.10
IAC	0.59 (0.40–0.88)	0.01
Labyrinthine	1.57 (1.03–2.40)	0.04
GG*	2.75 (1.70–4.44)	< 0.001
Tympanic	3.56 (2.39–5.30)	< 0.001
Mastoid	1.84 (1.24–2.73)	0.002
Parotid*	0.68 (0.34–1.34)	0.27

Fig. 4 Predictors of higher House–Brackmann grade by facial nerve segment involvement. *House–Brackmann grade collapsed into 1–2 and 3–6 because proportional odds assumption violated. CI, confidence interval; CPA, cerebellopontine angle; IAC, internal auditory canal; GG, geniculate ganglion. Source[44]

studies that focused on specific populations were excluded, the frequency of extratemporal schwannomas decreased and the other locations increased proportionally. We believe the latter totals are likely a more accurate representation of incidence of involvement of the various facial nerve segments by facial schwannomas. The geniculate ganglion, IAC, and tympanic segments are consistently the three most common sites of involvement in the largest studies performed previously.[7,34,45] The greater superficial petrosal nerve,[46] nerve to stapedius,[47] and chorda tympani nerve[48] have all been reported involved in case reports; however, they are extraordinarily rare. In studies used for this systematic review, there were only two patients with greater superficial petrosal branch involvement and both were in large tumors involving at least five facial nerve segments.[34] There were no patients with nerve to stapedius or chorda tympani involvement.

Table 8 Predictors of hearing loss

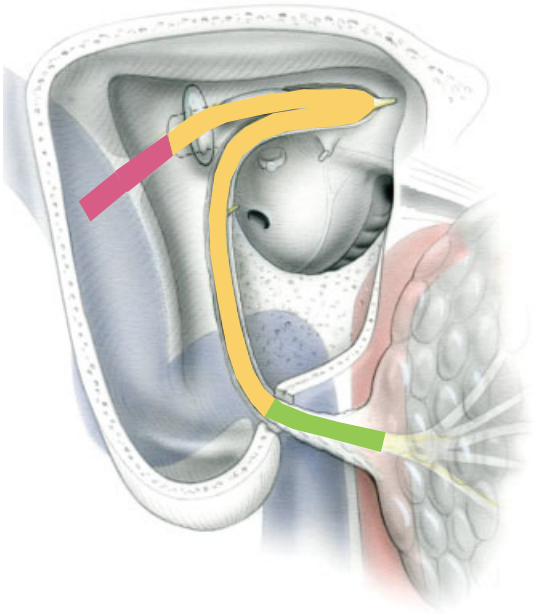
	n	Odds Ratio (95% CI)	p
Demographics			
Sex (female vs. male)	140	1.35 (0.67–2.75)	0.40
Age (y, older)	140	1.04 (1.01–1.07)	0.008
Side (left vs. right)	71	0.99 (0.34–2.86)	0.99
Tumor extent			
Tumor diameter (mm)	60	0.97 (0.92–1.02)	0.19
Facial nerve segments Involved	254	1.43 (1.13–1.82)	0.003
Sites			
Intradural	254	3.26 (1.88–5.65)	< 0.001
Intratemporal	254	0.60 (0.30–1.19)	0.14
Extratemporal	254	0.27 (0.09–0.77)	0.01

Abbreviation: CI, confidence interval.

Most patients had their presenting symptom(s) reported (79.6%). The most common presenting symptoms were facial weakness and hearing loss, with tinnitus, vertigo/imbalance, and parotid masses being the next most common. Facial spasm is a relatively uncommon (5.2%) but notable symptom which can help to differentiate facial schwannomas from a vestibular schwannoma.

It is critical to differentiate a vestibular schwannoma from an intradural facial schwannoma because the treatment paradigm of each is very different. Unfortunately, facial schwannomas confined to the IAC and CPA present similarly to vestibular schwannomas and can be impossible to differentiate preoperatively. A high index of suspicion is warranted if there are any facial nerve signs or symptoms or any extension past the fundus of the IAC radiologically.[23] Intraoperatively, facial schwannomas can be distinguished by the presence of spontaneous action potentials while drilling the bony IAC, action potentials when stimulating the tumor capsule, or the intimate involvement of the facial nerve with the tumor.[49] If encountered unexpectedly intraoperative, decompression or subtotal resection should generally be the treatment of choice.[23]

The most valuable conclusions that can be taken from this study are the factors associated with facial nerve weakness and hearing loss. These conclusions cannot predict prognosis



Location	Odds Ratio (95% CI)	*p*
CPA	4.49 (2.08–9.70)	< 0.001
IAC	2.82 (1.63–4.86)	< 0.001
Labyrinthine	1.76 (0.94–3.27)	0.08
GG	0.93 (0.54–1.60)	0.79
Tympanic	1.23 (0.71–2.13)	0.45
Mastoid	0.94 (0.54–1.63)	0.82
Parotid	0.027 (0.09–0.77)	0.01

Fig. 5 Predictors of hearing loss by facial nerve segment involvement. CI, confidence interval; CPA, cerebellopontine angle; IAC, internal auditory canal; GG, geniculate ganglion. Source[44]

because they are based on observations of single time points in the natural course of facial schwannomas. As with vestibular schwannomas,[50] there is no known way to predict if a facial schwannoma will continue to grow or not. However, it is reasonable to conjecture that if, for example, a patient presents with normal facial function but has variables associated with poor facial nerve function, that further tumor growth is perhaps more likely to cause facial weakness than a patient with variables associated with good facial nerve function. When making decisions regarding timing and type of intervention, knowing these associations could potentially impact clinical decision making.

A greater degree of facial weakness is positively associated with intratemporal tumor locations and negatively associated with intradural and extratemporal tumor locations. The mechanism of facial nerve weakness for facial schwannomas is currently unknown[7] but based on these findings it is likely related to compression of the nerve and/or vasa nervorum from growth of the neoplasm within the limitations of the fallopian canal. However, it is surprising that the tympanic segment involvement is trending toward being a stronger predictor for facial weakness compared with the labyrinthine segment. Considering the smaller caliber of the labyrinthine segment of the fallopian canal,[51] one would expect the labyrinthine segment to be more strongly associated with facial weakness.

We also found that the number of facial nerve segments involved is a positive predictor of facial weakness, whereas tumor diameter is not a predictor. This also suggests that facial weakness is likely propagated through a mechanism related to compression. Cell growth will either lead to increased pressure within a confined space or increased tumor volume, so tumors putting more pressure on their affiliated nerve segment will theoretically have less volume than they otherwise would. The fact that many segments are tightly grouped together in the intratemporal segment of the facial nerve could also have influenced this analysis. Age, gender, and laterality did not impact facial nerve status, although older age and left sided tumors were trending toward significance.

Hearing loss was not an inclusion criterion in this study but it was documented in over half of the patients. Unfortunately, across studies the documentation of hearing loss was inconsistent, so our analysis was limited to a simple positive or negative binary metric. The analysis still revealed meaningful results.

A patient was more likely to have hearing loss the more proximal the involvement of their schwannoma along the facial nerve. Intradural involvement, particularly in the CPA, was a positive predictor of hearing loss. Intratemporal involvement was a neutral predictor of hearing loss compared with other locations, and extratemporal involvement was a negative predictor. The mechanism for hearing loss in the IAC and CPA has been studied more extensively in vestibular schwannomas and the exact mechanism is still unclear but it is thought to be from nerve compression with resultant thinning of cochlear nerve fibers and/or impairment of blood supply to the auditory nerve or cochlea.[52] Hearing loss in patients with intradural facial schwannomas is likely via the same mechanism given the similar anatomic relationships. Intratemporal hearing loss is more likely from a conductive hearing loss secondary to either mass effect within the middle ear, ossicular erosion, or mass effect within the external auditory canal.[34] Among the relatively small number of patients ($n = 75$) where sensorineural and conductive hearing loss were differentiated, there was a fairly even mix that closely correlated with tumor location in the expected pattern.

As with facial weakness, the number of facial nerve segments involved was a positively associated with hearing loss whereas tumor diameter was not a predictor. Older age was a positive predictor of hearing loss which is likely because many older patients have hearing loss secondary to nontumor causes. Gender and laterality did not impact the likelihood of hearing loss.

The strengths of this study include the large sample size, the diversity of institutions where the patients presented, the uniformity of the HB grading system used with all patients and the level of detail mandated by the inclusion criteria created. Limitations include the lack of detail in hearing loss data available, the reliance on the reporting of others and the risk of publication bias inherent in a systematic review.

Conclusion

Facial schwannomas are extremely rare tumors with a wide variety of clinical presentations. The number of facial nerve segments involved were positively associated with both facial weakness and hearing loss, whereas tumor diameter is not a predictor for either. Intratemporal neoplasms are a positively associated with a greater degree of facial weakness. The more proximal a facial schwannoma is along the course of the facial nerve, the more likely a patient is to exhibit hearing loss. The type and timing of intervention should be tailored to individual patients with these findings in mind.

Note

This study was presented as a podium presentation at the North American Skull Base Society 28th Annual Meeting on February 17, 2018 in San Diego, California, U.S.A.

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Appendix A

Search strategies

1. PubMed–NCBI: Facial nerve (MeSH) and Neuroma (MeSH: No Exp) or ("facial nerve" or "seventh cranial nerve") and neuroma or "facial neuroma" or "facial nerve schwannoma." English only filter used.

2. Scopus: Keyword search–"Facial nerve neuroma" or "seventh cranial nerve neuroma" or "Facial neuroma" or "Facial nerve schwannoma" or "Facial schwannoma." English only filter used.