Impact of Demographics and Clinical Features on Initial Treatment Pathway for Vestibular Schwannoma

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Objective: To identify demographic and clinical features impacting initial treatment pathway for vestibular schwannoma.

Study Design: Retrospective chart review.

Setting: Tertiary care academic medical center.

Patients: Patients diagnosed with vestibular schwannoma between 2009 and 2019.

Interventions: Observation, stereotactic radiosurgery, or microsurgical resection.

Main Outcome Measures: χ^2 Test, one-way analysis of variance, and multivariate logistic regression were used to correlate demographic and clinical factors with initial treatment pathway for 197 newly diagnosed vestibular schwannoma patients.

Results: Among 197 patients, 93 (47%) were initially treated with observation, 60 (30%) with stereotactic radiation (Gamma Knife) and 44 (22%) with surgical resection. Age univariately had no statistically significant impact on initial pathway, but those undergoing surgery trended toward a younger demographic (49.1 yr [surgery] versus 57.2 yr [observation] versus 59.0 yr [Gamma Knife]).

INTRODUCTION

Vestibular schwannoma (VS) is a benign neoplasm arising along the cochleovestibular nerves in the internal auditory canal (IAC) or cerebellopontine angle. Although infrequently life-threatening, symptoms of presentation significantly impact quality of life (1,2). These symptoms include irreversible hearing loss, tinnitus, dizziness, facial nerve dysfunction, and

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Men were more likely to be initially observed than women (p = 0.04). Patients initially observed were more likely to have a lower Koos classification (p < 0.001) and have better tumor-ear hearing (p = 0.03). Only 34.4% of patients living outside the local geographic region were initially observed compared with 53.0% living locally (p = 0.055). Surgeon correlated with initial treatment (p = 0.04) but did not maintain significance when adjusting for hearing level or tumor size. A multiple linear regression model found age, maximum tumor diameter, and Koos class to correlate with initial treatment initial treatment pathway $(p < 0.0001, r^2 = 0.42)$.

Conclusion: Initial treatment pathway for newly diagnosed vestibular schwannoma is impacted by demographic factors such as age, sex, and geographic proximity to the medical center. Clinical features including hearing level and tumor size also correlated with initial treatment modality.

Key Words: Decision making-Treatment-Vestibular schwannoma.

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headache (2). Management options include active surveillance with serial magnetic resonance imaging (MRI), microsurgical resection, and stereotactic radiotherapy.

Relative frequency of treatment pathways has shifted over recent years, particularly with the advent of stereotactic radiotherapy modalities (3-5). For example, microsurgical resection can be planned as incomplete and subsequently combined with radiotherapy (6). Furthermore, increased frequency of brain imaging has led to increased identification of small VS or earlier identification of disease. Indeed, Carlson et al. (7) found no change in incidence between 2004 and 2011 but a significantly decreased tumor size at diagnosis. As such, there has been an increase in conservative management, which has been associated with increasing patient age and smaller tumors (<2 cm) (3,4). With several viable management options available to patients, counseling by providers is more complex and necessitates not only an understanding of potential outcomes, complications, and impact on quality of life but also patient factors that may influence decision making for treatment of newly diagnosed VS.

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Preference for treatment strategy is unique to each patient and dependent on a variety of sociodemographic factors. Patient age, race, sex, geographic location, and support system may play a role in their initial treatment decision (3,6-10). McClelland et al. (9) found patients who were elderly, Black, on Medicare or treated in a community hospital were more likely to receive observation as initial treatment. Babu et al. (8) found similar results, with elderly patients and Black patients more likely to undergo conservative management. In their study, this management pattern was found despite Black patients having large tumor sizes at diagnosis. Patients who are unmarried are also more likely to undergo observation and less likely to undergo surgery. A support system such as marriage correlates with overall survival and decrease tumor size at presentation (10). It has also been suggested that geographic location and access to tertiary care centers may also influence treatment chosen (11). The present study utilized a large cohort of patients across three different providers to identify demographic and clinic features that correlate with initial treatment pathway for newly diagnosed VS. Unlike previous studies examining decision-making patterns in VS management, the present study is novel in its incorporation of sociodemographic, geographic, clinical, and surgeon factors, providing a predictive model for initial management of VS.

METHODS

Data Source

This project was approved under our department-wide OTO Clinomics outcomes assessment platform, which facilitates retrospective chart reviews of our entire health system (institutional review board no. 1538127) (12,13). Using a cohort interrogation tool, i2b2, current procedural terminology codes 225.1 and D33.3 (benign intracranial tumors) were used to identify patients in our health system seen by the neurotology service between January 2009 and December 2019. This identified 1,634 patients for further review.

Patient Demographics and Study Design

Review of 1,634 patients with benign intracranial tumor diagnoses identified 684 patients with VS. Further review was performed to identify patients meeting the following inclusion criteria: 1) seen for initial consultation by one of three neurotologists in our department, 2) availability of a reviewable MRI of the IACs performed within 6 months of consultation, and 3) performance of an audiogram within 3 months of the time of initial assessment. These time frames were selected to ensure that tumor measurements and hearing levels would have been relevant to the decision-making process determining initial treatment pathway. This review identified 197 patients for further analysis.

Demographic data were recorded for each subject, including age, race, sex, zip code of residence, marital status, and employment status. Presenting MRI scans were reviewed by a single author (E. H.), with measurements taken in the axial plane to assess tumor size. Measurements were taken along the axis of the IAC, along the axis of the petrous ridge, and at any axial orientation that revealed the maximal tumor diameter. Tumors were also assigned a Koos classification based on extension out of the IAC and into the cerebellopontine angle (14). American Academy of Otolaryngology– Head and Neck Surgery (AAO-HNS) hearing class and Gardner– Robertson hearing class was determined from initial presenting audiogram. The initial treatment pathway was determined by review of the initial provider notes.

Statistical Analyses

The dependent variable was established as initial treatment pathway and was categorized as observation, Gamma Knife radiotherapy, or microsurgical resection. We did not include any patients with planned surgical debulking, followed by Gamma Knife. Thus, each initial treatment option was intended to be the therapeutic pathway, barring changes in status of the tumor. Univariate analyses were used to correlate patient demographics, population-level data, hearing status, and tumor characteristics with categorical treatment pathway. One-way analysis of variance was used for numeric versus pathway analyses (e.g., age versus treatment) and χ^2 test used for categorical versus pathway analyses (e.g., sex versus treatment) with significance set at p < 0.05.

We also performed linear regression analyses for continuous variables such as age and tumor measurements. For these analyses, the dependent variable was converted to an ordinal scale, with 1 for observation, 2 for Gamma Knife, and 3 for surgery, to reflect a graded degree of invasiveness. p Values and r^2 were calculated to determine significance and correlation strength, respectively. Finally, a multivariate regression model was developed to control for interaction among variables and included variables with the strongest Pearson correlation coefficients. All statistical tests were performed using R language (3.6.1).

RESULTS

Initial Treatment by Demographics

A total of 197 patients diagnosed with VS had necessary imaging and audiometric testing to meet the inclusion criteria. Average age was 55.9 ± 12.8 years, with 58.9%(116) female, 92.4% (182) White, and 97.0% (191) non-Hispanic (Table 1). Observation was the most common initial treatment pathway (47.2%), followed by Gamma Knife radiotherapy (30.5%) and surgical resection (22.3%).

Categorical analyses showed a nonsignificant trend toward surgery for those of younger age (Fig. 1). Specifically, patients who underwent initial observation had an average age of 57.2 \pm 13.5 years, those who underwent Gamma Knife treatments were similar at 59.9 \pm 11.3 years, but those who underwent surgery were younger at 48.6 \pm 10.6 years. Regression analysis, however, did show a significant correlation between older age and a lower probability of invasive treatment (p = 0.003). The correlation coefficient was quite low ($r^2 = 0.04$) indicating low predictive value of using age to identify initial treatment course.

Male and female patients alike were most commonly observed; although the majority of male patients underwent observation (57.0%), the majority of female patients (59.5%) had some form of intervention, either Gamma Knife or surgery (Fig. 1). The male preponderance for observation was significant at p = 0.04 (odds ratio, 1.93 [95% confidence interval, 1.09–3.43]). We did not observe a diverse racial or ethnic population, and thus, trends regarding initial treatment pathway could not be assessed.

Geographic location trended toward having an impact on initial treatment course (p = 0.055). We distinguished patients living in our health system's primary catchment area in the southeastern portion of our state, one of five designated department of health services healthcare regions, from those who lived outside the region (Table 1). The majority of patients were regional (n = 136; 69.0%), and the remainder

Demographic	Observation (47.2%)	Gamma Knife (30.5%)	Surgery (22.3%)	Total	
Age (yr)	57.2 ± 13.5	59.0 ± 11.3	49.1 ± 10.6	55.9 ± 12.8	
Location					
Regional	72 (52.9%)	37 (27.2%)	27 (19.9%)	136 (69.0%)	
Distant	21 (34.4%)	23 (37.7%)	17 (27.9%)	61 (31.0%)	
Sex					
Male	46 (57.0%)	23 (28.4%)	12 (14.8%)	81 (41.1%)	
Female	47 (40.5%)	37 (31.9%)	32 (27.6%)	116 (58.9%)	
Race					
White	87 (47.8%)	58 (31.9%)	37 (20.3%)	182 (92.4%)	
Black	2 (40%)	1 (20%)	2 (40%)	5 (2.5%)	
Asian	1 (50%)	0 (0%)	1 (50%)	2 (1.0%)	
Other	3 (42.9%)	1 (14.3%)	3 (42.9%)	7 (3.6%)	
Unknown	0 (0%)	0 (0%)	1 (100%)	1 (0.5%)	
Ethnicity					
Non-Hispanic	91 (47.6%)	60 (31.4%)	40 (20.9%)	191 (97.0%)	
Hispanic	2 (50%)	0 (0%)	2 (50%)	4 (2.0%)	
Other	0 (0%)	0 (0%)	1 (100%)	1 (0.5%)	
Unknown	0 (0%)	0 (0%)	1 (100%)	1 (0.5%)	

TABLE 1. Demographics and initial treatment pathway

Percentages under each treatment pathway represent proportion of patients with that demographic selecting that pathway. Percentages under total represent proportion of all patients with that demographic.

were largely from the northeastern portion of the state (n = 61; 31%). This catchment area for a specialized diagnosis like VS was distinctly broader than that noted for the entire otolaryngology clinics (Fig. 2). The majority of regional patients were observed (n = 72; 52.9%), whereas the majority of patients outside the region had some form of intervention (n = 40; 65.6%), with Gamma Knife being most common (n = 23; 37.7%) (Fig. 1).

Initial Treatment by Tumor Size

Our measures of tumor size were axial diameter through the axis of the IAC, along the petrous face, and any axis generating a maximal measure. Each initial treatment pathway had a significant difference in tumor size in all axial measures (Table 2). Specifically, those undergoing observation had significantly smaller tumors in all axes than those undergoing Gamma Knife (p < 0.0001) or surgery (p < 0.0001). Likewise, those having surgery had significantly larger tumors than those being observed (p < 0.0001) or having radiation treatment (p < 0.0001).

Koos classification showed a significant correlation with initial treatment course (p < 0.001; Fig. 3). Those in Koos class 1 had an overwhelming tendency toward observation, with 81.6% of patients presenting with these smaller tumors not having intervention. In contrast, 94.9% of those in Koos class 4 underwent either Gamma Knife (33.3%) or surgery (61.5%). Those in the middle classes, Koos 2 and 3, most commonly underwent Gamma Knife, followed by observation and then surgery.

Initial Treatment by Hearing Status

AAO-HNS Classification

Hearing status for the tumor ear was determined by audiometric assessment. We excluded five patients with bilateral tumors from this analysis. Most patients had class B hearing

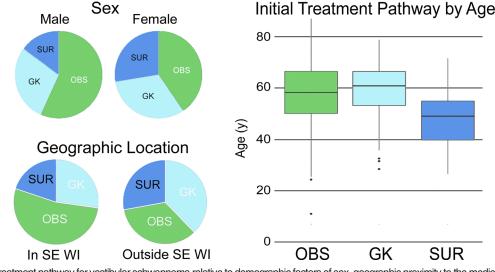


FIG. 1. Initial treatment pathway for vestibular schwannoma relative to demographic factors of sex, geographic proximity to the medical center, and age.

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Geographic Residence for Patients Evaluated by Otolaryngology

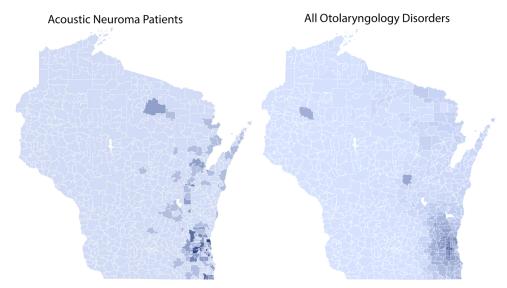


FIG. 2. Geographic residence of patients with vestibular schwannoma as compared with the overall catchment population seen in the otolaryngology clinics. Vestibular schwannoma patients have limited option for local care and therefore travel large distance for tertiary care, a factor that may influence treatment pathway.

(n = 57; 29%) (Fig. 3). Of the patients with class A hearing, 31 initially were observed. Thirteen of these patients had surgical intervention, and 11 underwent Gamma Knife. Of the patients with class B hearing, most (n = 28) were observed for their initial treatment, 15 had surgery, and 9 underwent Gamma Knife. Class C hearing was least prevalent, and the majority (n = 15) were observed, followed by 7 for Gamma Knife and 4 for surgical intervention. It was not until class D that the most common initial pathway was not observed. Gamma Knife remained more common than surgery, but those in class D had the highest proportion of surgical intervention among the cohort.

Gardner-Robinson Scale

Using the Gardner–Robinson scale showed similar results to using the AAO-HNS classification. The majority (n = 68) of patients in our study were Gardner–Robinson I (GR-I). Of these patients with GR-I, the majority were observed (n = 31). Fourteen additional GR-I patients had surgical intervention, and 13 had Gamma Knife. An equal number of patients with GR-II hearing had observation (n = 16) and Gamma Knife (n = 16) as their initial management strategy, with a minority undergoing surgery (n = 8). The majority of patients with GR-III hearing had intervention by Gamma Knife (n = 16), with 13 being

TABLE 2. Initial treatment pathway by tumor measurements

Mean \pm SD (cm)	Maximum Diameter	Axis of IAC	Petrous Face
Observation Gamma Knife Surgery Overall	$\begin{array}{c} 1.04 \pm 0.82 \\ 1.66 \pm 0.60 \\ 2.61 \pm 1.15 \\ 1.57 \pm 1.03 \end{array}$	$\begin{array}{c} 1.00 \pm 0.80 \\ 1.62 \pm 0.59 \\ 2.27 \pm 0.99 \\ 1.46 \pm 0.93 \end{array}$	$\begin{array}{c} 0.73 \pm 0.78 \\ 1.24 \pm 0.61 \\ 2.30 \pm 1.23 \\ 1.23 \pm 1.04 \end{array}$

IAC indicates internal auditory canal; SD, standard deviation.

observed and 8 having surgery. There were only three patients with GR-IV hearing status; one had Gamma Knife, and two were observed. The majority of 16 patients with GR-V hearing had surgical intervention (n = 9), whereas 5 others had Gamma Knife and 2 were observed.

Initial Treatment by Surgeon

Patients in this study were seen by one of three neurootologic surgeons in our department. Surgeon 1 evaluated 126 patients (63%), surgeon 2 saw 47 (24%), and surgeon 3 saw 24 patients (12%). This mirrors surgeon time in the department, with surgeon 1 being well established for the entire 10-year study period and surgeon 3 having joined the group in the last 3 years of this span. Both surgeons 1 and 3 were privileged in Gamma Knife, whereas surgeon 2 was not. Regardless of surgeon, patients were more commonly observed rather than either of the other two pathways (Fig. 3). Surgeon 1 had a higher proportion of patients undergoing Gamma Knife than surgery, whereas surgery was the second most common pathway for surgeons 2 and 3. χ^2 Analysis showed that surgeon had a significant correlation with initial treatment pathway (p = 0.04); however, when controlling for tumor size and hearing status, this no longer showed a statistically significant correlation.

Multivariable Predictors of Initial Treatment Pathway

Correlation analyses were performed between multiple numeric or ordinal variables and the dependent variable of initial treatment pathway. Treatment pathway, as noted earlier, was converted to an ordinal variable by ranking the intensity of intervention from observation (1) to Gamma Knife (2) to surgery (3). Multiple linear regression was performed using the three variables with the highest Pearson correlation: age, Koos classification, and maximum tumor

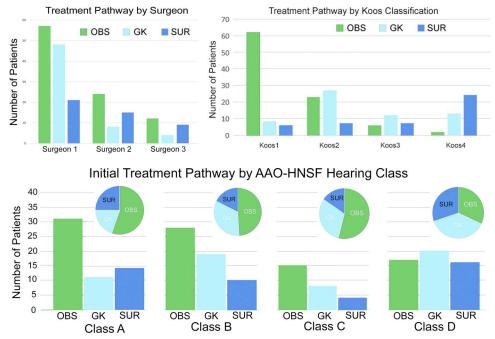


FIG. 3. Initial treatment pathway for vestibular schwannoma relative to clinical features of treating surgeon, Koos classification, and hearing status.

diameter (Table 3). The three variables were incorporated into a predictive formula of initial treatment, which had an r^2 of 0.42 (p < 0.0001). The largest contributors to the model were Koos class 4, followed by Koos class 3, then Koos class 2. Age and maximum diameter had minor contributions to the predictive model.

DISCUSSION

Understanding factors significantly influencing the shared decision-making process for treatment options for VS is paramount to providing a patient-centered approach in neurotology. Findings from our study may inform this discussion, specifically as to whether patient treatment choice is influenced by patient sex, age, race, or geographic location. Understanding these factors may help the provider guide patients to evidence-based treatments providing the best outcomes for their specific biological status (e.g., tumor size, functional status) while recognizing the sociodemographic factors that may influence patient decision making.

Age

In our study, age showed an association with treatment pathway, with younger patients more likely to have surgical intervention and older patients more likely to be observed. Babu et al. (8) reported a similar disproportion, with 23.3% of patients older than 65 years undergoing surgery compared with 57.4% of patients younger than 65 years. Similarly, Nellis et al. (15) reported an odds ratio of 0.19 (p = 0.011) for those older than 65 years to undergo surgical resection, arguing that this could be due to elderly patients having increased incidence of surgical complications. This perception of increased surgical complications and mortality in the elderly may account for reports of younger patients electing surgical intervention, whereas older patients may opt for radiotherapy or observation (16). However, Bower and co-workers (17) found no difference in complications, facial nerve outcome, or hearing preservation for patients older than 65 years. In addition, Oghalai et al. (18) found no difference in complications in elderly patients but did report lower rates of hearing preservation. Although age impacts treatment pathway, the factors behind it remain unclear and likely include not only surgeon and/or patient perception of surgical risk but also issues of longevity, which may favorably shift the riskbenefit ratio for observation. Gamma Knife may, therefore, be the default intervention for older patients without a reasonable option for observation.

Race

In an analysis of a national population-based tumor registry, Carlson et al. (19) found that the median annual incidence of VS was highest among White patients. Indeed, in

TABLE 3. Pearson correlation coefficients between initial treatment pathway and clinical variables

	Age (yr)	Surgeon	Tumor Ear AAO-HNS	Nontumor Ear AAO-HNS	Tumor Ear G-R	Nontumor Ear G-R	Max Tumor Diameter	Koos Class
Initial Tx	-0.24	0.04	0.12	-0.17	0.19	-0.18	0.30	0.62

AAO-HNS indicates American Academy of Otolaryngology-Head and Neck Surgery; G-R, Gardner-Robinson; Tx, treatment.

our study, 92.4% of subjects were White, which is consistent, albeit higher, than other reported cohorts, with ranges from 82.5 to 90.5% (8,19). The slightly higher White representation in our study may miss the full diversity of VS patients in our region as the medical center is on the periphery of one of the most segregated cities in the United States (20). The 14 non-White patients in our study, whether Black, Asian, or other, followed treatment pathways across the spectrum with no preponderance to either observation or intervention. This contrasts with Babu et al. (8), who found that Black patients were half as likely to receive surgery and twice as likely to have conservative management as White patients regardless of tumor size.

Hearing Status

We found that patients with functional hearing were more likely to be observed, perhaps because of competing evidence as to the best intervention in those with good hearing. For example, the probability of hearing preservation after microsurgery has been reported as 30 to 75% and is most influenced by baseline hearing, although tumor size and a fundal cap are also contributory (21,22). Similarly, Gamma Knife in those with better baseline hearing has higher rates of hearing preservation rates as opposed to Gamma Knife in those with existing hearing loss (23,24). Adding to the confusion are reports of similar hearing preservation at 2 years with radiosurgery and observation in those with class A or GR-1, and that these levels are similar to those at 10 years after surgery (25). However, if patients are observed, they should be counseled that the highest hearing preservation probability, if they instead had intervention, is in the first 2 years after diagnosis, with decline in the following years (22). At our institution, middle fossa surgical approaches for VS are less commonly used, and by default, this may account for the higher levels of observation in excellent hearing subjects, which typically have small tumors. In contrast, we found surgery to be used most commonly in those without serviceable hearing. This is consistent with other reports in which patients with worse PTA thresholds or documented hearing deterioration were most likely to undergo surgical intervention (26).

Tumor Size

Koos class, a categorical measure of tumor size, along with tumor diameter in several planes, correlated with invasiveness of intervention. Those patients in our study who were observed had the smallest average tumor maximal diameter, around 1 cm. Other studies have similarly demonstrated a preference for observation in those with small tumors, 1.10 to 1.18 cm (8,27). It was suggested that these patients are less symptomatic and elect observation after weighing the risks of intervention (27). We recognize, however, that these tumor sizes represent the most favorable hearing preservation outcomes for middle cranial fossa approach (28).

In contrast, the average maximal diameter among patients undergoing surgery in our cohort was greater than 2.5 cm. In our program, 2.5 cm represents an informal limit for the utilization of Gamma Knife. Such a limit is commonly considered among radiation oncologists and neurotologists performing stereotactic radiosurgery (29). In addition, tumor size at initial presentation positively correlates with the likelihood of subsequent growth when observed (30). As such, patients in our program presenting with these larger tumors typically undergo counseling in which observation and Gamma Knife are not considered viable long-term options and are reserved for those with significant medical comorbidities or far-advanced age. This likely accounts for the preponderance of surgery among this larger tumor group.

Surgeon

Looking at surgeon alone showed a distinct difference in the proportion of patients undergoing each type of intervention. Surgeons 2 and 3 showed similar treatment profiles in which Gamma Knife was least utilized in contrast to surgeon 1 with whom there was a high proportion of patients undergoing Gamma Knife. Several local potential explanations for this difference include that surgeon 1 has been Gamma Knife privileged the longest among this group, thus getting referrals specifically for Gamma Knife treatment. Surgeon 1 also experienced significant inconsistency in neurosurgical support in the early years of this cohort. That said, when controlling for tumor size and hearing status, the difference between pathway treatments among surgeons is not significant.

This latter finding may provide insight into how the process of shared decision making between surgeon and patient ultimately functions. One explanation for the similarity in pathways based on tumor size and hearing, regardless of surgeon, would be that our neurotology team is very consistent in their counseling of patients regardless of personal experience or preference. In shared decision making, this necessitates that providers recognize personal bias and utilize, to the best that is available, evidence-based approaches to counseling regarding treatment options. An alternative explanation for our findings is that regardless of potential surgeon bias toward a specific treatment pathway, the patient is most influenced by tumor size and/or hearing status. In our cohort, observation was the most common initial treatment pathway, as opposed to surgery, and is consistent with previous reports suggesting that shared decision making for elective surgical procedures tends to skew away from surgical intervention (31).

Geographic Location

A majority of patients from outside the local region received intervention, either Gamma Knife or surgery, rather than observation. This was a notable contrast to those living locally in which observation predominated. Similar patterns have been noted by Ostler et al. (32) demonstrating increased odds of intervention, as opposed to observation, for each additional mile from the medical center. This was despite finding no association between median income and tumor size and management plan. In addition, Leon et al. (33), found that patients who lived more than 25 miles from the center were more likely to choose a treatment option. Further study is needed to identify whether there are differences in outcome

for VS because of these identified differences in treatment based on geography.

As a retrospective review, these data are limited by including only those patients with VS who also had complete radiographic and audiometric data. Potentially, there are sociodemographic factors associated with those without complete datasets skewing the study cohort. Missing data are also possible, but the extracted data were supplemented by further manual review. Generalizability of our results is a concern regarding demographics and also treatment approaches. Some neurotology practices do not include stereotactic radiosurgery privileges, and some practices have unique surgical philosophies, utilize other approaches, or collaborate differently with neurosurgical services.

CONCLUSIONS

Initial treatment pathway for VS is associated with patient age, sex, and geographic proximity to the tertiary medical center. Clinical features including hearing level, Koos classification, and tumor size were most impactful on treatment pathway. Surgeon did not associate with treatment pathway when controlling for clinical factors, suggesting that provider bias, privileging, and surgical experience are less impactful in the shared decision-making model than demographic and tumor-specific characteristics.

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