Wait and Scan Management of Intra-canalicular Vestibular Schwannomas: Analysis of Growth and Hearing Outcome

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Objective: To report on the results of intracanalicular vestibular schwannomas (ICVS) that were managed by wait and scan and to analyze the possible predictors of tumor growth and hearing deterioration throughout the observation period.
Study Design: A retrospective case series.
Setting: Quaternary referral center for skull base pathologies.
Patients: Patients with sporadic ICVS managed by wait and scan.
Intervention: Serial resonance imaging (MRI) with size measurement and serial audiological evaluation.
Main Outcome Measure: Tumor growth defined as 2 mm increase of maximal tumor diameter, further treatment, and hearing preservation either maintain initial modified Sanna hearing class, or maintain initial serviceable hearing (class A/B).
Results: 339 patients were enrolled. The mean follow-up was 36.5 ±31.7 months with a median of 24 months. Tumor growth occurred in 141 patients (40.6%) either as slow growth (SG) in 26.3% of cases or fast growth (FG) in 15.3% of cases. Intervention was performed in only 64 cases (18.8%). Out of 271 patients who underwent hearing analysis, 86 patients (33.5%) showed hearing deterioration to a lower hearing class of the modified Sanna classification. Tumor growth and older age were predictors of hearing deterioration. Of the 125 cases with initial serviceable hearing (Class A/B), 91 cases (72.8%) maintained serviceable hearing at last follow-up. Tumor growth and a worse initial pure tone average (PTA) were predictors of hearing deterioration.
Conclusions: Wait and scan management of ICVS is a viable option and only 18.8% of patients needed further treatment. Hearing tends to deteriorate over time.
Key Words: Follow-up—Hearing loss—Vestibular schwannoma—Wait and scan.

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The three main management options for newly diagnosed sporadic vestibular schwannoma (VS) are surgery, radiation therapy (RT), and wait and scan conservative management (1). With the recent advances and the increasing availability of MRI, the incidence of newly diagnosed small vestibular schwannomas has dramatically increased (2). Many of these tumors have few symptoms or are asymptomatic and were discovered incidentally. While surgery is crucial for the management of large VS, the decision in smaller tumors is more complex.

With the increased diagnosis of small tumors and the evolving reports showing that many of these tumors stop growing or do not grow, a lot of centers started to adopt the wait and scan policy for their management (3–6).

Advantage of the wait and scan policy is the likely preservation of hearing and the avoidance of complications related to the other treatment modalities. Disadvantages of the wait and scan policy are deterioration of hearing over time, and the development of other symptoms as vertigo. In addition, tumor growth, particularly in cases showing fast growth may eventually necessitate intervention on a comparatively large tumor risking a worse outcome. The choice of a proper management strategy ultimately aims at functional preservation and increasing the patient's quality of life (4,5,7).

The aim of the present work is to report on the results of ICVS that were managed by wait and scan in our center and to analyze the possible predictors of tumor growth and hearing deterioration throughout the observation period.

METHODS

Out of nearly 4,800 VS treated at our center, surgery was performed in nearly 3,800 cases while approximately1000 cases were managed conservatively. In the early years of our practice, surgery was performed in the majority of ICVS. We

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gradually started to adopt the wait and scan policy that currently became our standard of care for newly diagnosed cases (Fig. 1). A retrospective analysis of the database of all cases of sporadic ICVS that were initially managed by wait and scan policy between 1994 and 2019 was performed in the present study. The study was approved by the ethics committee in our center.

Exclusion Criteria

These included patients with neurofibromatosis type II, cases with previous treatment whether surgery or RT before presentation and cases with doubtful diagnosis. Patients who lacked at least two serial MRI or those lost to follow-up were also excluded.

The decision of adopting the wait and scan policy was taken after discussing the other options with the patient (namely surgery and RT).

A follow-up MRI and audiological evaluation were performed after 6 months from presentation, then yearly for 3 years and every 2 years thereafter. After 10 years, follow-up was performed every 5 years.

The information retrieved from the database included patient demographics, initial presentation, tumor size, growth features at follow-up, initial hearing level, and hearing outcomes.

Tumor Size and Growth

Tumor size was defined as the largest tumor diameter in mm, in the gadolinium enhanced-MRI images. Slow growth (SG) was defined as tumor growth more than or equal to 2 mm and less than 4 m/yr. In addition, cases that had a growth of more than 2 mm between the initial and last follow-up MRI were also considered as tumor growth. Anything less than 2 mm was considered as no growth (NG) as it could be due to interobserver variability or a difference in slice position between the two scans. FG was defined as growth more than or equal to 4 mm/yr. A decrease in tumor size of one or more mm is considered involution or shrinkage (I). Tumor growth rate/yr was calculated as the difference between the initial size at the last follow-up MRI divided by number of years.

Hearing Evaluation

PTA was calculated as the mean of hearing thresholds at 0.5, 1, 2, and 4 kHz. Speech discrimination score (SDS) was obtained at an intensity of 40 dB above speech reception threshold or at most comfortable threshold. Patients' hearing was classified from A to F according to the modified Sanna classification (8). Patients who had no complete audiological data (pure tone average [PTA] and SDS) at follow-up or those who had initial profound hearing loss were excluded from the hearing evaluation. Hearing deterioration was defined as a decline in hearing by at least one class of the modified Sanna classification. Class A and B were considered serviceable hearing. A separate analysis was performed for cases presenting initially as classes A/B hearing. In these cases, maintaining class A or B was considered a hearing preservation.

Statistical Analysis

Both descriptive and inferential statistics, including parametric and nonparametric methods, were used as appropriate. Comparison of two categorical variables was performed using x^2 test. For continuous data, independent-samples *t* test was used in case of normal distribution and Mann–Whitney U test for non-normal distribution. Logistic regression was used to estimate the odds of tumor growth and of hearing deterioration associated with patient demographics and tumor characteristics. Multivariable models were developed with a backward selection process. Kaplan–Meier survival curves were used to assess tumor growth and hearing deterioration with time. A $p < 0.05$ value was considered significant in all analyses. Statistical analysis was performed with SPSS version 22.0 statistics program (SPSS Inc., Chicago, IL).

RESULTS

Out of 449 cases of ICVS that were initially managed by wait and scan policy, 339 cases were enrolled in the current study. The remaining 110 cases were excluded due to different causes as mentioned in our exclusion criteria. There were 162 men (47.8%) and 177 (52.2%) women. The right

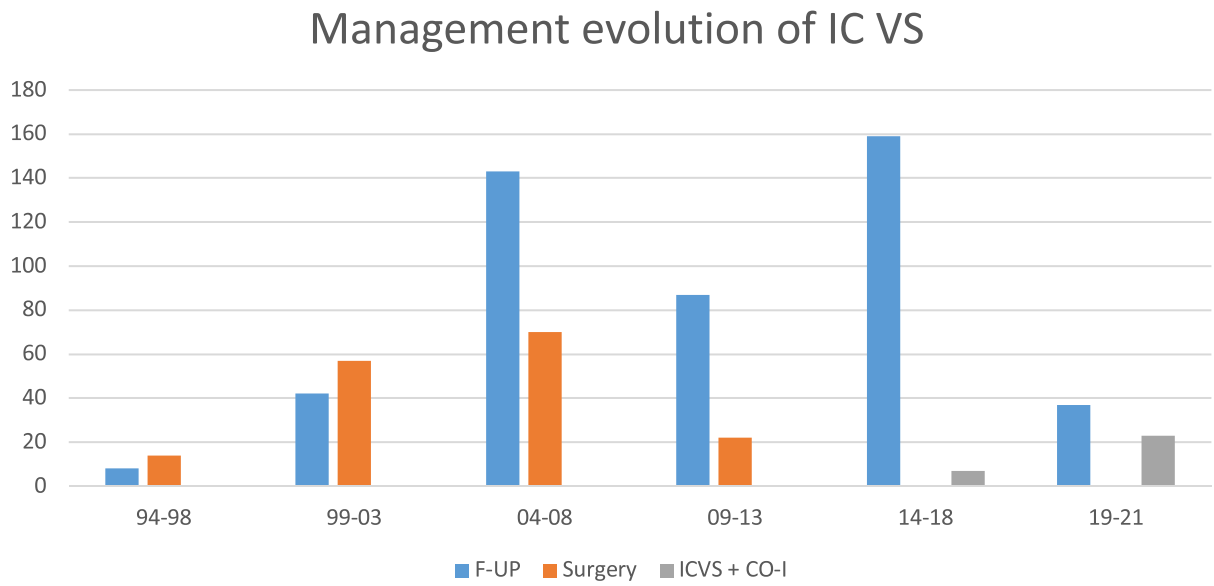


FIG. 1. The evolution of the management strategy of ICVS in our center. ICVS indicates intracanalicular vestibular schwannomas.

side was affected in 163 cases (48.1%) and the left in 176 cases (51.9%). Their ages ranged from 16 to 89 years with a mean of 58.3 ± 12.2 years and median of 60 years. Hearing loss was the commonest initial symptom and was present in 204 cases (60.2%). Dizziness was present in 89 cases (26.3%) whereas tinnitus was present in 83 cases (24.5%). Forty-two cases (12.4%) were asymptomatic and were incidentally discovered. Follow-up ranged from 6 to 182 months with a mean of 36.5 ± 31.7 months and median of 24 months. Eighty-two patients (24.2%) missed their scheduled follow-ups after initial compliance.

Tumor Growth

At the last follow-up, no tumor growth was observed in 195 cases (57.5%). In three cases (0.9%) tumor involution occurred. Thus, a total of 198 cases (58.4%) showed NG or I. Tumor growth was seen in 141 cases (41.6%) presenting either as SG in 89 cases (26.3%), or as FG in 52 cases (15.3%). In 27 cases showing tumor growth, a mixed growth pattern was observed. They all showed random, non-linear growth. The commonest was NG + SG in 10 cases and SGþNG in six cases. Other patterns included FG + NG + SG, NG + FG, FG + SG, NG + SG + NG, and SG + FG. The mean tumor growth was 1.51 ± 2˙7 mm/yr. The fastest growing tumor showed a 15 mm growth/yr. Of the FG tumors, 17 cases (32.7%) started to grow within 6 months, 34 cases (65.4%) within the first year, and 47 (90.4%) within 2 years. Of the SG tumors, five cases (5.6%) started to grow within 6 months, 28 cases (31.5%) occurred within the first year, and 54 (60.7%) within 2 years. Thus, most cases showing tumor growth occurred within 2 years (101 cases = 71.6%) and slightly less than half (43.7%) were in the first year. Tumor growth started to occur after 5 years in 11 patients (7.8%), onlyone of whom showed rapid growth. Figure 2 shows the Kaplan–Meier survival curve depicting probability of tumor growth over time. A comparison between groups of patients showing tumor growth and those showing NG/I was performed. There was a statistically significant worse initial PTA for cases showing tumor growth. All other variables were not significant (Table 1). Univariate and multivariate logistic regression studying the patient's demographics (age, sex, laterality) and initial clinical presentation (PTA, SDS, tinnitus, and vertigo) failed to show any predictive factor. In 111 patients (32.7%), extra-canalicular tumor (EC) extension occurred. Intervention was performed in 64 patients (18.88%), in the form of surgery in 61 cases and RT in the remaining three. The reason for surgery was pure EC tumor extension in 31 cases and FG in another 22 cases. In seven cases, surgery was performed due to deterioration of hearing, whereas in one case it was due to worsening vertigo.

Hearing Analysis

Only 271 cases had complete records of their hearing during initial evaluation and at follow-up. Fourteen cases had profound deafness at initial presentation and were excluded from the analysis. The remaining 257 cases were included for the hearing analysis. There were 125 men (48.6%) and 132 women (51.4%). The right side was affected in 129 cases and the left on 128 cases. The mean age at presentation was 57.6 years. The mean

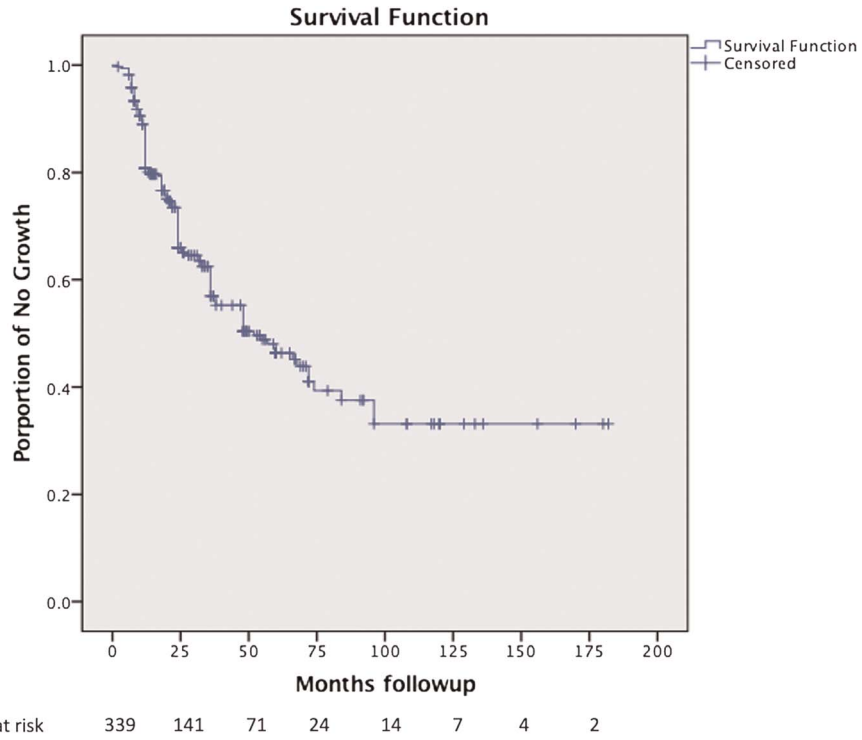


FIG. 2. Kaplan–Meier survival curve depicting probability of tumor growth over time (months of follow-up).

TABLE 1. *Comparison of demographics and clinical findings at presentation between the group of patients showing no tumor growth (NG/IG) and those showing tumor growth (SG/FG)*

Parameter	No Growth (n = 198)	Growth (n = 141)	Significance
Age (yr) (Median, IQR)	60 (51.7–67)	61 (51–67)	NS
Side			
Rt (no, %)	98 (49.5%)	66 (46.8%)	NS
Lt (no, %)	100 (50.5%)	75 (53.2%)	
Sex			
Male (no, %)	97 (49.0%)	65 (46.1%)	NS
Female (no, %)	101 (51.0%)	76 (53.9%)	
Initial hearing			
PTA	43.4	49.5	0.043*
SDS	75.3%	73.5%	NS
C/O At Presentation			
Tinnitus (n = 83)	53 (26.8%)	30 (21.3%)	NS
Vertigo (n = 89)	55 (27.8%)	34 (24.1%)	NS

*$p < 0.05$, Mann–Whitney U test.
NS indicates non-significant.

duration of follow-up was 30.9 months. The mean PTA at presentation was 40.9 ± 19.5 dB and the mean SDS was 80.9% ± 27.1. At presentation good hearing class (A or B) patients were 125 cases (48.6%) whereas classes (C–F) were 132 cases (51.4%). At the last follow-up, classes (A–B) were 93 cases (36.2%) and classes (C–F) were 164 cases (63.8%) (Fig. 3). At the last follow-up, 169 patients (65.6%) maintained their initial hearing class, two patients (0.8%) had improvement of their hearing to classes A and B whereas 86 patients (33.5%) showed hearing deterioration. For cases that had audiological data more than 5 years from presentation, only 46.1% preserved their hearing class. Figure 4 shows the Kaplan–Meier survival curve depicting probability of hearing deterioration over time. Patient demographics and tumor growth were compared between the group with hearing preservation/improvement at last follow-up and those who showed hearing deterioration. Univariate analysis showed a statistically significant correlation between hearing deterioration and older age, tumor growth and worse PTA at initial follow-up (Table 2). Multiple regression analysis showed same correlation for age and tumor growth.

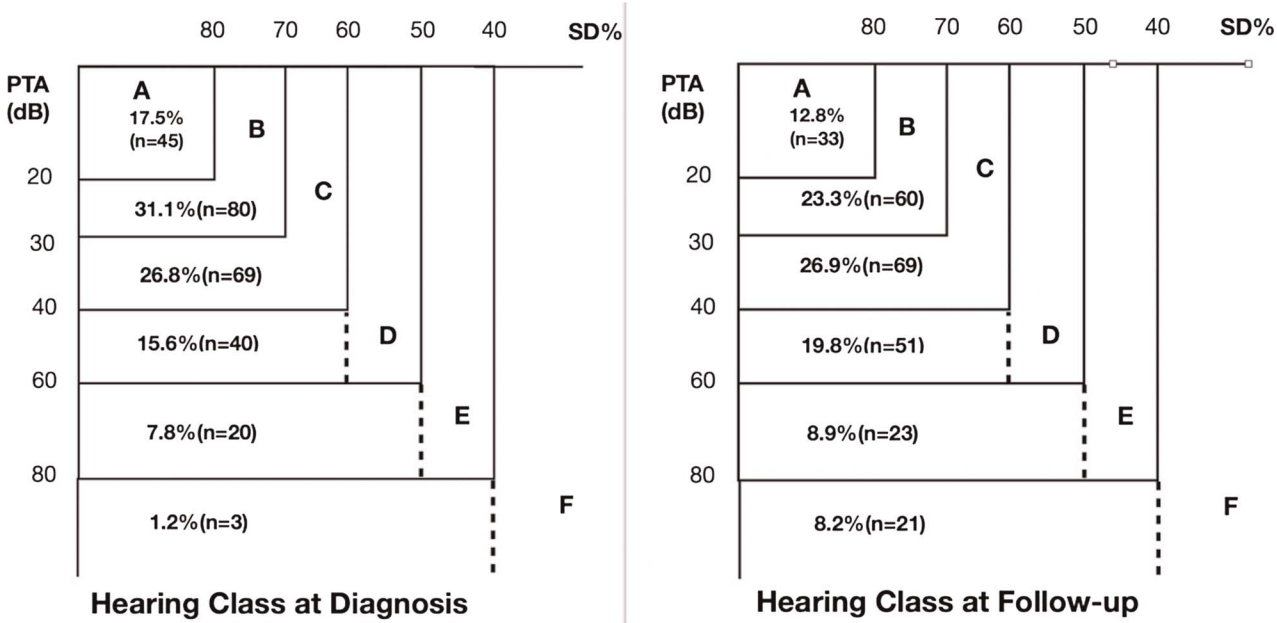
Cases with serviceable initial hearing (Class A–B) were also analyzed separately. There were 125 cases and of those 91 cases (72.8%) maintained their A/B hearing class at the last follow-up, the remaining 34 cases (27.2%) deteriorated into classes (C–F). For cases who had audiological data more than 5 years from presentation, only 55.5% maintained their A–B hearing class. The demographics and univariate analysis of these cases are shown in Table 2. In multiple logistic regression, there was a correlation between serviceable hearing deterioration and worse initial PTA and tumor growth. No correlation was found between serviceable hearing deterioration and age, sex, or initial patient's complaints.

DISCUSSION

Management of small VS is still controversial. Surgical intervention and RT both carry their own risks and complications. On the other hand, growth of an untreated tumor might lead to more symptoms. In addition, definitive treatment (surgery or RT) on a larger tumor and advanced age might carry a relatively more morbidity and a worse final outcome. A study of the natural course of these tumors in a trial to define the factors that correlate with growth or hearing deterioration is therefore needed for decision making and proper counseling of the patient. Multiple reports have studied the conservative management of VS (9–12), but few studies, including ours, only focused on ICVS (13–17).

Tumor Growth

In the literature, the rate of tumor growth for all wait and scan VS varied from 6 to 74% (18). These reports included both intra and extrameatal VS and also included cases of NFII. In the current study, tumor growth occurred in 41.6% of cases. Comparable results of ICVS growth were reported by Kirchmann et al. (19) (37%) and by Lees et al. (20) (45.3%). Our results differ significantly from a large study by the Danish group who showed that only 17% of ICVS showed growth (9). Those authors defined IC tumor growth as extrameatal extension of the tumor. According to this definition, very small tumors that grew but remained in the IAC were not counted as growing. Fayad et al. (12) found also that 52% of tumor growth occurred during the first year. Moffat et al. (21), reported that 52.4% of growing tumors showed radiologically demonstrable first growth within 18 months of presentation, whereas Younes et al. (17) demonstrated that 76.5% of growing ICVS occurred in the first year of follow-up. The majority of growing tumors in our study (71.6%) occurred in the first 2 years. It is noteworthy that most FG in our series occurred early (32.7% within 6 months, and 65.4% within 1 year). These findings highlight the importance of early frequent serial imaging. Some authors advised to stop imaging for nongrowing tumors after 5 years based on their findings that none of the tumors grew after that (9,12). On the contrary, we still recommend lifelong surveillance as 7.8% of our cases started to grow after 5 years. Prolonged surveillance has also been



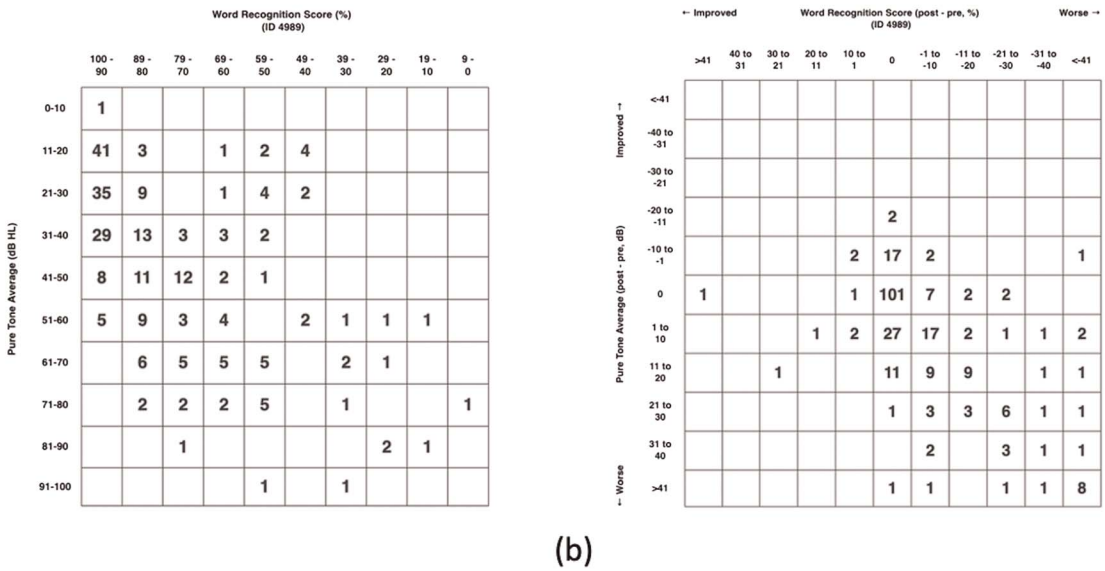


FIG. 3. Hearing class (*A*) in the ear with tumor at diagnosis and at the last follow-up according the modified Sanna classification and scattergram (*B*) of patients at diagnosis and at last follow-up (n = 257).

recommended by other investigators based on similar findings (10,11,21–24).

In a systematic review of the literature, the mean growth rate for all tumors was found to vary between 1 and 2 mm/yr (18). In accordance with the literature, the growth rate for all tumors in the current work was 1.51 mm/yr. We also identified complex patterns of tumor growth and not just simple growth or no growth. Few studies have shown similar patterns highlighting that predicting the behavior of VS is not a simple task (25,26). Different authors tried to study the predicting variable that correlate with tumor growth with contradictory results. Age, sex, side, duration of symptoms, and tumor size at diagnosis did not predict tumor growth (11,27–30). In the present study, PTA was significantly worse in the cases who manifested tumor growth when compared with NG. However, with regression analysis, the difference was not statistically significant. No other predictors of tumor growth were identified in the present work; a finding also confirmed by other investigators (11,27). On the other hand, other reports found that tumor growth was correlated with larger size at diagnosis in

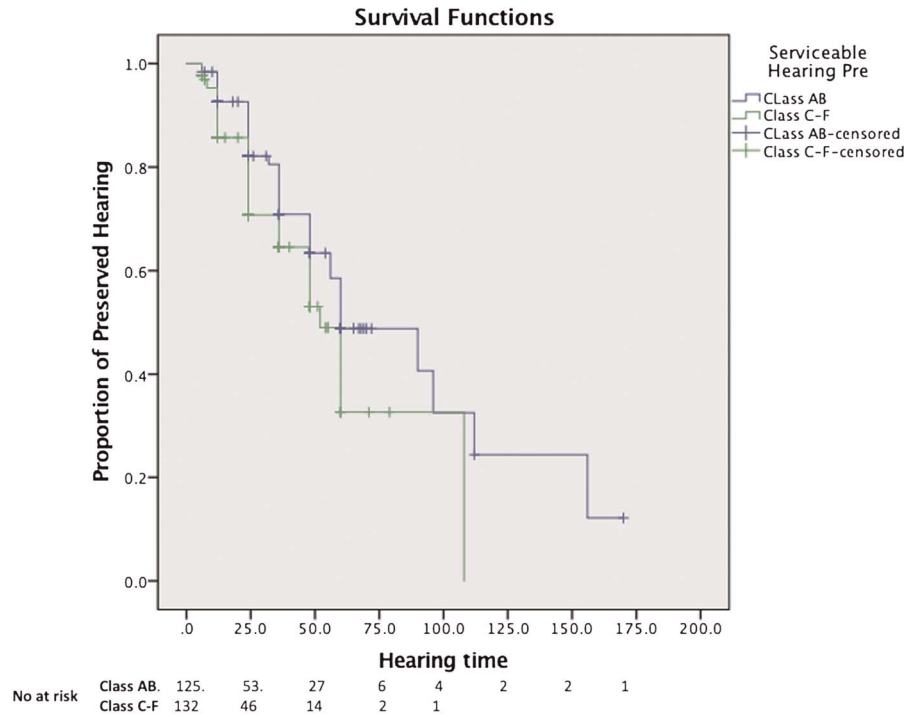


FIG. 4. Kaplan–Meier survival curve depicting probability of hearing deterioration over time (months of follow-up) with the cohort divided into patients with serviceable hearing at diagnosis (class A/B) and those with unserviceable hearing at diagnosis (class A–F). Log rank test: x^2 4.18, $p = 0.041$*.

association with tinnitus (31), disequilibrium (29,32), or with balance symptoms and hearing loss of less than 2 years at the time of diagnosis (33). The discrepancy in determining predictive values for tumor growth can be attributed to the heterogeneity of studies, the variable methods of recording tumor growth and the fact that our series included only ICVS. Failure to identify tumor growth predictors highlights the importance of serial imaging in all cases and the need to stress this fact during patient counseling.

Hearing Results

The results of hearing preservation in the wait and scan VS patients vary in different series. There are a lot of controversies in what is meant by hearing preservation.

TABLE 2. *Predictive values of hearing preservation (all cohort n = 257) and maintenance of serviceable hearing (n = 125) in univariate and multivariate logistic regression*

	Hearing Preservation All Cohort (n = 257)			Maintain Serviceable Hearing (n = 125)		
Variable	OR	95% CI	*p*	OR	95% CI	*p*
Univariate analysis						
Age	0.968	(0.945–0.992)	0.008**	0.959	(0.924–0.996)	0.029*
Sex (one female)	0.944	(0.562–1.585)	0.826	0.781	(0.352–1.734)	0.544
Side (one left)	1.456	(0.870–2.436)	0.153	2.666	(1.163–6.109)	0.020*
Initial PTA	0.984	(0.984–0.971)	0.020*	0.879	(0.829–0.932)	0.0001**
Initial SDS	1.008	(0.997–1.018)	0.154	0.977	(0.942–1.012)	0.199
Tinnitus at presentation	1.1541	(0.799–2.2972)	0.179	2.391	(0.758–7.540)	0.137
Vertigo at presentation	1.148	(0.619–2.128)	0.661	2.537	(0.807–7.975)	0.111
Tumor growth	0.252	(0.146–0.435)	0.0001**	0.162	(0.068–0.382)	0.0001**
Multivariate analysis						
Age	0.965	(0.938–0.993)	0.16	N	N	N
Side	N	N	N	2.822	(0.840–9.478)	0.093
Initial PTA	N	N	N	0.857	(0.788–0.932)	0.0001**
Tinnitus at presentation	2.217	(0.954–5.152)	0.64	N	N	N
Tumor growth	0.282	(0.148–0.537)	0.0001**	0.138	(0.40–0.469)	0.002**

*$p < 0.05$.
**$p < 0.01$.
N indicates excluded from model.

Many authors used the American Academy of Otolaryngology Head & Neck Surgery classification and considered hearing preservation as maintenance of good hearing (>70% SDS and PTA <30 dB), and/or serviceable hearing (>50% SDS and PTA <50 dB) (12–14,34). Others used the consensus meeting classification (17), considered hearing deterioration as a decline in hearing by at least one class (35), or the mere decrease of PTA by at least 10 dB (14). For those reporting maintenance of good hearing (>70% SDS and PTA <30 dB), the results varied from 17 (19) to 74% (6), with an average of 50% as reported in a systematic review (36). Pennings et al. (15), reported a 74% preservation of serviceable hearing according to the 50/50 rule and concluded that the majority of hearing loss in ICVS occurs early and that after 3 years of observation the likelihood of hearing deterioration is very small. The mean follow-up of their cases was 3.6 years. However, in series with long mean follow-up, hearing preservation results were low as it was observed that irrespective of tumor growth hearing deteriorates with time (19,36,37). Our results of maintaining serviceable hearing at the last follow-up was 72%. However, in patients who had audiological data for more than 5 years, only 55% maintained their serviceable hearing which is comparable to the average rate of hearing preservation in the literature and with the findings of hearing deterioration over time.

Some studies showed that favorable factors for hearing preservation include good hearing at presentation (38–40), and slow or no tumor growth (12,13,19,35). In accordance with these findings, we found that no tumor growth and good hearing at presentation were predictive factors for preservation of serviceable hearing at followup. Other investigators, however, found no relation between tumor growth and hearing deterioration (15,17,37), whereas others found that tumor growth was associated with the annual hearing decreasing rate only in ICVS but found no correlation in extracanlicular tumors (41). In the current series, we also concluded that hearing preservation was correlated with younger age. A possible explanation is that younger people may tolerate the tumor effect better than the more elderly which is evidenced by the finding that normal hearing in VS was more prevalent in younger population (42).

Termination of Follow-up and Comparison With Other Lines of Treatment

Mere SG is not an absolute indication for intervention. Fast or continuous growth with EC extension, impending brainstem compression, younger age group, worsening symptoms, and patient's will all favor active treatment. It is noteworthy that failure of wait and scan and a shift to intervention was performed in only 18.8% of our patients. This means that nearly 81% of patients would have been overtreated if active intervention had been chosen from the start with unnecessary exposure of added risks and complications of these modalities. Though surgery after failure of the wait and scan might carry a poorer facial nerve (FN) outcome because of larger tumor size, a previous report showed no increased risk of injury to FN due to wait-and-scan per se over initial surgery between similar sized tumors (43). We, therefore, think that primary active treatment in ICVS should be offered only if hearing preservation is aimed at. In this context, the results of the hearing preservation treatment should be superior to the natural course of the disease.

Some authors argue that hearing preservation outcomes are better in RT in comparison to wait and scan (14). However, in a systematic review of hearing preservation after RT, a clear tendency of hearing deterioration with time has been noticed. Using the class B of AAOHNS, a decline of preservation of hearing from 73% at less than two years of follow-up, 59% at two to five years of follow-up, 48% at five to ten years follow-up, and 23% at ten years or greater was observed (44). In our series, a 55% preservation of serviceable hearing class A/B of modified Sanna classification (which is comparable to class A of AAO-HNS) was seen after 5 years and, therefore, a wait and scan policy gives equivalent if not better results of hearing preservation. In addition, reported RT tumor control rate carries a selection bias. In a review of literature, Putanik et al. (26), found that most of the RT series do not follow a wait and scan policy before initiation of treatment. Since the natural history of small VN shows no growth in most cases, some of these irradiated tumors would not have grown irrespective of whatever treatment they received. Moreover, RT raises some concerns of long-term tumor control and the rare potential of malignant transformation (45). In cases in which tumor continues to grow despite RT, facial nerve outcomes of microsurgical resection are worse when compared with nonradiated patients (46).

Peng and Wilkinson (47) recommended microsurgical resection for small VS via the middle fossa in patients under 65 years as a primary treatment to preserve hearing. They argued that surgery offers better hearing preservation than wait and scan, particularly in patients with hearing symptoms which are predictors of hearing deterioration if wait and scan is adopted. Zanelloti et al. (48), favored a hearing preservation surgery rather than wait and scan in small VS with class A/B of the modified Sanna classification, as long-term hearing outcome would be more favorable. In a systematic review of the literature, using the A/B class of the AAO-HNS, 58% of patients with preoperative serviceable hearing retained serviceable hearing at last follow-up assessment after microsurgical resection of small VS with a mean follow-up of 52 months (49). This is comparable to the 55% of retained serviceable hearing after 5 years in our series. It is true that unlike wait and scan, hearing after surgical removal is generally stable over time (50), but when the results are adjusted to the serviceable hearing (classes A and B) of the modified Sanna classification, the hearing preservation rates are much less than reported as we have previously shown (51). In addition, the added morbidity of surgery should be considered. It is noteworthy, that Markov decision analysis comparing the three management strategies for small VS and a study of the quality of life determined that a period of observation

resulted in higher quality-adjusted-life-year totals than immediate surgery or RT treatment (4,52).

A word of caution in the wait and scan management is that some patients discontinue their follow-up. This has been shown in our series and documented by others (53). Moreover, tumor growth, as seen in our series, is not predictable and not necessarily linear. It is therefore of paramount importance to stress the necessity of adherence to lifelong follow-up during patient's counseling as these tumors may grow despite initial quiescence.

Limitations and Strength of the Study

Limitations of the current study include the retrospective design, the loss of follow-up in several patients, the selection bias, and the relatively short mean followup period.

The advantages are the focus on ICVS, the strict inclusion/exclusion criteria, and the large number of patients in comparison to the most series in the literature.

CONCLUSIONS

The wait and scan treatment proved to be a valid option in the management of ICVS. Tumor growth occurred in 41.6% of the wait and scan patients. Only 18.8% needed intervention. In patients with initial class AB hearing, serviceable hearing was maintained in 55% after 5 years of follow-up.

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