Decision Making on Vestibular Schwannoma: Lessons from a Multidisciplinary Board

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BACKGROUND: **Management of vestibular schwannoma (VS) is a complex process aimed at identifying a clinical indication for fractionated stereotactic radiotherapy (sRT) or radiosurgery, microsurgical resection, or wait and scan (WS). We describe the experience of our VS multidisciplinary team (MDT) at a tertiary university referral center created for diagnosis, treatment, and follow-up of VS patients.**

METHODS: **We conducted a retrospective study on 132 consecutive patients referred to the MDT and managed by observation (WS), microsurgery, or fractionated sRT. The analysis included patient age, tumor size, hearing level, facial nerve function, tumor control, complications, and quality of life questionnaires.**

RESULTS: **Among the patients, 21% were subjected to microsurgery, 10% to sRT, and 69% to WS. The median follow-up time was 30 months. Outcomes based on different management modalities are described. Statistically significant differences among groups were detected in terms of quality of life (physical domain).**

CONCLUSIONS: **MDT may provide the best individualized therapy for VS patients compared with a single gold-standard strategy.**

INTRODUCTION

Decision making in the treatment of vestibular schwannoma (VS) has become progressively more complex. Major advancements have been made in VS management: fractionated stereotactic radiotherapy or radiosurgery (sRT) provides a treatment alternative to microsurgical resection, especially in patients with increased risk of perioperative complications, advanced age, and tumor size <2.5 cm.[1-3] Surgery remains the mainstay of treatment for larger tumors, with the main approaches being translabyrinthine and retrosigmoid.[4-6]

At present, VS-specific mortality is near zero and most patients benefit from durable tumor control, regardless of the type of treatment.[7] Therefore adequate counseling is necessary and must give realistic expectations. For this reason, an increasing interest in quality of life (QoL) measurements has arisen in the field of VS treatment.[3] Since our understanding of the natural history of VS has improved, there has been a trend toward more conservative management without significant degradation of QoL.[8] Many centers have now foreseen the presence of a multidisciplinary team (MDT) composed of different professionals, specializing in not only the diagnosis and staging of the tumor but also the best individualized therapy and adequate supportive care for each patient. The objective of this manuscript is to describe the experience of the MDT at our tertiary university referral center created for diagnosis, treatment, and follow-up of VS patients. We describe the algorithm used in treatment decision making, summarizing the results of 3 main strategies (surgery, sRT, and wait and scan) in terms of QoL, tumor control, hearing function, and complications.

Key words
- Management
- Multidisciplinary
- Vestibular schwannoma

Abbreviations and Acronyms
AAOHNS: American Academy of Otolaryngology—Head and Neck Surgery
MDT: Multidisciplinary team
MRI: Magnetic resonance imaging
MS: Microsurgery
PCS-12: Physical Component Summary
QoL: Quality of Life
SF-12: Short Form 12
sRT: Stereotactic radiotherapy or radiosurgery
TL: Translabyrinthine
VS: Vestibular schwannoma
WS: Wait and scan

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Citation: World Neurosurg. (2022) 157:e506-e513. https://doi.org/10.1016/j.wneu.2021.10.140

Journal homepage: www.journals.elsevier.com/world-neurosurgery

Available online: www.sciencedirect.com

METHODS

Patient Characteristics

This is a retrospective study on 132 consecutive patients who were referred to the vestibular schwannoma MDT of the Department of Head and Neck Surgery of the Catholic University–Rome from June 2016 to December 2019. The MDT was composed of an otolaryngologist, neurosurgeon, and radiotherapist and was held once/twice a month. Exclusion criteria were follow-up time <12 months, patients affected by type 2 neurofibromatosis, patients unwilling to fulfill the questionnaires, and patients whose clinical documentation was not fully available. Data collected for the analysis included patient age, tumor size, date of diagnosis, type and date/period of treatment, hearing level, and facial nerve function according to the House Brackmann scale. Radiologic assessment data refer to magnetic resonance imaging (MRI) scan with gadolinium, which was scheduled in all patients 7–10 days before each consultation. Tumor size was measured by MRI (T1 contrast-enhanced thin slice) and evaluated according to the Koos classification.

Hearing Assessment

Hearing assessment consisting of pure tone audiometry and speech discrimination test was performed in all patients on the same day of the MDT meeting. The pure tone audiometry value was obtained as an average of the 0.5, 1, 2, and 4 kHz frequencies. In the speech discrimination test, the score was calculated as a measure of percentage of words recognized and repeated by the patient, taken from a standardized list presented at suprathreshold levels. Hearing characteristics were categorized according to the American Academy of Otolaryngology–Head and Neck Surgery (AAOHNS) guidelines.[9]

Treatment Options. Following radiologic and hearing assessment, the strategy regarding treatment was chosen during MDT consultations on the basis of tumor characteristics, symptoms, age, and general health. An algorithm was used in decision making, as follows:

1. The observation option "wait and scan" (WS) was indicated in all patients with a first diagnosis of VS, except in those with a lesion >3 cm or affected by disabling symptomatology. Patients underwent a 6-month follow-up by MRI + MDT consultation, and after 2 consecutive examinations documenting no tumor growth, yearly MRI + MDT consultation was prescribed and the patient remained under the observational option. In case of a significant growth of the tumor (i.e., >3 mm), the strategy was abandoned.
2. Microsurgery (MS) was proposed immediately for tumors ≥3 cm in diameter, for tumors <3 cm with documented growth, and for patients with disabling symptomatology. The MS approaches performed were translabyrinthine (TL) and retrosigmoid, and the choice usually depended on hearing function and the dimension and location of the tumor. After MS, patients are followed by a yearly MRI + MTD consultation for the first 2 years and later every 2 years in case of growing residual disease.
3. sRT was indicated in patients older than 65 years, with growing tumors <2.5 cm that led to minimal morphologic alterations of adjacent brain structures. The treatment was performed using LINAC (VARIAN CLINAC 2100 CD) in photon mode with a nominal energy of 6 MeV. The total dose administered was 1800 cGy with fractioning of 600 cGy per day for 3 consecutive days. In all patients, images of the anatomic district were acquired. The measurement of the mean volume reduction was performed as previously indicated by Söderlund Diaz and Hallqvist.[10] After sRT, patients were followed by yearly MRI + MTD consultation. **Figure 1** shows the flowchart depicting the possible strategies for individualized VS treatment.

Quality of Life Questionnaire. Two questionnaires were administered to all patients on the same day of the MDT meeting. The first was the Short Form 12 (SF-12),[11] a multipurpose measure of health status. The 2 main items are the Mental Component Summary–12 and Physical Component Summary (PCS-12). Higher scores indicate better health status. The second was a 6-question survey specifically designed by the authors (**Table 1**) that investigated previous clinical experiences on VS management and satisfaction related to the consultation. The questionnaire scores were compared among groups (MS, sRT, and WS groups). The questionnaires administered at the 6-month posttreatment consultation in the MS and sRT groups and those administered at the last consultation in the WS group were used for comparison.

Statistical Analysis

Continuous variables were described using means and standard deviations (SD) when their distribution was normal and medians and ranges when their distribution was skewed. Comparisons of baseline demographics, clinical outcomes, and QoL outcomes among patients in the 3 groups were evaluated using Kruskal-Wallis tests for continuous and ordinal data. The statistical analysis of the results was performed using SPSS for Windows (IBM SPSS Statistics, Chicago, Illinois, USA). The results were considered as significant for P values <0.05 with a confidence interval of 95%. This study was approved by our institutional review board and carried out in accordance with the Declaration of Helsinki. All patients received comprehensible information about the surgical procedures and surveys and gave their consent for participation.

RESULTS

Patient Characteristics

On the basis of inclusion criteria, the analysis was performed on 107 patients; 25 patients abandoned MDT consultations (18.9%). The median age of patients at the time of the first MDT meeting was 60 years (range: 48–84 years). The male-to-female ratio was 0.84. The median pretreatment Koos grading was 2 (range: 1–4). All patients had pretreatment grade I facial nerve function. The median time from diagnosis was 35 months (range: 0–252 months). The median time from the first to the last MDT meeting, at the time of data analysis, hereafter referred to as follow-up time, was 30 months (range: 12–54).

Twenty-two patients (21%) were subjected to a microsurgical procedure (MS group), performed by a TL approach in 16 patients and a retrosigmoid approach in 6 patients. Surgery was indicated

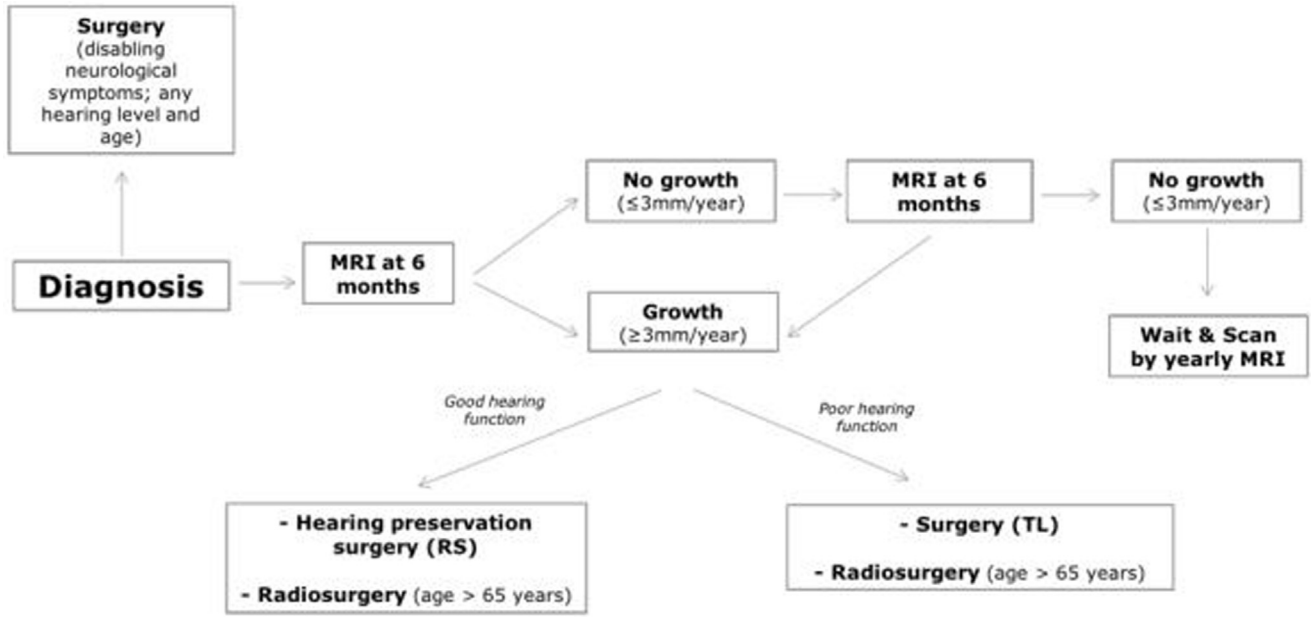

Figure 1. Decision making flowchart depicting the possible strategies for individualized treatment. MRI, magnetic resonance imaging; RS, retrosigmoid approach; TL, translabyrinthine approach.

after a mean time of 4.3 months (range: 0–36) from the first MDT meeting. Fractionated stereotactic radiotherapy was performed in 11 patients (10%; sRT group) and was indicated after a mean time of 6.5 months (range: 0–24) from the first MDT meeting. Seventy-four patients (69%) were subjected to WS strategy.

Baseline demographic and clinical data and significant differences between groups are summarized in Table 2. The 3 groups were heterogeneous in terms of the following baseline characteristics: age, Koos grade, AAOHNS grade, and follow-up time. At pairwise analysis, age was significantly higher in the sRT versus MS group and in the sRT versus WS group ($P < 0.05$ for both comparisons). Median Koos grade was significantly higher in MS versus sRT and in MS versus WS ($P < 0.05$ for both comparisons). Preoperative AAOHNS grade was significantly higher in MS versus WS and in sRT versus WS ($P < 0.05$ for both comparisons). Follow-up time was significantly longer in sRT versus WS ($P < 0.05$).

Outcomes Based on Different Treatment Modalities. In the MS group, 4 of 22 patients (18%) had postoperative facial nerve dysfunction (2 with grade IV and 2 with grade III facial nerve palsy). No serviceable hearing (AAO-HNS Class > B) was present after surgery. One complication was reported: a cerebrospinal fluid leak through the retroauricular wound that resolved after 8 days of conservative therapy (bed rest and diuretics). All patients underwent complete removal of the tumor.

In the sRT group, one patient complained of facial paresthesia and postural instability after treatment, both symptoms resolved spontaneously in 2 weeks. No other complications were reported. One patient had posttreatment hearing worsening (class B to class D). The tumor control rate was 100%, and the mean volume reduction was 6.3 mm (range: 4–8.7 mm). The comparison was performed between pretreatment and last MRI, with a mean interval of 31 months (range: 12–42 months). Among those patients, 3 had transitions from stage III Koos to stage II Koos. The remaining 8 patients had unchanged Koos stage after treatment.

In the WS group, during follow-up time hearing class worsened in 5 patients, as measured at the last examination (Figure 2). No further symptoms occurred during observation and tumor size remained unchanged at subsequent MRI examinations in all cases.

Quality of Life Questionnaires

Median overall PCS-12 score was 47 (range: 23–62), with a median difference compared with the U.S. average of −3.2 (see Table 2). Median overall Mental Component Score–12 score was 44.7 (17–63), with a median difference compared with the U.S. average of −4.8. Significant differences between groups were detected in the PCS-12 item, with higher scores in the WS group compared with the MS and sRT groups ($P < 0.05$ in both comparisons). Detailed results from the SF-12 administration are reported in Table 3. Responses to the second part of the survey are shown in Table 1.

DISCUSSION

The multidisciplinary approach to VS management has led to a shift in older treatment paradigms. During the present experience of the MDT board for VS, we noted several advantages such as comprehensive assessment of otoneurologic symptoms, careful

Table 1. Specific Information and Results Collected from the Survey

Question	Answer Options	Results
1. In what year were you diagnosed with VS?		
Mean time from diagnosis (months; SD; range)		35.2 (±35; 0—252)
2. How many physicians have you already consulted because of the VS?		
Median; range		2 (0—5)
3. What field did they belong to?	General medicine	0
	Otolaryngology	84 (79%)
	Neurosurgery	38 (35%)
	Radiotherapy	22 (21%)
	Neurology	6 (6%)
	Other	0
4. Were all the physicians consulted in agreement on a single treatment?		
Yes		97 (91%)
No		10 (9%)
5. How did you find the medical examination carried out at our institution in general?	There was enough time to clarify my doubts	42 (39%)
	I was pushed toward a specific treatment	7 (7%)
	All the various possibilities have been explained to me in detail	57 (53%)
	I didn't feel adequately informed	1 (1%)
6. What sources of information do you usually use?	Medical books or scientific journals	11 (10%)
	Internet: pages dedicated to patients	51 (48%)
	Internet: technical pages dedicated to health professionals	33 (31%)
	Internet: Patient Forum	24 (22%)
	Information and advice from friends and relatives	29 (27%)

SD, standard deviation.

neuroradiologic evaluation, easier flow of patients among specialists, high surgical specialization, addressing functional and quality of life items, creation of local registries, and limitation of loss to follow-up. Before reaching the MDT, patients had already consulted an average of 2 physicians. Preventing dispersion of patients during follow-up is a further advantage: the possibility to schedule appointments in advance and to perform contextual radiologic examinations represents a significant benefit for patients and allows them to always interface with the same specialists. In addition, current EANO guidelines[10] state that compliance of patients is crucial for failure of follow-up and that conservative management requires a program of MRI scanning, audiometry, and outpatient consultation. The role of the MDT is strengthened by these recommendations. The main difference, compared with a traditional approach, resides in an individualized proposal of procedures compared with a single gold-standard approach. In recent years, other coordinated MDTs have been shown to improve patient outcomes.[11,12]

An algorithm was adopted to facilitate treatment indications. However, in some situations (i.e., strong patient motivation for surgical removal, impairing symptoms, etc.) different approaches can be suggested. Moreover, decisions on "borderline" cases should be made considering the experience of the center and individual skills of surgeons, since the results of VS surgery are operator dependent. Especially in the choice among different surgical indications, strict observance of the flowchart is not always possible.

The main result is that of a numerical discrepancy between groups. The majority of patients were, in fact, assigned to a WS strategy. Following MDT evaluation, the role of surgery seems to be downsized to a reduced number of cases. The authors advise against immediate surgical indication, unless disabling neurologic symptoms are present. The age cutoff for radiotherapy administration was chosen on the basis of previous experiences,[1,13-16] and it is likely that it will undergo further changes in the future.

When intergroups characteristics were compared, we found that WS patients had significant differences in terms of Koos stage and hearing compared with the other groups. During the observational time, significant changes, in terms of tumor size and symptoms, were detected. Those who undertook treatment (30% of the overall

Table 2. Baseline Demographic and Clinical Data Expressed as Median/Range

		MS Group					*P* Value			
Feature	**Overall**	**Overall**	**TL**	**RS**	**SR Group**	**WS Group**	**Overall Comparison**	**MS vs. SR**	**MS vs. WS**	**SR vs. WS**
Age (years)	60 (48–82)	60 (48–80)	59	71	70 (69–82)	59 (50–82)	<0.05	<0.05	>0.05	<0.05
Sex										
Female	58	11	7	4	9	38	>0.05			
Male	49	11	9	2	2	36	>0.05			
Follow-up time (months)	30 (12–66)	30 (12–54)	38	30	42 (11–54)	29 (12–66)	<0.05	>0.05	>0.05	<0.05
Pretreatment tumor size										
Median Koos grade	2	4	4	4	2	2	<0.001	<0.001	<0.001	>0.05
Koos I (number of patients)	24	0	0	0	0	24				
Koos II (number of patients)	39	7	6	1	5	27				
Koos III (number of patients)	14	2	2	0	0	12				
Koos IV (number of patients)	30	13	8	5	6	11				
Pretreatment hearing (AAOHNS grading)										
Grade A (number of patients)	25	2	0	2	0	23	<0.05	>0.05	<0.05	<0.05
Grade B (number of patients)	16	1	0	1	2	13	<0.05	>0.05	<0.05	<0.05
Grade C (number of patients)	22	6	6	0	0	16	<0.05	>0.05	<0.05	<0.05
Grade D (number of patients)	44	13	10	3	9	22	<0.05	>0.05	<0.05	<0.05

MS, microsurgery; TL, translabyrinthine; RS, retrosigmoid; SR, stereotactic radiotherapy; WS, wait and scan; AAOHNS, American Academy of Otolaryngology—Head and Neck Surgery.

population) abandoned the WS group after an average short period (4–6 months). This may be because many patients were referred to MDT since they were already symptomatic or because they were affected by a large tumor and wanting to adopt a therapeutic solution. The remaining patients in the WS group, after a median time of 29 months, did not show evidence of tumor growth or symptomatology onset/worsening, leading to a change in strategy. Although our results were collected during a relatively

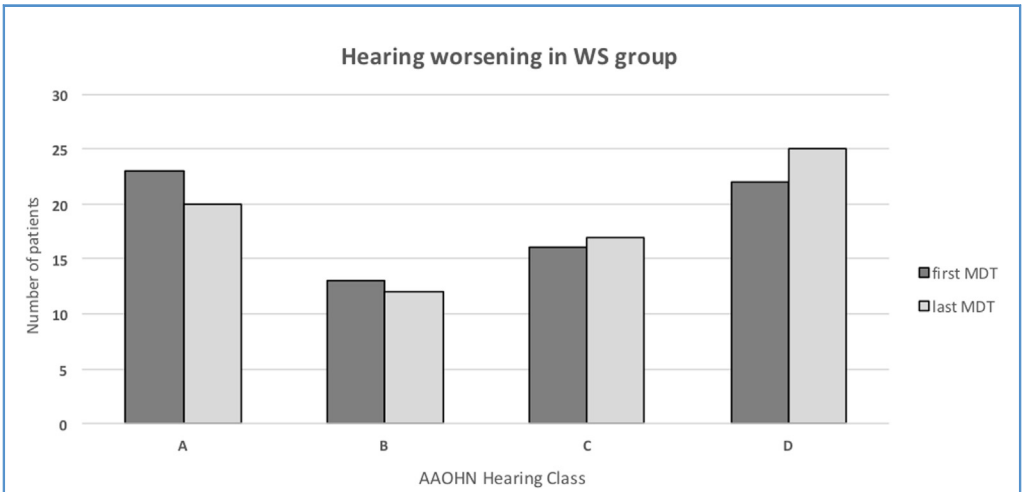

Figure 2. American Academy of Otolaryngology—Head and Neck Surgery hearing class worsening in the wait and scan group during follow-up. WS, wait and scan; MDT, multidisciplinary team.

Table 3. Results from Short Form-12 Survey Expressed as Median/Range

Feature	Overall	MS	SR	WS	*P* Value			
					Global comparison	Pairwise MS vs. SR	Pairwise MS vs. WS	Pairwise SR vs. WS
PCS-12	47 (23 to 62)	46.6 (23 to 54)	43.7 (27 to 54)	50.1 (26 to 62)	<0.05	>0.05	<0.05	<0.05
Difference from U.S. average	−3.2 (−27 to 11)	−3.9 (−27 to 4)	−7.2 (−23 to 3)	1 (−25 to 11)	<0.05	>0.05	<0.05	<0.05
MCS-12	44.7 (17 to 63)	43.7 (26 to 61)	49.5 (23 to 58)	44.7 (17 to 63)	>0.05	>0.05	>0.05	>0.05
Difference from USA average	−4.8 (−33 to 19)	−6.2 (−23 to 11)	−0.4 (−26 to 8)	−4.8 (−33 to 19)	>0.05	>0.05	>0.05	>0.05

MS, microsurgery group; SR, stereotactic radiotherapy group; WS, wait and scan group; PCS-12, physical component score; MCS-12, mental component score.

short observational time, they are consistent with those reported in similar populations. Fayad et al[17] described 114 VS patients receiving conservative management during a mean interval of 3.8 years and found that 31% of patients required further treatment with surgery or radiation therapy. Analogous results on longer follow-up time (11–12 years)[18,19] demonstrated a similar drop-out rate with a conservative strategy, between 22% and 35%.

In the sRT group, age was significantly higher compared with both the MS and WS groups and Koos stage was significantly lower compared with the MS group, thus confirming the rationale for sRT. No significant toxicity was detected during follow-up: only 1 patient had hearing deterioration after treatment, although a low mean hearing level at baseline (81% of patients with pretreatment unserviceable hearing) must be considered. No facial palsy or other permanent complications were reported. Other studies have shown more pronounced neurologic morbidities, with 1.6% of patients experiencing new facial weakness, 2.8% of patients new trigeminal nerve damage, 0.9% hydrocephalus, and 0.5% with possible radiation-induced malignancies.[20] Other studies have described analogous toxicity rates, with a hearing preservation rate of 85%–87% of cases.[13-22] However, the comparison of these findings should take into consideration the low sample size of our study (11 patients in the sRT group).

While surgery may cause sudden neurologic impairment, radiation can affect neurologic function even after many years. For this reason and in the event a tumor regrows, we do not suggest sRT for those younger than 65 years. Some authors recommend radiation therapy only in older patients.[14-16] Carlson et al,[1] comparing RT with MS, observed a significant difference in terms of age (66 vs. 58 years, respectively). However, this indication is still debated. A precise cutoff has not been suggested to date, and recent EANO guidelines[10] do not mention the issue.

A recent systematic review[23] has demonstrated differences in terms of hearing preservation comparing stereotactic radiosurgery versus fractionated radiotherapy, with slightly better results obtained by the latter (49% vs. 45% of average deterioration for patients with serviceable hearing, respectively). On the other hand, nonreproducible findings were obtained from comparison of tumor control between the 2 methods. In our hospital, only LINAC fractionated radiotherapy is routinely administered, and thus these results could not be confirmed.

The length of follow-up is crucial and can influence the incidence of neurologic impairment on hearing function after radiation. As far as tumor control is considered, after a median follow-up of 29 months we observed a local control rate for the 11-patient cohort of 100%, with a mean volume reduction of 6.3 mm. Our results are consistent with other midterm follow-up studies: A review by Apicella et al[24] listed a range of studies with different follow-up times, and the majority of those with comparable observational intervals (35–55 months)[2,18,25,26] showed a local control rate of 90.5%–100%. Along with increasing observational time, a progressive reduction of tumor control rates may be expected.[19] Although encouraging, our results need further confirmation with extended follow-up times.

As expected, the MS group was composed of younger patients compared with the sRT group and with a higher median Koos grade. Baseline hearing levels were worse, compared with the WS group, but not with the sRT group. A low complication rate was registered in this population: no patient needed revision surgery and only 18% of patients manifested some degree of postoperative facial nerve impairment. The overall facial dysfunction rate lies well below the range limits described in the literature, with values from 43% to 63%.[20,27-29] However, the limited size of our surgical sample may partially account for this result. On the other hand, no patient preserved a sociable hearing level and the reasons for this are related to the low baseline hearing level (86% of patients with AAOHNS grade >B) and in the high proportion of patients subjected to a TL approach with consequent loss of cochlear function.

The mean SF-12 scores demonstrated overall deterioration in both physical and mental aspects of QoL in all patients. All management strategies, in fact, deviated negatively from the average norm. Most VS patients have minimal disability at presentation, and treatment of VS is aimed at dealing with the disease rather than patient symptoms per se. A significant difference was observed in the WS group, compared with the MS and sRT groups (physical item of the SF-12), whereas no differences were noticed considering MS versus sRT. Many previous papers have already reported QoL deterioration in patients undergoing surgery for VS,[30-32] underlining the importance of possible conservative treatment. Some studies have described significantly improved QoL outcomes in sRT patients versus surgery,[2] whereas others stressed the need for long-term follow-up to detect late improvements in the MS group.[33] Pollock et al[34] compared sRT versus microsurgical, finding that the former did not experience any deterioration, while the latter had early decline in the physical component score at 3 months post treatment, which subsequently returned to near baseline. Similarly, Myrseth et al[35] found greater impairment in the microsurgical group versus sRT, which was partially reduced at 1- and 2-year follow-up. In our study, we compared 6-month posttreatment survey results and therefore longer-term data are needed since late modifications may occur.

The present study has some limitations. First, the baseline characteristics of groups were not homogeneous, thus compromising the interpretation of QoL comparisons. This intrinsic bias cannot be eliminated since the different strategies are chosen on the basis of different clinical features, and this is shared by all analogous studies. The second limitation resides in the discrepancies in sample sizes of different groups. This is because, according to the decision-making algorithm, a minority of subjects were candidates for 2 treatment options. Moreover, no patient in the present series was operated on after radiotherapy administration. This constitutes an interesting topic,[36] which must be answered in the years to come.

The main strength is the novelty of the subject: the current study is, to the best of our knowledge, the first one analyzing the results from a standardized multiyear MDT for VS at a tertiary referral center.

CONCLUSION

MDT can offer an individualized management proposal to VS patients compared with a single gold-standard strategy. In our analysis, the majority of patients were assigned to a WS strategy and the use of surgery was downsized to a reduced number of cases.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Bruno Sergi: Conceptualization, Investigation, Writing — original draft. **Mario Balducci:** Investigation. **Gaetano Paludetti:** Supervision. **Alessandro Olivi:** Conceptualization. **Pasqualina Maria Picciotti:** Methodology, Validation, Writing — review & editing. **Eugenio De Corso:** Formal analysis, Software. **Giulio Cesare Passali:** Formal analysis, Methodology. **Anna Rita Fetoni:** Validation, Visualization. **Daniela Lucidi:** Data curation, Writing — original draft, Writing — review & editing.

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Conflict of interest statement: The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received 22 September 2021; accepted 20 October 2021

Citation: World Neurosurg. (2022) 157:e506-e513. https://doi.org/10.1016/j.wneu.2021.10.140

Journal homepage: ***www.journals.elsevier.com/world-neurosurgery***

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