Nervus Intermedius Outcomes after Vestibular Schwannoma Surgery and Radiosurgery: A Single Institution Experience

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Purpose

To present NI outcomes in our series of patients who have undergone all treatment modalities for vestibular schwannoma and a review of the existing literature.

Introduction

Nervus intermedius (NI) dysfunction in vestibular schwannoma (VS) is significant and is present in up to 75% of patients following treatment [1-9]. The NI comprises afferent sensory fibers from the nasopharynx, nose, external auditory meatus, and taste from the anterior two-thirds of the tongue. Additionally, it is responsible for parasympathetic innervation of the nasal mucosa, lacrimal gland, and the submandibular and sublingual salivary glands [10-11]. Currently, there are sparse reports of NI outcomes following either radiation and/or surgical resection. Moreover, it is unclear how specific tumor characteristics and treatment modalities affect the NI. Herein, we present NI outcomes from our series of patients undergoing all treatment modalities for vestibular schwannoma and perform a review of the existing literature in order to determine which treatments and patient factors predispose to NI dysfunction following VS treatment.

Methods

We obtained institutional review board (IRB) approval for the study. A retrospective review was performed of all patients who underwent either gamma knife radiosurgery and/or open surgery for treatment of VS between January 1, 2008 and December 31, 2018. Inclusion criteria included a diagnosis of a vestibular schwannoma and post-treatment follow-up for at least 1 month. A total of 222 patients were identified and classified as having undergone open microsurgery, gamma knife or both microsurgery and gamma knife. Patients' charts and Pre and Post-treatment T1 contrast MRI studies were then reviewed for assessment of tumor volume, radiation treatment dose, surgical approach and Koos grade [12]. Post-treatment clinical notes were used to define post-operative facial weakness and classified according to the House-Brackmann grades [13]. Extent of resection was described in operative reports and confirmed with radiographical data by comparing pre-operative MR images to immediate post-operative MR images. Resection was classified as either gross total (GTR) when there was no visible residual, near total (NTR) with 95-99% resection, or subtotal resection (STR) with < 95% resection. Patients were then contacted via phone and taken through a questionnaire [6] that included pre and post-operative assessment.

Statistical Analysis: After compilation of the data, descriptive statistics were used to characterize the NI dysfunction in patients and statistical analysis was performed using Graph Pad Prism 8. Statistical significance was accepted at a probability of 0.05. For subgroup analysis, statistical significance was determined by Fisher's exact test, student t-test or ANOVA..

Table 1. Patient Demographics

Patient Demographics	N		
Total Number of Patients	98		
Total Number of Radiation Patients	54		
Total Number of Surgical Patients	27		
Total Number of Patients with Rad and Surgery	17		
Male Patients [Total]	55		
Female Patients [Total]	43		
OVERALL TUMOR SIZE		Average Size (mm^3)	P-Value
All Patients	92	6210.61	<0.00001
Radiation Patients	50	1524.33	
Surgical Patients	26	11018.90741	
Patients with Radiation and Surgery	16	13864.84	

Table 2: Current published studies with early post-treatment NI dysfunction rates

Author	Year Published	Study	Post-Operative NI Dysfunction			
			Lacrimation	Dry Eye	Crocodile Tears	Gustatory Dysfunction
Nakamizo et al.	2012	Surgery	-	-	10.9%	-
Metwali et al	2018	Surgery	76.6%	-	-	19.9%
Irving et al.	1995	Surgery	72%	-	44%	48%
Watanabe et al.	2003	Surgery	-	-	-	34.3%
Stripe et al.	2007	Surgery	44%	40%	45%	33%
Noonan et al.	2016	Surgery	5%	38%	-	28%
		Radiosurgery	22%	11%	-	33%
Tamura et al.	2008	Surgery	-	25.3%	12.1%	-
		Radiosurgery	-	13.2%	1.5%	-
Park et al.	2013	Radiosurgery	11.1%	10%	2%	16%
Ung et al.	Current Study	Surgery	22%	74%	-	44%
		Radiosurgery	9%	30%	-	11%
		Surgery + Radiosurgery	23.5%	47.1%	-	29.4%

Results

98 patients responded to the questionnaire and were included within this study (44.1% response rate). Patients were stratified into three groups: Group 1 included 54 patients who underwent radiation, Group 2 with 27 patients who underwent surgical treatment, and Group 3 with 17 patients who underwent both radiation and surgery. Twenty-eight percent of patients presented with pre-operative NI dysfunction; most commonly dry eye followed by taste dysfunction and dysfunction with lacrimation (crocodile tears). Following treatment, 79% of patients experienced NI dysfunction most commonly dry eye. Statistical differences in dry eye and taste were observed when comparing the treatment groups.

Long-term follow-up of patients demonstrated recovery of NI function in our patient cohort. Of the 14 patients who experienced dysfunction in lacrimation, 4 patients (28%) demonstrated resolution of their symptoms. Rates of recovering from dry eye were much less and only 7/41 patients (17%) had resolution of their dry eye at two years. In comparison to dry eye and lacrimation dysfunction, gustatory dysfunction had higher rates of improvement and 50% of patients had improvement of their taste at 2 years (11/22 patients).

Figure 1 (a) Pre-treatment NI Dysfunction in All Patients: In total, 27 patients presented with pre-treatment NI Dysfunction. Three patients presented with lacrimation dysfunction, 16 patients presented with dry eyes, and 8 patients presented with gustatory dysfunction. (b) Post-treatment NI Dysfunction in All Patients: In total 77 patients presented with pre-treatment NI Dysfunction. Fourteen patients experienced lacrimation dysfunction, 41 patients had dry eye, and 22 patients had post-treatment gustatory dysfunction.

Figure 1A

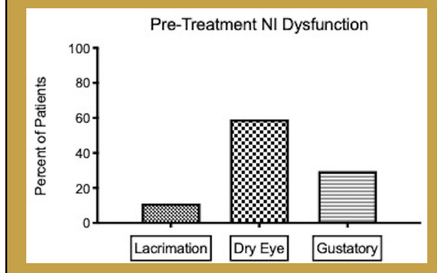


Figure 1B

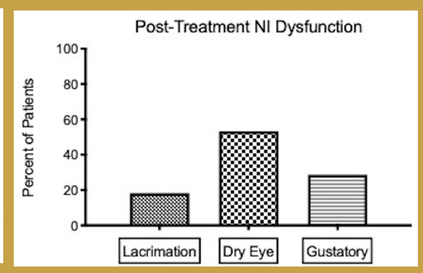


Figure 2 (a) Post-Treatment Dysfunction in Lacrimation: Post-treatment, 4/44 patients treated with radiation, 6/27 patients who underwent microsurgery, and 4/17 patients who underwent both radiosurgery and surgical resection experienced post-operative dysfunction. No statistical significance was observed between the groups, p-value 0.3. (b) Post-Treatment Dry Eye: After treatment, 4/44 patients treated with radiation, 20/27 patients treated with microsurgery, and 8/17 patients treated with a combination approach, experienced dry eyes attributed to NI dysfunction. P-value = 0.001 (c) Post-treatment Gustatory Dysfunction: In total, 5/44 radiation patients, 12/27 surgical patients, and 5/17 combined therapy patients experienced post-treatment taste dysfunction. P-value = 0.005

Figure 2A

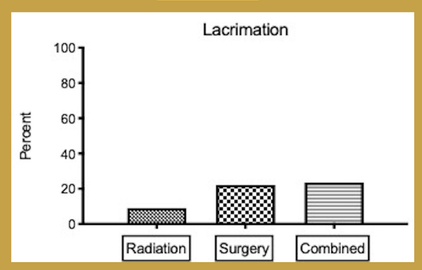


Figure 2B

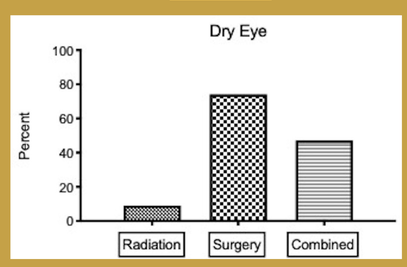
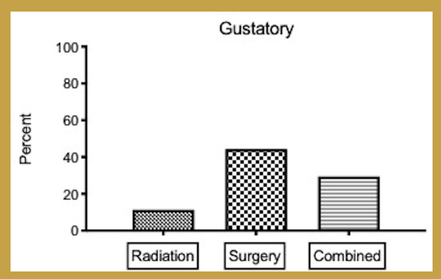


Figure 2C



Discussion

Our study showed that a variable NI dysfunction was present prior to treatment of vestibular schwannoma in 27% of patients. Following treatment, 79% of patients experienced NI dysfunction and most commonly was in the form of a dry eye. Statistical differences in dry eye and taste were observed when comparing the treatment groups and is more prevalent in the surgical group as compared to radiosurgery. In our series, many patients demonstrated an overall improvement of their NI dysfunction. Fifty percent of patients with gustatory dysfunction demonstrated improvement at 2 years, while rates of symptomatic improvement were much less in patients with dry eye and lacrimation dysfunction. These findings suggest that perioperative NI dysfunction is more common than generally believed and necessitates pre-treatment counseling as it may impact treatment choice and post-treatment care.

To the best of our knowledge, our study is the first to comparatively assess all treatment modalities including long term follow up. Given our findings, we believe that it is necessary to discuss the possibility of having NI dysfunction after treatment of VS. Although the ramifications of NI injury are relatively mild compared to facial motor deficits, NI dysfunction alters how patients interact with their environment and can impact patients' quality of life. In addition, advanced HB grade weakness and dry eye can have serious consequences such as exposure keratopathy and visual loss. Importantly, the rate of NI dysfunction can be observed in a majority of patients undergoing treatment with less than a half experiencing functional improvement.

Study Limitations:
Our study is limited by the single institutional and retrospective nature. Although we initially identified 222 patients within our initial review, only a limited number of patients responded to our questionnaire and thus were included into our study. The large regional demographic referral network to our institution impacts patients' follow-up and patients were lost to follow-up or had changed their contact information. Furthermore, the limited amount of responses may be attributed to a known tendency where only patients with post-operative symptoms respond to study questionnaires and continue to follow-up clinically. Another observation is the higher response rate among the radiosurgery group (around 50%). This may reflect their concern of the fact that they're still bearing the tumor and hence the need for long term follow up. Despite these limitations, our study illustrates the significant incidence of NI dysfunction associated with VS even prior to treatment. The differences observed in different treatment groups is likely attributed to selection bias with more small tumors undergoing radiosurgery and large tumors treated surgically. However, all treatment modalities can cause NI dysfunction. Future large prospective studies are warranted.

Conclusion

NI dysfunction is considerable before and after treatment of vestibular schwannoma most commonly in the form of dry eye. NI dysfunction is more prevalent in the surgical group as compared to radiosurgery and can be independent of facial motor palsy. Post-treatment gustatory dysfunction tends to improve over time more than dry eye and lacrimation dysfunction. These findings should be explained in pre-treatment counseling as they may impact treatment choice and quality of life.

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