

A Systematic Review of Interventions for Balance Dysfunction in Patients With Vestibular Schwannoma

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Objective: Dizziness is a major contributing factor to poor quality of life for patients with vestibular schwannoma (acoustic neuroma). We wished to review the literature on interventions for balance dysfunction in these patients.

Data Sources: A systematic literature review was performed identifying studies that measured balance function before and after treatment for vestibular schwannoma. Data sources include Medline (1950–present), EMBASE (1974–present), Cochrane Library (issue 3, 2008), NHS Centre of reviews and dissemination, Clinical Evidence, Cochrane central register of controlled trial, and CINAHL.

Study Selection: A minimum follow-up of 6 months was required, to estimate long-term balance function. Eight articles were identified, including five studies with surgical intervention, two studies with stereotactic radiotherapy, and one comparing the two. Study design was generally poor with a high risk of bias. These studies all utilized the

Dizziness Handicap Inventory (DHI) as a measure of pre- and postintervention balance function.

Data Extraction: Results showed that overall DHI scores are not statistically affected by intervention irrespective of modality (surgery or stereotactic radiotherapy). Patients selected with severe dizziness, who undergo surgery, improved postoperatively. No other studies for severe dizziness were noted for comparison.

Conclusions: Age, sex, and tumor size have no statistically significant effect on DHI outcomes, and no evidence to suggest which treatment modality has better dizziness related outcomes. No specific treatment modality was superior in terms of long-term balance function. Patients with severe dizziness may benefit from surgery, although no comparator studies were identified. **Key Words:** Acoustic neuroma—Balance—DHI—Dizziness—Vestibular schwannoma.

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Vestibular schwannomas (historically also known as acoustic neuroma) are a benign neoplasm arising from the vestibular nerves. The estimated annual incidence of vestibular schwannoma is 17.4 per million people (1). Vestibular schwannomas most commonly present with hearing loss, tinnitus, and dizziness.

The incidence of balance disturbance or dizziness has been reported as between 49 and 66% in patients with vestibular schwannoma (2). Of the symptoms experienced by those with vestibular schwannoma, dizziness has the greatest detrimental effect on quality of life, even when compared with facial nerve dysfunction and hearing loss (3). Balance dysfunction and dizziness may occasionally be debilitating symptoms, limiting an individual's day-to-day function and ability to work (4).

Vestibular schwannomas are usually managed by three different approaches: surveillance with serial

MRI imaging, radiotherapy-based treatments (including stereotactic radiosurgery [SRS]), or surgical resection. Published evidence regarding the efficacy of vestibular schwannoma management tends to concentrate on removing the lesion and/or preventing growth of the tumor. Secondary outcomes often include preservation of hearing (if serviceable) and facial nerve function. Comparatively less attention has been focused on other symptom control, including dizziness.

It is likely that each treatment modality interacts differently with the vestibular system and it remains unclear how this may affect long-term symptoms. The prevalence of persistent postsurgery disequilibrium was highlighted in a number of articles, with rates ranging from 10 to 78% (5,6).

The aim of this study is to review published evidence regarding the long-term effect of treatment on the symptoms of imbalance caused by vestibular schwannoma.

METHODS

A systematic review on August 23, 2017 was conducted using Medline (1950–present), EMBASE (1974–present), Cochrane Library (issue 3, 2008), NHS Centre of reviews and dissemination, Clinical Evidence, Cochrane central register of controlled trial and CINAHL were searched. The search

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strings acoustic neuroma, vestibular schwannoma, dizziness, balance, disequilibrium, and vertigo were combined with Boolean operators. Results were limited to English language. Full, peer-reviewed articles were included. Abstracts, posters, and proceedings of academic conferences were excluded. Duplicate results were filtered and removed. Reference lists were cross-referenced for additional relevant studies.

Full article publications were included that met the following criteria:

1. Patients with vestibular schwannoma undergoing any form of therapeutic intervention (whether specifically for balance rehabilitation or for removal/control of schwannoma).
2. Pre- and postintervention measurements of dizziness, vertigo, or balance impairment. Outcome measures should be validated and specific to dizziness (including objective tests of balance function or patient-reported outcome measures).
3. Studies looking at long-term dizziness outcomes rather than initial postop balance compensation (minimum follow-up 6 mo).

RESULTS

We identified 372 unique articles published between 1974 to present, of which 353 did not meet the inclusion

criteria (Fig. 1). Eleven of the remaining 19 articles were excluded as their main outcome measures were the Short Form Health Survey (SF-36) questionnaire or Glasgow Benefit Inventory, both of which are general quality-of-life measures and not specific to dizziness/imbalance.

Eight unique articles were included in the review where pre- and postintervention measurements of balance function were reported. No systematic reviews or randomized prospective studies were found measuring balance function in vestibular schwannomas. Seven studies were prospective studies and underwent formal data extraction, one study was a reported retrospective cross-sectional design. Study details are outlined in Table 1

Study Design and Reporting

In all studies, recruitment of participants was selected or restricted to consecutive patients with a diagnosis of vestibular schwannoma who presented to their center for treatment. All studies were observational, convenience-sample trials with no randomization. Three studies had small sample sizes, and therefore subject to selection bias (7–9). No study commented on power calculations.

None of the studies looked at conservative (surveillance) management alone. One study included two cohorts, who received surgery or SRS (10). Two studies

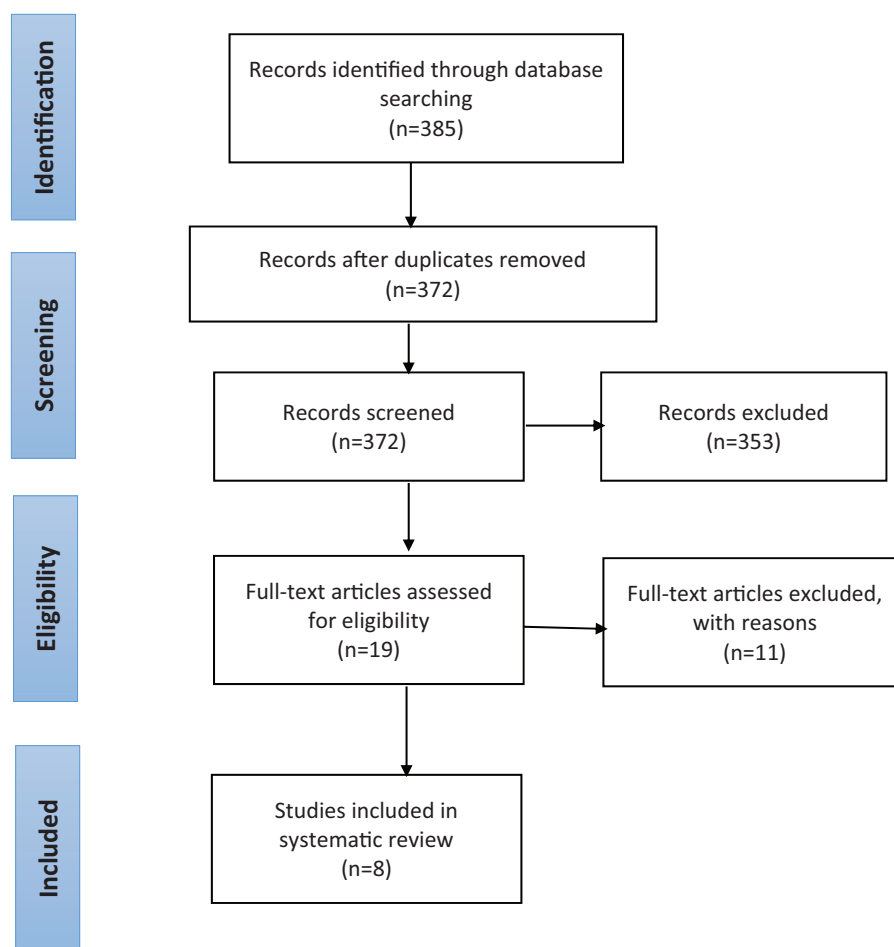


FIG. 1. PRISMA based flow-diagram showing systematic review search.

TABLE 1. Studies included in the systematic review of interventions for balance dysfunction in patients with vestibular schwannoma.

Author	Year	Design	Participants	Treatment Group (s)	Comparator Group (s)	Follow-up	Outcomes	Results
Humphriss et al. (13)	2003	Consecutively sampled prospective observational cohort study, retrospective review of case notes.	100	Surgery via Translabyrinthine approach with Vestibular rehabilitation before and after surgery	NA	12 mo	DHI	DHI done pretreatment, 3 and 12 mo posttreatment. Statistically significant change between pre- and 12 mo scores. 21% were worse and 5% improved, no <i>p</i> values provided. Most DHI does not worsen postop (73%) Cohort where DHI worsened up to 3 mo postop then plateaued. No <i>p</i> value given. Greater canal paresis made improvement more likely Tumor size can affect the degree of change in handicap. Age, the presence of central vestibular system abnormalities, and the nature of the patient's principal presenting symptom have no effect on this handicap change Findings: No statistical significant change, if does worsen will plateau after 3 mo
Pollock et al. (11)	2006	Consecutively sampled prospective observational cohort study	82	Surgery (36 patients) for vestibular schwannomas >3 cm in size or SRS (46 patients)	NA	12 mo	HSQ and DHI	DHI done pretreatment, 3- and 12- mo post. Eighty-two patients selected with unilateral VS less than 3 cm (excludes many patients we tend to operate on). Three patients had surgery and 46 patients had SRS, unclear as to how patients were selected, potential risk of bias. Patients who underwent surgery tended to be younger, may introduce significant bias. All surgical approaches used Analysis of DHI scores is incompletely described but reported at 12 mo 35% of surgical patients had no dizziness, compared with 61% of SRS patients. Mean DHI lower in SRS group at last follow-up ($p = 0.02$) which is statistically significant. Findings: difficult to make a conclusion as DHI analysis needs to be more rigorous and potential risk of selection bias. Study suggests SRS is better for dizziness in small to moderate VS, but unable to generalise findings. Eighteen patients' prospective surgery translab – all have disabling vertigo despite preop vestibular rehab, risk of selection bias. 88% reportedly improved at 12 mo ($p < 0.05$) Final DHI correlates with other postsurgical VS patients (i.e., those without baseline disabling vertigo). Age or sex did not correlate with changes in DHI scores. Findings: although small sized tumor, in cases with severe vertigo not responding to rehab, surgery can improve symptoms.
Godefroy et al. (8)	2007	Consecutively sampled prospective observational cohort study. Included if small, non-cystic, intracanalicular tumors, with no extrameatal growth.	17	Surgery (Translabyrinthine approach) and Vestibular rehabilitation before and after surgery	Dutch population, age and sex adjusted control group (n = 1063)	12 mo	SF-36 and DHI	

(Continued)

TABLE 1 (Continued)

Author	Year	Design	Participants	Treatment Group (s)	Comparator Group (s)	Follow-up	Outcomes	Results
Park et al. (12)	2011	Consecutively sampled prospective observational cohort study	59	GKS (12.5 Gy median dose) with a vestibular schwannoma size of 0.1 cm to 4.3 cm	NA	6 to 18 mo (mean 15 mo)	SF-36 and DHI	Fifty-nine patients undergoing GKS with preoperative and 1,3,6,12, and 18 mo follow-up. Mean VS size 1.3 cm, risk of selection bias. Baseline mean DHI 17. Post-treatment mean 14.5 No significant decline noted in DHI at any point. Only 46 patients had follow-up for 6 mo or greater (unable to exclude the 13 based on the data presented). Paired <i>t</i> test used for statistical analysis, normally used for distributed data, risk of method bias. Findings: no significant decline in DHI, however numbers in the study decrease at 6, 12, and 18 mo. Results may be confounded by selection bias.
Uehara et al. (14)	2011	Consecutively sampled prospective observational cohort study	38	Surgery (Retrosigmoidal approach). Patients were divided into groups dependent on initial caloric response (present or not).	NA	9 mo	DHI	Thirty-eight patients included: surgery 26 small VS; 12 large VS (no difference in age), no mention of remaining two patients. Risk of selection bias High drop-out rate of study (18 out of 58). <i>t</i> test used for statistical analysis – may not be appropriate. DHI deteriorated in “caloric response” group, and returned to preop baseline at 3 mo DHI returns to baseline 3 mo after surgery Worse scores in older patients (50 yrs and up) 6 and 9 mo postsurgery Findings: DHI worsened in Group 1 then normalized by 3 mo with no balance dysfunction postsurgery. Only refers to the statistically significant change and not the 18 point DHI “clinically significant” change. Vestibular compensation facilitates a more rapid or complete recovery after unilateral vestibular loss in younger patients than older patients.
Stavas et al. (9)	2014	Consecutively sampled prospective observational cohort study	10	SRS/FSRT (20 Gy mean dose)	NA	12.8 mo	DHI	Small sample size—10 patients. Risk of selection bias. Two patients were significantly worse post SRS (even at 12 mo), clinically and statistically significant. Radiation dose to vestibule not contributing to worse outcome. Findings: No overall group analysis provided, and with small sample size we cannot generalise the findings from this study.

TABLE 1 (Continued)

Author	Year	Design	Participants	Treatment Group (s)	Comparator Group (s)	Follow-up	Outcomes	Results
Thomeer et al. (10)	2015	Consecutively sampled prospective observational cohort study	48	Surgery (Transpetrosal approach) and Vestibular rehabilitation after surgery	NA	6 mo	DHI	Baseline DHI mean 14.1 (77% of patients). Postop 71% stable/improved—DHI 19.8 at 6 mo. Vestibular rehabilitation was beneficial if started early (<1mo post) Age, tumor stage, and cystic transformation had no statistical significance No effect of early initiation of vestibular rehab postop Preservation of ipsilateral cVEMPs had lower postop DHI scores. Larger sample size needed Findings: Improvement was not statistically significant
Samii et al. (15)	2017	Retrospective consecutively sampled prospective cohort study. The sample comprised those with Grade IV dizziness on the Kanzaki scale	19	Surgery (Retrosigmoidal approach)	Control group of randomly selected patients with intracranialicular VS, with no vestibular symptoms at presentation.	12 mo	DHI	Nineteen patients with disabling vertigo and small intracranialicular VS included. Risk of selection bias Preop DHI score >54 in all patients. Age, sex, duration, size and location had no effect on postop DHI score. No significant decline in DHI score postoperatively, in fact worse than control group at 3 wks and 1 yr. After 1 yr vertigo improved in all patients and resolved in 17/19. 12 mo no statistically significant difference between control group, BUT vertigo improved in all cases. Findings: Larger VS associated with better outcomes due to well-developed central compensation. Pro surgery for intracranialicular VS, at 12 mo process of compensation completed after stabilization of vestibular input, hence improvement in scores. Suggests surgery can help improve poor DHIs back to baseline for these specific patients.

TABLE 2. Studies included in the systematic review with their reported DHI (Dizziness Handicap Inventory) findings.

Author	Management	Follow-up	Number	Pre-DHI Score Mean	Post-DHI Score
Humphriss et al. (13)	Translabyrinthine surgery	12 mo	100	14.0 median	21.0 median
Pollock et al. (11)	Surgery group	12 mo	36	11.9	16.5
	SRS group		46	11.0	8.4
Godefroy et al. (8)	Translabyrinthine surgery	12 mo	17	51.3	19.4
Park et al. (12)	GKS	6 to 18 mo (mean 15 m)	59	16.1	14.5
Uehara et al. (14)	Surgery smaller VS	9 mo	26	7.5	17.0
	Surgery larger VS		12	17.0	8.0
Stavas et al. (9)	SRS/FSRT	12 mo	10	8.4	18.5
Thomeer et al. (10)	Surgery (Translab/retrosig)	6 mo	48	14.4	19.8
Samii et al. (15)	Surgery (retrosig)	12 mo	19	66.3	4.3

reported on radiosurgery outcomes only (8,11). Five studies reported on surgical resection only (7,9,12–14). One study reported that their control group were patients undergoing conservative management of vestibular schwannoma (VS) (14) and another study used an external comparator population control group (7). Most of the articles state their study cohorts were chosen by consecutive sampling of selected patients. Patients were usually allocated to certain study groups depending on patient preference and clinical condition. In one study, older patients were specifically recruited to the radiosurgery group (10). Follow-up duration for patients was an average of 14 months over the nine studies, ranging from as little as 6 months (9) to 12 months (15). Interim follow-up and dizziness handicap inventory (DHI) measurements also varied, making it difficult to appreciate the pattern and change in DHI over time.

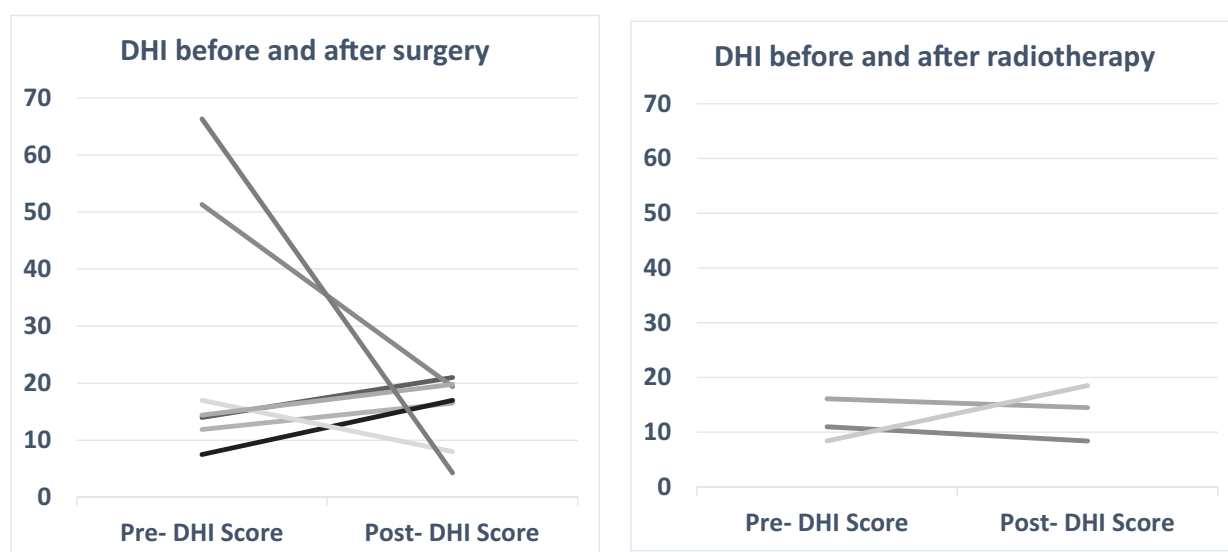
Differences in data analysis were evident. One study excluded patients who failed conservative management protocol and then subsequently underwent surgery or radiosurgery (11). With these exclusion criteria, patients who successfully underwent conservative management strategies (such as vestibular rehabilitation) are more

likely to have a better DHI score, and as such the accurate interpretation of these study findings is difficult.

Dizziness Handicap Inventory

All included studies used the DHI questionnaire as a measure of balance function. This is a 25-question questionnaire focusing on the perceived effect dizziness can have on emotional, physical, and functional aspects of daily life (1,7). The DHI has been shown to be reliable and valid (16). The DHI scores range from 0 (best possible measured health) to 100 (the worst possible function), with a change in DHI score of 18 or more considered to be clinically significant (16). Pre- and postintervention DHI scores are summarized in Table 2 and Figure 2.

Two studies selected patients specifically due to severe rotatory vertigo failing to improve despite extensive vestibular rehabilitation (7,14). Both groups were classified as Grade IV according to the Kanzaki et al. (17) grading system for VS. Average DHI scores were above 50 in both cohorts. Surgery was undertaken in these patients, either by trans-labyrinthine or retro-sigmoid approach. Both articles observed a statistically and

**FIG. 2.** Dizziness Handicap Inventory (DHI) scores demonstrated before and after intervention.

clinically significant reduction in long-term DHI score (see Table 2).

Subgroup Analysis of Dizziness Handicap Inventory

A number of studies undertook subgroup analysis of patients' age, sex, and tumor size, with respect to impact on long-term DHI postintervention. We discuss each of these in turn briefly below.

Age

Four studies concluded that age had no measurable effect on postintervention DHI score (7,9,12,14). The mean age of cohorts' studies ranged from 47 to 56 years. One study excluding patients aged over 75 (9).

Sex

Two studies concluded that sex had no statistically significant effect of long-term postintervention DHI (7,14). Two articles suggested that initial postintervention DHI results may be worse in male patients, but these differences were not noted beyond 3 months postintervention (9,12).

Size

Two studies commented that size had no effect on the degree of long-term postintervention dizziness (9,15). Humphriss et al. (12), however, suggested tumor size and the magnitude of preoperative canal paresis can significantly affect the degree of change in DHI. Tumor sizes in the studies included were categorized ranging from <1.5 cm to >4 cm, with three studies not stating specific size but categorized as "small" (7,9,12).

Clinical Tests of Balance Function

Two studies used instrumental tests of balance function (in addition to DHI), with a minimum follow-up of 6 months.

Uehara et al. (13) undertook static posturography testing of 38 patients, before and after surgery for vestibular schwannoma. Patients were observed over a 9-month follow-up period. No significant difference was found in shifting lengths and envelope areas in both groups before and after surgery. Posturography is a noninvasive measure used to quantify the central nervous system adaptive techniques involved in the control of posture and balance. It is carried out by placing the patient on a standing instrumented platform connected to force and movement transducers, which are able to detect small movements of the body and changes in the center of gravity.

Stavas et al. (8) undertook vestibular testing for 10, before and after stereotactic radiotherapy for VS. Testing included caloric and cervical vestibular-evoked myogenic potential testing, in addition to DHI scoring. They found no statistically significant change in caloric responses and also no statistical change in cervical vestibular-evoked myogenic potential responses, with most patients having absent response preintervention.

DISCUSSION

This review summarizes the studies reporting balance outcomes in patients with vestibular schwannoma. The eight studies reviewed are generally of poor quality and would all be categorized as "Level 4 Evidence" (18). They are limited by study design, selection bias, and lack of appropriate control/comparator groups. None of the studies include power calculations. This makes it difficult to generalize findings or formulate robust conclusions. Given the results we were not able to conduct a meta-analysis. This highlights the need for further high-quality studies in this area. The routine collection and reporting of long-term validated balance outcomes should be considered for all patients with vestibular schwannoma, given the profound impact on overall quality of life.

Treatment Modality

No study demonstrated a significant change in DHI for nonselected patients undergoing routine treatment for VS. The studies by Godefroy et al. (7) and Samii et al. (14) selected VS patients with severe/disabling vertigo (mean DHI over 50), who had not responded to vestibular rehabilitation. There was a significant reduction in long-term postsurgery DHI, suggesting that surgery can be helpful with respect to more severe balance dysfunction. In this highly selected cohort of patients, postsurgery DHI returned to a baseline level comparable with the wider VS patient population. Neither comparator nor control data are available to know how this cohort may respond to other, nonsurgical treatments.

Age, Sex, and Size of Vestibular Schwannoma (VS)

A number of the studies reviewed considered the potential impact of age, sex, and tumor size and the subsequent impact on dizziness outcomes in these patients.

Age had no measurable effect on postintervention DHI score (7,9,12,14). The mean age of patients in the studies ranged from 47 to 56 years (minimum age of 18 yrs old and maximum age of 88 yrs old). Older patients may be more prone to disequilibrium from confounding comorbidities, such as visual impairment, musculoskeletal, and arthritic disorders, generalized weakness, and neurological lesions (2). Therefore, these results are subject to selection bias, particularly by excluding older patients. With regards to sex we found no statistically significant effect of long-term postintervention DHI (7,14).

One study found that larger VS were associated with better outcomes due to already well-established central compensation mechanisms (15). The largest study (n = 100) by Humphriss et al. (12) showed evidence that tumor size did not have a significant effect on functional compensation status following surgery and was one of the few studies to include large VS >4.4 cm. The remaining studies had a much smaller sample sizes and had a mean VS size of 2 cm (7–11,13). From these studies, we

can conclude that it appears tumor size may affect the process of vestibular compensation, but not the final prognosis.

Interventions Not Covered Within This Review

A number of published case series have reported on treatments other than surgery or radiotherapy for the management of dizziness associated with VS. Treatments include vestibular rehabilitation and intratympanic gentamicin. These series were excluded from this review, usually due to a lack of pretreatment dizziness scores, or insufficient follow-up time. These are discussed in brief below, to give further context to this subject.

Vestibular Rehabilitation

Thomeer et al. (9) could not find any statistical significance of vestibular rehabilitation on postoperative DHI score, and found no benefit if started early (less than 1 mo postoperatively). Godefroy et al. (7) in their study concluded that patients with severe disabling vertigo, who did not respond to vestibular rehabilitation, may benefit from surgery. From these two studies, we can conclude vestibular rehabilitation had no impact on postoperative DHI scores; however, sample size and lack of statistical analysis needs to be considered.

Intratympanic Gentamicin

A number of case series have reported on the use of intratympanic gentamicin (ITG) for patients with VS. These studies fall into two categories: ITG given before surgery in an attempt to prehabilitate the patient to vestibular loss (19–21) and ITG given for patients with unoperated VS as an attempt to control balance symptoms (22–24). Studies of preoperative ITG have suggested a potential improvement in postoperative rehabilitation (18). Gentamicin is potentially cochleotoxic and can result in worsening dizziness and increases the risk of hearing loss (25). Cada et al. (20) administered preoperative intratympanic gentamicin in 10 patients with VS who then underwent vestibular rehabilitation 2 months before surgery. They found no statistically significant improvement in DHI scores in comparison with a control group.

Covelli et al. (23) reported a case of an intralabyrinthine VS in a patient with severe vertigo. The patient opted for ITG over surgery and found her vertigo symptoms resolved, with no further symptoms 6 months post-intervention but developed a moderate sensorineural loss (22,24). Similarly, Yang et al. (22) looked at eight patients with severe vertigo with small VS who also received ITG. They found that all patients showed a drop in DHI scores consequently over time, but three patients also experience significant hearing loss as a result.

Tjernström et al. (19) compared 20 patients with VS who received preoperative ITG to a control group who underwent surgery only. They found that patients who had ITG demonstrated better postural stability at follow-up. They attributed the difference to active and continuous motor learning as the vestibular function slowly

attenuates; with no concomitant central nervous dysfunction due to effects from neurosurgery, thus allowing time for a separate unimpeded recovery process with more limited challenges and objectives; and the initiation and certain progression of sensory reweighting processes allowed before surgery. Magnusson et al. (21) also reported similar findings with the administration of preoperative gentamicin and vestibular rehabilitation, they found that ablating vestibular function and achieving compensation before surgery resulted in no cases of vertigo in the immediate postop period.

A randomized control trial is required to truly understand the potential impact of intratympanic gentamicin on dizziness in VS patients with long-term patient follow-up data.

Posturography

Posturography generally lacks validity as a sole measure of vestibular function and is subject to a number of biases (26,27). Most reviews of posturography as a tool for assessing balance function conclude that it rarely provides useful diagnostic information or influences clinical decision making (27,28). Posturography has shown some benefit in identifying patient at risk of falls, especially in the elderly population and those with multiple sclerosis (29–31)

How Does Vestibular Schwannoma Cause Dizziness?

There are no clear studies looking at how VS causes dizziness in the first instance. The current literature suggests that dizziness in VS patients may be due to a number of causes including direct action of the tumor on the vestibular nerve via compression or invasion, labyrinthine artery compression, compression of the pons, and/or cerebellum, communicating, and noncommunicating hydrocephalus and the release of toxic metabolites can contribute, some of which is demonstrated histologically and radiologically (32–34). Some theories suggest that smaller VS can irritate the vestibular nerve causing initial vertigo, and that larger VS can cause disequilibrium (35). The dizziness may also be coincidental, and due to other conditions, such as peripheral neuropathy and vestibular migraines.

CONCLUSION

Based on Level III and IV evidence, we can conclude the following:

1. In VS patients there seems to be no statistically significant difference in DHI score pre- and post-intervention.
2. Significantly dizzy patients improve with surgical intervention. With the lack of comparison studies, however, it is difficult to conclude whether they would have improved with other interventions.
3. We cannot comment on the role of conservative management, vestibular rehabilitation, and the use of intratympanic gentamicin.

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