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The Relation Between Tinnitus and a Neurovascular Conflict of the Cochleovestibular Nerve on Magnetic Resonance Imaging

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Introduction: Magnetic resonance (MR) imaging is often used in diagnostic evaluation of tinnitus patients. Incidental findings like a neurovascular conflict (NVC) in the cerebellopontine angle are often found; however, the diagnostic value of this finding remains unclear. The aim of this study is to investigate whether the type or degree of compression of the vestibulocochlear nerve is of diagnostic value in patients with a NVC.

Methods: A retrospective study was performed in 111 tinnitus patients with available MR imaging between 2013 and 2015. Clinical and audiometric variables were gathered and MR imaging was reevaluated by two neuroradiologists. NVCs were analyzed using a grading system based on previous research by Sirikci et al.

Results: In total, 220 ears were available for assessment. In patients with unilateral tinnitus a loop compression and an indentation of the cochleovestibular nerve were more frequent than in patients with bilateral tinnitus. However, there

was no significant difference in distribution of the type of compression between tinnitus and nontinnitus ears. Patient with unilateral tinnitus had a significantly higher degree of hearing loss in the symptomatic ear, compared with the asymptomatic ear and with the bilateral tinnitus group. Also, it was found that the degree of hearing loss did not differ between the various types of compression.

Conclusion: This study did not find a diagnostic value of specific types of compression in patients with a NVC. Although the distribution of NVC classification was different in patients with unilateral and bilateral tinnitus, there was no definite relation between the type of NVC and the presence of ipsilateral tinnitus. Also, the degree of hearing loss was not related to specific types of NVC.

Key Words: Cochleovestibular nerve—Neurovascular conflict—Tinnitus.

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Tinnitus is a common condition, affecting 5% to 15% of the adult population (1). When an otorhinolaryngologist is consulted for tinnitus complaints, a targeted patient history, physical, and audiological examination is performed. In case of for example unilateral tinnitus, pulsatile tinnitus, focal neurological abnormalities or an asymmetrical hearing loss, further diagnostic evaluation often includes routine magnetic resonance imaging (MRI) (2). The most important purpose of using MRI in tinnitus patients is to exclude pathology in the cerebellopontine angle (CPA), such as a vestibular schwannoma. In 41% of the MRI studies an incidental finding is reported, such as the presence of a vascular loop in the CPA with close contact to the vestibulocochlear nerve

(3), which is often referred to as a neurovascular conflict (NVC). This is a phenomenon in which a cranial nerve is compressed by a nearby artery or vein, which presumably causes ectopic excitation and thereby symptoms related to the affected nerve (4). For example, a NVC is a well-known cause of hemifacial spasms in case of facial nerve compression and trigeminal neuralgia in case of trigeminal nerve compression (5,6). A neurovascular conflict of the vestibulocochlear nerve visible on imaging is suggested to cause a “vestibulocochlear nerve compression syndrome” consisting of ipsilateral symptoms of unilateral tinnitus, hearing loss, and/or vertigo (7). However, the diagnostic value of finding an NVC on MRI remains unclear, as not all patients with an NVC on MRI experience tinnitus and not all patients with tinnitus have an NVC on MRI. In fact, tinnitus has multiple etiologies.

Previous studies investigating the relationship between the vestibulocochlear nerve and the anterior cerebellar inferior artery (AICA) show that close contact between the two was observed in 25% to 53% of patients with tinnitus (8,9). In both studies, the percentages of NVCs in

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tinnitus patients did not significantly differ from the percentage that was found in asymptomatic patients (8,9). Several previous studies were aimed at finding characteristics of a NVC that predicted that the NVC was indeed symptomatic. For example, it is suggested that the root entry zone (REZ) of a cranial nerve, which is the transition zone of the peripheral nerve segment to the central nerve segment, is more susceptible to injury and therefore a NVC in the REZ possibly is more likely to be symptomatic than when the NVC is located at the peripheral nerve segment (10,11). Also, the type of symptoms or the type of compression might be an indicator that a NVC is symptomatic. In trigeminal neuralgia and hemifacial spasms, it has been demonstrated that the degree or severity of compression and atrophy of the nerve correlate with good clinical outcome after decompression surgery. This suggests that in these more profound compression cases, a neurovascular contact is the correct underlying pathology (12–14). This might also be the case for patients with NVC of the vestibulocochlear nerve. Siricki et al. (15) developed a classification system for types of compression of the vestibulocochlear nerve. In this study we hypothesize that the type or degree of compression can be of diagnostic value in tinnitus patients with a neurovascular compression. The goal of this study is to investigate whether there is a correlation between the type of neurovascular compression and the presence of tinnitus.

METHODS

Patients

All consecutive patients referred to the tertiary specialized outpatient clinic for patients with tinnitus in the University Medical Center Groningen between September 2013 and November 2015 were analyzed. Baseline data and questionnaires were gathered prospectively into an anonymized database and analyzed retrospectively. All patients 18 years and older with an available MRI scan of the CPA were included. This research was submitted to the Institutional Review Board of the University Medical Center Groningen, who decided that no full review was needed due to the retrospective nature of this study.

Clinical Variables

All tinnitus patients in our specialized outpatient clinic were evaluated by a multidisciplinary group of medical professionals including an otolaryngologist, audiologist, and psychologist. Information is gathered structurally and includes demographics, clinical complaints related to tinnitus (e.g., presence of vertigo, lateralization of the tinnitus, type of tinnitus), audiometric information, and results from questionnaires, i.e., the Hospital Anxiety and Depression Scale and the Tinnitus Handicap Index (THI). The Hospital Anxiety and Depression Scale is divided in no anxiety or depression (score ≤ 8) versus indication for anxiety or depression (score > 8). The THI is divided in slight tinnitus (grade 1: 0–16 points), mild tinnitus (grade 2: 18–36 points), moderate tinnitus (grade 3: 38–56 points), severe tinnitus (grade 4: 58–76 points), and very severe tinnitus (grade 5: 78–100 points).

Audiological information from tone audiometry was classified into four categories based on PTA (pure-tone average at

1, 2, and 4 kHz in decibel): minimal (10–30 dB), moderate (30–55 dB), severe (55–90 dB), and very severe (> 90 dB) hearing loss.

Radiological Analysis of MR Imaging

All patients with available MRI were reevaluated by a highly experienced neuroradiologist and a last-year radiology resident specializing in neuro- and head and neck radiology. Both were blinded for clinical information. Although there were differences in interpretation in this reevaluation, overall consensus was reached in all cases. Most patients already had a scan in secondary hospitals, the indications for scanning were mostly unknown. Reevaluation included scoring of: the presence of a vascular compression of the vestibulocochlear nerve in the CPA; the specific anatomical vessel causing the compression; whether compression occurred in the REZ and if there was any other CPA pathology. The type of compression of the vestibulocochlear nerve was classified based on the grading system by Siricki et al. (15). The classification divides NVC on MRI into five categories: no neurovascular conflict on imaging (no NVC), point compression (grade 1), longitudinal compression (grade 2), loop compression (grade 3), and indentation (grade 4). The NVC classification was determined on the left and right cochleovestibular nerves. For unilateral tinnitus, the results were stratified with respect to the symptomatic tinnitus side and to the asymptomatic nontinnitus side. In patients with bilateral tinnitus, the classifications were stratified as left and right-sided.

Statistical Analysis

Comparison between categorical groups was performed with the Pearson chi square test and univariate logistic regression analysis. In the logistic regression analysis, the dependent variable THI was split into two groups (THI grades 1 and 2 versus THI grades 3–5). Continuous data was analyzed using the Student *t* test. A *p* value of < 0.05 was considered statistically significant. SPSS software version 22 (SPSS Inc, Chicago, IL) was used for all analyses.

RESULTS

Patient Characteristics

The consecutive cohort consisted of 297 tinnitus patients. In 182 of these patients, no MRI was available and in four patients, the MRI was of inadequate quality to properly evaluate the CPA. In the remaining scans, one left ear and one right ear could not be reliably assessed due to insufficient quality of MRI, leaving 111 patients with 220 ears available for radiological assessment (Fig. 1). The MRI was also evaluated for other pathologies: there was one patient with dehiscence of the superior semicircular canal. There were no patients with a tumor or other pathology in the CPA or petrous bone.

The characteristics of included patients are summarized in Table 1. The total percentage of women was 41% and the age distribution ranged from 23 to 77 years with an average of 55 years. Most patients (83%) had complaints of subjective nonpulsatile tinnitus, the other 17% experienced pulsatile tinnitus, for example. Tinnitus was unilateral, i.e., either only in the right or in the left ear, in 49 patients (44%) and bilateral in 62 patients (56%). When stratified with respect to severity of the hearing

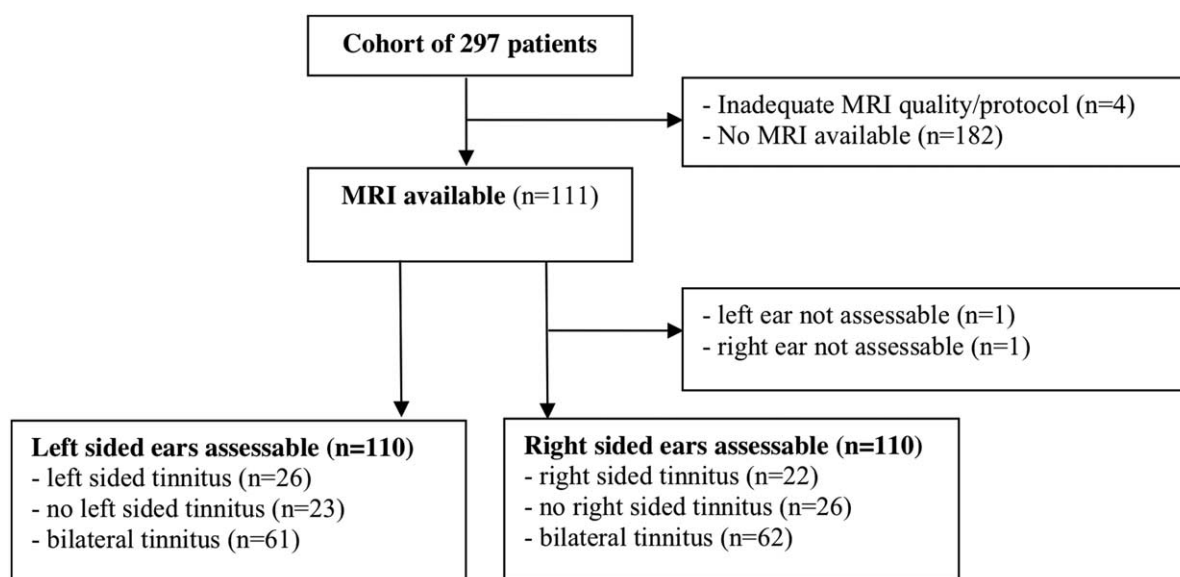


FIG. 1. Flow chart of included patients with tinnitus. MRI indicates magnetic resonance imaging.

TABLE 1. Characteristics of included patients (n=111)

Number	Total (n = 111)	Unilateral Tinnitus (n = 49)	Bilateral Tinnitus (n = 62)	p Value
Age (n=111) (yrs)				
Mean [range]	55 [23–77]	52 [23–76]	58 [30–77]	0.01
Sex (n=111) (%)				
Male	65 (59%)	24 (49%)	41 (66%)	0.07
Female	46 (41%)	25 (51%)	21 (34%)	
Type of tinnitus (n = 111) (%)				
Subjective nonpulsatile tinnitus	92 (83%)	40 (82%)	52 (84%)	0.76
Other	19 (17%)	9 (18%)	10 (16%)	
Neurovascular conflict (n = 111) (%)				
No NVC present	14 (13%)	3 (6%)	11 (18%)	0.23
Left NVC	25 (23%)	13 (27%)	12 (19%)	
Right NVC	21 (19%)	8 (16%)	13 (21%)	
Bilateral NVC	51 (46%)	25 (51%)	26 (42%)	
Vertigo (n = 110) (%)				
Vertigo/dizziness	34 (31%)	16 (33%)	18 (30%)	0.72
No vertigo/dizziness	76 (69%)	33 (67%)	43 (70%)	
THI grade (n = 107) (%)				
Grade 1	12 (11%)	5 (11%)	7 (11%)	0.71
Grade 2	29 (27%)	16 (34%)	13 (22%)	
Grade 3	32 (30%)	12 (20%)	20 (33%)	
Grade 4	19 (18%)	8 (13%)	11 (18%)	
Grade 5	15 (14%)	6 (10%)	9 (15%)	
[0,1-4]HADS-depression ^a (n = 106) (%)				
No indication depression	79 (75%)	35 (76%)	44 (73%)	0.75
Indication depression	27 (25%)	11 (24%)	16 (27%)	
HADS-anxiety ^a (n = 106) (%)				
No indication anxiety	72 (68%)	34 (74%)	38 (61%)	0.25
Indication anxiety	34 (32%)	12 (26%)	22 (37%)	
Hearing loss in tinnitus affected ear(s) (n = 111) (%)				
Mild (10–30 dB)	53 (48%)	22 (37%)	31 (50%)	0.128
Moderate (35–55 dB)	37 (33%)	13 (27%)	24 (38%)	
Severe (60–90 dB)	15 (14%)	10 (20%)	5 (8%)	
Very severe (>90 dB)	6 (5%)	4 (8%)	2 (3%)	

^aCut-off score for HADS-depression/anxiety: indication for depression or anxiety is present when scores ≥ 8 .

dB indicates decibel; HADS, Hospital Anxiety Depression Scale; THI, tinnitus handicap inventory; NVC, neurovascular conflict on imaging.

TABLE 2. Characteristics of the contact between cochleovestibular nerve and a compressing vessel on evaluated MRI scans (per ear, n=220)

	n (%)
Classification of compression (n=219) (%)	
No NVC	73 (33%)
Grade 1	52 (24%)
Grade 2	30 (14%)
Grade 3	61 (28%)
Grade 4	3 (1%)
Compromising vessel (n=144) (%)	
AICA	115 (80%)
PICA	1 (1%)
Venous	28 (20%)
Root entry zone on ipsilateral side of complaints (n=143) (%)	
Yes	21 (15%)
No	122 (85%)

AICA indicates anterior inferior cerebellar artery; PICA, posterior inferior cerebellar artery; NVC, neurovascular conflict on imaging.

loss, a mild hearing loss (PTA 10–30 dB) was most frequently present (48%).

Vascular Compression of the Vestibulocochlear Nerve

Characteristics of the evaluated MRI scans (per ear, n=220) are depicted in Table 2. In 146 ears (67%) a NVC was found by radiological assessment. Regarding the

type of compression, loop compression (grade 3) was most frequently found (28%), followed by point compression (grade 1; 24%), longitudinal compression (grade 2; 14%), and nerve indentation (grade 4; 1%). Of those NVCs, the AICA was the compromising vessel found most frequently (80%).

Table 3 compares patients with unilateral and bilateral tinnitus. For patients with unilateral tinnitus, the NVC on the tinnitus side (symptomatic side) and nontinnitus side (asymptomatic side) was recorded. For bilateral tinnitus, also the NVC was evaluated on both sides (left and right ears). Table 3 shows a cross tabulation of: the classification of compression; the degree of hearing loss (PTA in dB); the compromising vessel; and compression in the REZ; in relation to these two groups (unilateral tinnitus versus bilateral tinnitus). The distribution of NVC classification on the tinnitus side (symptomatic side) of unilateral cases was significantly different from that in bilateral cases ($p=0.014$), with loop compression (grade 3) and indentation (grade 4) being more common in the group of unilateral cases. The distribution of NVC classification in the asymptomatic ears was not significantly different from bilateral tinnitus ($p=0.099$). There was no significant difference in NVC classification within the unilateral tinnitus group (asymptomatic versus symptomatic ears) ($p=0.80$).

The degree of hearing loss was significantly higher ($p=0.042$) in the unilateral tinnitus group (44 dB), compared with the bilateral tinnitus group (36 and 32 dB for left and right ears, respectively). The compromising

TABLE 3. Neurovascular conflicts in the CPA and their characteristics on MRI related to unilateral tinnitus versus bilateral tinnitus ears

	Unilateral Tinnitus (n=97)			Bilateral Tinnitus (n=122)		Total n (%)	a	b
	Total n (%)	Symptomatic Side n (%)	Asymptomatic Side n (%)	Left n (%)	Right n (%)			
Classification of compression NVC (n=219)							0.01	0.10
No NVC	73	12 (25%)	14 (29%)	23 (38%)	24 (39%)	47 (39%)		
Grade 1	52	8 (17%)	11 (22%)	20 (33%)	13 (21%)	33 (27%)		
Grade 2	30	8 (17%)	5 (10%)	5 (8%)	12 (20%)	17 (14%)		
Grade 3	61	18 (38%)	18 (37%)	13 (21%)	12 (20%)	25 (20%)		
Grade 4	3	2 (4%)	1 (2%)	0	0	0		
Mean PTA (dB)	33	44	21	36	32	34	0.04	0.00
Compromising vessel (n=147)							0.23	0.02
AICA	115	27 (75%)	28 (80%)	32 (84%)	27 (71%)	59 (78%)		
Venous	28	7 (19%)	4 (11%)	6 (16%)	11 (29%)	17 (22%)		
PICA	1	1 (3%)	0	0	0	0		
Unclear	4	1 (3%)	3 (9%)	0	0	0		
Compression in the root entry zone (n=143)							0.84	0.31
No	122	31 (86%)	28 (80%)	34 (90%)	29 (85%)	63 (88%)		
Yes	21	5 (14%)	7 (20%)	4 (11%)	5 (15%)	9 (13%)		

The two rightmost columns show the statistical significance of the difference in grade distribution between the symptomatic ($p=0.01$) and asymptomatic side ($p=0.10$) in unilateral patients and the combined left and right sides of the bilateral patients.

^aUnilateral symptomatic versus total bilateral p value.

^bUnilateral asymptomatic versus total bilateral p value.

AICA indicates anterior inferior cerebellar artery; NA, not available; NVC, neurovascular conflict on imaging; PICA, posterior inferior cerebellar artery; PTA, pure-tone average (mean over 1, 2, and 4 kHz).

vessels did not significantly differ between unilateral and bilateral tinnitus ($p=0.227$). Also, whether or not there was compression in the REZ did not significantly ($p=0.839$) differ among the two groups (unilateral symptomatic versus bilateral).

Figure 2 shows a boxplot with the different types of compression in relation to the degree of hearing loss (PTA) for tinnitus ears (symptomatic ears) versus asymptomatic ears. For each type of compression, asymptomatic ears had less hearing loss than tinnitus ears. No significant difference in degree of hearing loss was found between any grade of NVC versus “no NVC”. The boxplot in Figure 3 shows the relation between the type of compression and the degree of hearing loss on the side of the compression, regardless of any tinnitus symptoms. The degree of hearing loss does not significantly differ between the various types of compression, indicating that there is no causal relation between the type of compression and the degree of hearing loss.

Univariate Analysis of Different Clinical Factors Influencing Tinnitus Severity

A univariate logistic regression related various variables to tinnitus handicap (Table 4). For this analysis, the patients were divided in two groups: group 1: THI 0 to 35, mild tinnitus, and group 2: THI 36 to 100, moderate to very severe tinnitus. There was no significant relation between the presence of a NVC or the type of compression and the tinnitus handicap. Univariate analysis within the patient groups revealed no significant links between age, sex, severity of hearing loss, type of tinnitus, and tinnitus handicap. However, there was a significant association for both anxiety and depression in relation to severity of tinnitus ($p=0.012$, OR 3.62 CI: 1.33–9.82 and $p=0.003$, OR 1.45 CI: 0.50–4.86 respectively),

showing that patients with moderate to very severe tinnitus more often have an indication for anxiety and depression.

DISCUSSION

Summary of Findings

In this retrospective study, we evaluated the relation between the type of contact between the cochleovestibular nerve and a nearby blood vessel (using the grading system of Sirikci et al. (15)) and the presence of unilateral tinnitus.

We found that loop compression and indentation of the cochleovestibular nerve were more common in the patient group who had unilateral tinnitus; however, there was no significant difference in distribution of NVC classification between symptomatic (tinnitus) and asymptomatic (no tinnitus) ears. The degree of hearing loss did not differ between the various types of compression. The vessel causing the compression or the fact that the compression was found in the root entry zone, was not significantly related to the presence of unilateral tinnitus. Finally, we found that the severity of tinnitus was not related to the presence of a NVC, the type of hearing loss or the type of tinnitus.

Interpretation of Results

In concordance with other studies, this study demonstrated that when an NVC of the vestibulocochlear nerve is found, this does not necessarily correlate with tinnitus symptomatology (8,9). This phenomenon is also seen in NVCs of the trigeminal nerve: a study by Miller et al. (14) showed that an arterial NVC of the trigeminal nerve without symptoms of trigeminal neuralgia was observed in 17% of patients.

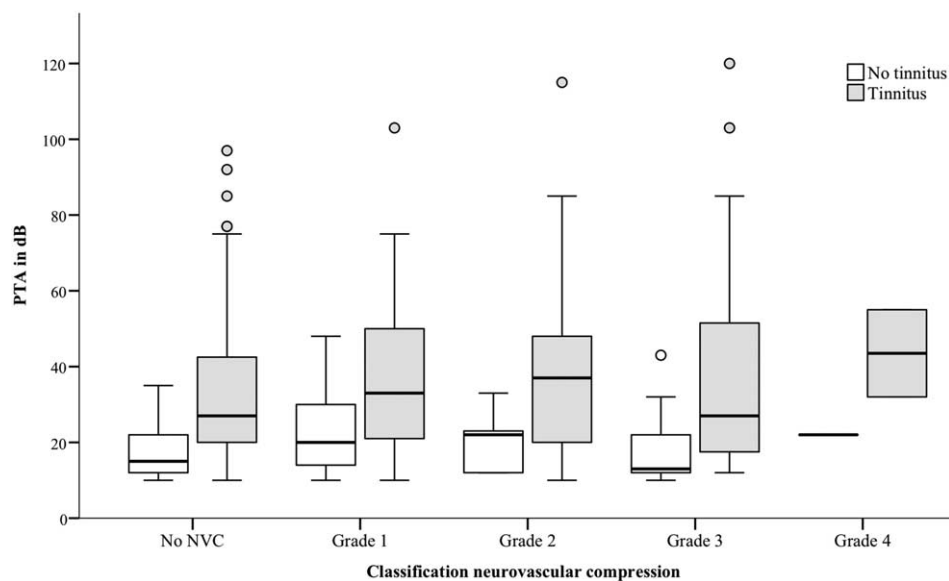


FIG. 2. Boxplot with classification of the NVC versus the mean PTA at 1-2-4 kHz in symptomatic versus asymptomatic tinnitus ears. NVC indicates neurovascular conflict on imaging.

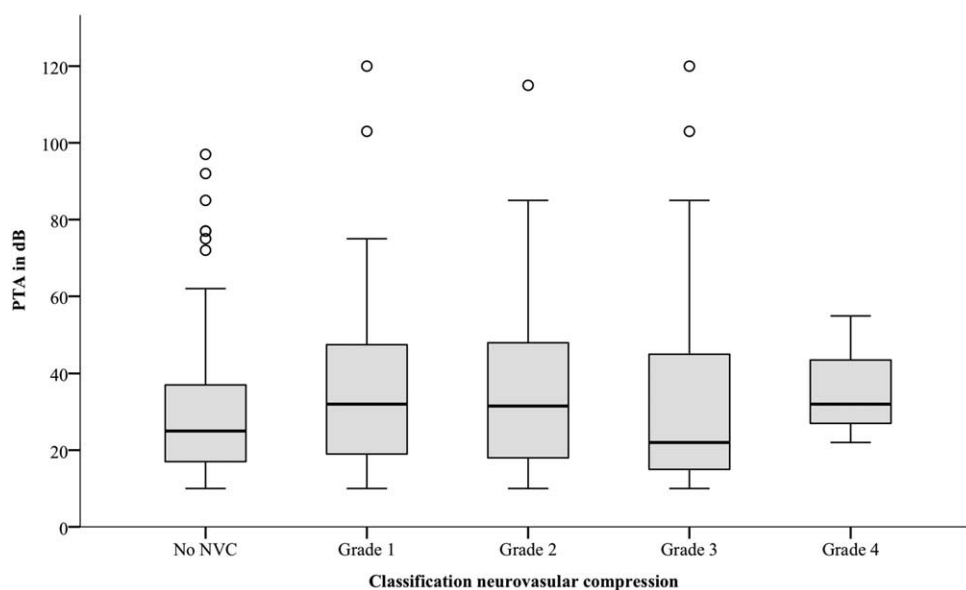


FIG. 3. Boxplot showing the type of compression in relation to degree of hearing loss on the ipsilateral side.

In trigeminal neuralgia and hemifacial spasms, a significant predictor of symptomology was compression of the proximal nerve and nerve indentation or displacement (13,14). In our study we found that in the group of patients with unilateral tinnitus, loop compression and nerve indentation (grades 3 and 4) were

significantly more present and the point compression and longitudinal compression (grades 1 and 2) were less often found, as compared with the bilateral tinnitus group. We hypothesized that specific types of compression are more likely to have a causal relation with tinnitus when it causes unilateral symptomatology, as

TABLE 4. Univariate analysis of different factors in relation to tinnitus handicap (Group 1: THI 0–35 versus Group 2: THI 36–100)

Variable		Odds Ratio [CI]	<i>p</i> Value
Age group	18–40 yrs	1 (reference)	0.521
	40–60 yrs	1.04 [0.28–3.83]	
	Older than 60 yrs	1.80 [0.77–4.24]	
Sex	Male	1 (reference)	0.878
	Female	0.94 [0.42–2.10]	
HADS anxiety	No anxiety	1 (reference)	0.012
	Anxiety	3.62 [1.33–9.82]	
HADS depression	No depression	1 (reference)	0.003
	Depression	9.55 [2.11–43.18]	
	Very severe	1.83 [0.22–15.3]	
Severity of hearing loss	Minimal	1 (reference)	0.748
	Moderate	0.97 [0.16–5.82]	
	Severe	0.63 [0.10–3.94]	
	Very severe	1.83 [0.22–15.3]	
Type of tinnitus	Subjective non pulsatile tinnitus	1 (reference)	0.454
	Subjective pulsatile tinnitus	1.45 [0.50–4.68]	
NVC	No	1 (reference)	0.936
	Yes	1.03 [0.56–1.87]	
Type of compression	No NVC, grade 1 or 2 compression	1 (reference)	0.937
	Grade 3 or 4 compression	0.98 [0.55–1.73]	

Severity of tinnitus was measured with the THI and was divided into two groups (THI 0–35 versus 36–100). Tinnitus-related findings (neurovascular conflict and type of compression) were analyzed in 220 separate ears; patient-related variables were analyzed in 111 separate patients.

CI indicates confidence interval; HADS, hospital anxiety depression questionnaire; NVC, neurovascular conflict on imaging; THI, tinnitus handicap inventory.

observed in the “vestibulocochlear nerve compression syndrome” (7). It may be that when there is compression by a loop around the nerve (grade 3), a larger contact surface with the nerve exists, causing more disruption of neuronal transmission. The same theory applies for nerve indentation (grade 4), as it is plausible that an indentation in the nerve causes local irritation and ectopic excitation. This is in line with a recently published study of Bae et al. (16), who found that a NVC of the cochlear nerve (with >50% extension of contact in the internal auditory canal) was more frequently detected on symptomatic sides of patients with typewriter tinnitus. In our study, although loop compression and indentation were more frequently found in the unilateral tinnitus group, the distribution in types of NVC did not significantly differ between within the unilateral tinnitus group (asymptomatic side versus symptomatic side), which does not affirm our hypothesis. Possibly, the presence of a higher graded NVC is more of a risk factor for development of (unilateral) tinnitus rather than a cause. Unfortunately, the indentation type of NVC was rare in our patient sample (n=3); therefore firm conclusions are not possible.

This study also showed that the severity of hearing loss was significantly higher in the symptomatic ears in patients with unilateral tinnitus. Also, in our analysis the degree of hearing loss was equal in relation to the different types of NVC, including “no NVC”. No specific relation between degree of hearing loss and a specific type of compression could be found. In our patient sample, it could not be confirmed that hearing loss is a symptom of the cochlear nerve compression syndrome and a result of compression and thereby irritation of the auditory nerve (17,18). The significant difference in degree of hearing loss in the unilateral symptomatic tinnitus versus bilateral tinnitus ears can be explained by the fact that hearing loss is a known risk factor for the development of tinnitus. In conclusion, lateralization of tinnitus (i.e., unilateral tinnitus) was the result of asymmetry in hearing loss (caused by other etiologies) and the degree of hearing loss could not be related to a specific type of NVC.

Interestingly, in this study a rather high percentage of NVCs were found (67%). Other studies demonstrated percentages of tinnitus patients with an NVC caused by an AICA loop varying from 14% to 65% (3,9,15). Possibly, the rather high percentage of NVCs in our study can be partially explained by the fact that not only the AICA was scored in our study, but also other compromising vessels such as the posterior inferior cerebellar artery and venous vessels.

Limitations of the Study

As the patients included in this study visited a tertiary outpatient clinic, more severe tinnitus symptoms can be expected in comparison with the general tinnitus population. This selection bias may have influenced our data, especially in terms of severity of tinnitus burden.

The current study has one of the largest sample sizes in comparison with previous studies investigating the relation between symptoms and NVC on MRI. However, still a larger number of patients would be preferable, mainly because some types of NVCs (i.e., loop compression and especially indentation) are only present in small numbers. Moreover, a standardized protocol of imaging should be used in a prospective study as our study consisted of MRI scans from different hospitals, preferable in higher quality imaging such as three Tesla MRI. Also, a control group would be recommendable, as a NVC is known to also be present in patients without tinnitus.

Moreover, tinnitus is a subjective complaint and description by patients is difficult to interpret objectively. For some patients, the difference between unilateral and bilateral tinnitus can be difficult to distinguish, which may have influenced our data. Future research should therefore concentrate on prospectively gathering standardized clinical and imaging data to confirm the results that were found in this study.

CONCLUSIONS

The mere presence of an NVC on MRI or the involvement of the REZ does not correlate with symptoms of tinnitus. Although the distribution of NVC classification is different in patients with unilateral and bilateral tinnitus, there was no definite relation between the type of NVC and the presence of ipsilateral tinnitus or the degree of hearing loss. Further prospective research is warranted to confirm these findings to assess and confirm the clinical relevance of NVC on MRI.

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