博士学位論文

真珠腫性中耳炎に対する鼓室形成術後のめまい発症のリスク因子の検討

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Doctoral Dissertation

Examination of risk factors for postoperative vestibular symptoms in patients with cholesteatoma

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論文題目

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Examination of risk factors for postoperative vestibular symptoms in patients with cholesteatoma

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Abstract

Background: In cholesteatoma, the prognosis of tympanoplasty has been well discussed in terms of hearing outcomes and residual or recurrent lesions. Postoperative dizziness and vertigo are major complications of tympanoplasty; however, few reports are available.

Aims/Objectives: We investigated each condition of cholesteatoma postoperative vestibular risk using the STAM system and staging published by EAONO/JOS, as well as findings on bony destruction.

Material and Methods: From April 2010 to March 2021, 156 patients (166 ears) with cholesteatoma who underwent primary microscopic tympanoplasty at our hospital were registered. Subjective vestibular symptoms were recorded the day after surgery.

Results: Postoperative vestibular symptoms were observed in 13.9% of subjects. All of them were stage II and had both attic and mastoid lesions. Attic ($p<0.05$) and mastoid ($p<0.01$) lesions were risk factors. Multivariate analysis showed that significant differences were found in past histories of vestibular symptoms ($p<0.05$) and exposure of the dura mater ($p<0.01$).

Conclusions and Significance: In the exposed dura group, the length of the prominence of the lateral semicircular canal to the middle cranial fossa dura was significantly shorter than that of the non-exposed group ($p<0.01$). Narrow working space and downward operation may increase vestibular risk.

Keywords: Cholesteatoma, tympanoplasty, postoperative vestibular symptoms

Introduction

Cholesteatoma is a disease in which lesions increase in a destructive manner. The progression of the lesions can lead to sensorineural hearing loss, dizziness, facial nerve paralysis, and intracranial complications [1-5]. Generally, there is a risk that operative invasion causes the same complications in middle ear surgery. The prognosis of tympanoplasty has been well discussed in terms of hearing outcomes and, especially in cholesteatoma cases, residual or recurrent lesions. However, few reports have discussed postoperative dizziness and vertigo, which are important complications.

For cholesteatoma cases, the European Academy of Otology and Neurotology/Japanese Otological Society (EAONO/JOS) published a consensus on the localisation of lesions and staging system in 2017 and obtained an index to appropriately evaluate the severity of each cholesteatoma patient [6]. As a result, the residual/recurrence rate of cholesteatoma according to stage and localisation has been clarified [7]. Since the prognosis of hearing and recurrence rate varies greatly depending on the focal localisation and stage, it is expected that the occurrence of postoperative vestibular symptoms will have the same result. Using this index, we hypothesised that it would be possible to examine the risk factors more accurately for vestibular symptoms that reflect the severity and location. Ability to evaluate risk factors in advance is beneficial for surgeons with regards ensuring the safety of surgery and for patients with regards providing informed consent using accurate information.

We previously reported the risk factors of postoperative vestibular symptoms in tympanoplasty cases, which included chronic otitis media cases and cholesteatoma cases, that were performed during 2 years from 2012 to 2014, and found that cholesteatoma lesions in the mastoid area, exposure of the dura mater, and thinning of the prominence of the lateral semicircular canal (blue line appearance) are the vestibular risks [8]. In this

study, the cases, especially those of cholesteatoma, included various pathologies and thus involved primary and secondary operations. In our previous studies, those with bone-destruction findings were predominantly cholesteatoma cases, and the results were considered to strongly reflect the outcome of cholesteatoma cases. In the case of secondary surgery, it was difficult to determine whether bone destruction had already occurred at the time of the primary operation or due to a recurrent lesion. From the above, it is necessary to select the target cases and then perform a more accurate analysis.

To investigate the risk factors involved in the incidence of postoperative vestibular symptoms in cholesteatoma cases, we investigated the occurrence of postoperative vestibular symptoms only in primary operation cases of cholesteatoma surgeries performed at our hospital and investigated the relationship between the localisation of cholesteatoma lesions, staging, and the findings of bone destruction.

Subjects and Methods

Subjects

From April 2010 to March 2021, 166 ears of 156 patients with cholesteatoma who underwent microscopic tympanoplasty at our hospital were registered (Table 1). All patients underwent a postauricular approach under general anaesthesia. Of all cases, 31 cases were performed in one stage, and 135 were performed in a two-stage policy. Considering that the outcome of tympanoplasty varies greatly depending on the skill of the surgeon, the operations performed by the same surgeon (KD) who was an expert who had more than 30 years of surgical experience at the start of the study was extracted. The selection of cases excluded children under 6 years of age, who were expected to have difficulty complaining of subjective dizziness and vertigo. This study was reviewed and approved by the institutional review board of our hospital (Approval number: R03-131).

Vestibular symptoms

We recorded the subjects' complaints about the presence or absence of subjective vestibular symptoms on the day after surgery. Regardless of the presence of nystagmus, vertigo, or dizziness, those who complained of vestibular symptoms were judged to have vestibular symptoms.

STAM system and staging

The location and extent of cholesteatoma were evaluated according to the STAM system reported by EAONO/JOS based on the contents described in the operation records. "S1" was a supratubal recess, "S2" was a sinus tympani, "T" was a tympanic cavity, "A" was an attic, and "M" was a mastoid region (Figure 1). Staging was evaluated as stage I: cholesteatoma localised in the primary site; stage II, cholesteatoma involving two or more sites; stage III, cholesteatoma with extracranial complications; and stage IV, cholesteatoma with intracranial complications.

Evaluation of the risk factors

According to the result of our previous study, we investigated the location of lesions in the STAM system, and whether there was bone thinning in the prominence of the lateral semicircular canal (blue line), the dehiscence of the fallopian canal, and exposure of the dura mater, as well as whether there was a past history of vestibular symptoms. In addition, the shortest distance from the apex of the prominence of the lateral semicircular canal to the middle cranial fossa dura in the coronal section of the temporal bone computed tomography (CT) image was measured. Similarly, in cases of cholesteatoma in the mastoid area and having soft tissue appearance above the bony edge of superior semicircular canal in the CT image, the shortest distance from the superior semicircular canal to the adjacent bony edge was measured (Figure 2). In cases with bone destruction, the presence of obvious inner ear fistula and semicircular canal fistula, which are considered to be inevitable for inner ear disorders and vestibular disorders, were excluded.

Statistical analysis

Fisher's exact test was performed to examine the correlation between each explanatory variable and the occurrence of vestibular symptoms. In addition, multivariate analysis by logistic regression was performed among the items for which a significant difference was found. Welch's test was performed to determine the distance between the prominence of the lateral semicircular canal and the dura mater, and similarly for the distance between the superior semicircular canal to the adjacent bony edge. The variance was statistically significant when the p-value was less than 0.05. The analysis was performed using the R statistical software ver4.0.2.

Results

There were 22 patients who complained of vestibular symptoms the day after the operation, accounting for 13.9% of the total. Vertigo occurred in six cases and dizziness in 16 cases. In one case, the hospitalisation period was extended by 1 week due to vertigo, but in all other cases, the symptoms improved, and the patient was discharged as scheduled.

There were more vestibular symptoms among the subjects having a history of vestibular symptoms ($p<0.01$) (Table 2).

During examination by the stage of cholesteatoma revealed more vestibular symptoms among stage II cases with pars flaccida (Table 3); however, examination by the focal origin revealed no significant difference among different stages. Furthermore, examination by the STAM system revealed significantly more vestibular symptoms in cases with lesions at the attic ($p<0.05$) and mastoid ($p<0.01$). In addition, vestibular symptoms were observed only in the stage II cases (Table 4).

In relation to bone destruction, patients with exposure of the dura mater ($p<0.01$), bone dehiscence of the Fallopian canal ($p<0.01$), and blue line ($p<0.01$) revealed significant differences and were considered to be at high risk (Table 5). Multivariate logistic regression analysis was performed for each item, and significant differences were observed in the past histories of vestibular symptoms ($p<0.05$) and exposure of the dura mater ($p<0.01$) (Table 6).

Pathologically, it is not considered that exposure of the dura mater causes vestibular symptoms. However, because it was the greatest risk factor, we hypothesised that the narrowing of the working space around the mastoid antrum in mastoidectomy may be a background factor in cases with exposure of the dura mater. Therefore, as an additional study, the shortest distance from the prominence of the lateral semicircular canal to the middle cranial fossa dura was measured in the coronal image of the temporal bone CT of all cases in this study. It was confirmed that the length was significantly shorter in the exposed dura group than in the non-exposed group ($p<0.01$) (Table 7). In addition, in cases with cholesteatoma in the mastoid area and need to remove epithelial

tissue from the bony surface adjacent to the superior semicircular canal, we thought that by thinning the bony wall adjacent to the superior semicircular canal, the procedure might also threaten the vestibular function by stimulating the superior semicircular canal. We measured the length from the superior semicircular canal to the bony edge. However, as a result of the examination, no correlation was found between the thickness of the bony wall and the occurrence of vestibular symptoms ($p=0.53$) (Table 8).

Discussion

In the primary operation for cholesteatoma, the incidence of postoperative dizziness at our hospital was 13.9%. The issues so far in cholesteatoma have been reported to be the rate of residual/recurrence of the lesion and hearing improvement results; few studies have discussed postoperative vestibular symptoms. This study is the first to investigate the incidence of dizziness in detail based on the STAM system and staging, as well as the findings of bone destruction. In our previous study, we reported that patients who underwent canal wall down mastoidectomy (CWD) had a higher incidence of vestibular symptoms than those who underwent canal wall up mastoidectomy (CWU) [7]. The reason for this was that the surgical invasion was large in CWD cases and thus it was likely that the impact of drilling was transmitted more to the vestibular organ; further, the extent of cholesteatoma lesions was relatively larger in CWD cases. In this study, a significant difference was observed in the comparison of the number of cholesteatoma regions based on the STAM system, with 1.73 regions in CWU cases and 2.82 regions in CWD cases ($p<0.01$). Therefore, it is difficult to simply compare the risk of dizziness due to variations in mastoidectomy.

In the STAM system and staging by EAONO/JOS, cases where the lesions extends beyond the origin region to multiple regions are defined as stage II. All vestibular symptoms in this study corresponded to stage II. Among the cases judged to be stage II, there were cases in which bone destruction was remarkable and cases in which the lesions were widespread in mastoid cells, and on the other hand, there were cases in which the lesions were spread over two regions but were relatively localised. James et al. reported that stage II accounted for a large proportion of staging by the STAM system and could

not fully express the severity. They assumed that dividing stage II into subgroups based on ossicular status or extension beyond the antrum into deeper mastoid air cells would allow a more even and useful distribution [8]. In our study, we also found a significant difference in the items related to bone destruction, suggesting that the findings of bone destruction function more as a predictor of prognosis than the staging system. All patients with vestibular symptoms had both attic and mastoid lesions. Considering that cholesteatoma lesions originating from the mastoid are extremely rare, it is considered that the condition most associated with the development of vestibular symptoms is the condition in which cholesteatoma has progressed to the mastoid.

Multivariate analysis revealed significant differences in past histories of vestibular symptoms and exposure of the dura mater. Leonetti et al. reported patients who had complaints of preoperative history of vertigo that improved after canal wall down mastoidectomy [9]. In some cases, the cholesteatoma lesion itself may cause vestibular disorder, and removal of the lesion also result in the risk of postoperative vestibular disorders. Additionally, the sensitivity or vulnerability of vestibular symptoms may also cause postoperative vestibular disorders. The reason why the exposure of the dura mater had the highest odds ratio, and that no significant difference was observed in the blue line cases, was due to the difference in the consciousness of the surgeon and the difficulty of the operation. Since the surgeon may proceed with the operation so as not to touch the dangerous part, such as the blue line and the exposed part of the dura mater, as much as possible, in the case with the blue line, the operation is protectively minimally invasive to the part. On the other hand, when the dura mater is exposed, invasion on the cranial side is restricted to avoid damage to the dura mater. As a result, it was considered that the operative procedure close to the vestibular organ may be related to the occurrence of vestibular symptoms. It is known that otitis media with effusion and cholesteatoma in childhood inhibits the growth of the mastoid [10]. Keratag et al. reported that when comparing between cases of exposed and unexposed dura mater, the height of tegmen was significantly lower in exposed cases, and that the volume of mastoid air cells was generally smaller in cases with low tegmen. They suggested that downward operation to avoid dural damage increases the risk of complications other than dural damage [11]. In our study, the distance from the lateral semicircular canal to the tegmen was significantly

narrower in the exposed cases of dura. The distance from the lateral semicircular canal is more selective from the perspective of examining the risk of vestibular symptoms and more strongly reflects the purpose of this examination. It was suspected that the small space in the mastoid antrum transmitted a larger drilling impact from a short distance, which may be related to vestibular symptoms. In the temporal bone CT scan, it is difficult to accurately evaluate the spread of cholesteatoma lesions because they are visualised in the same colour as cholesterol granulomas and liquid components.

Mahmutoglu et al. reported that temporal bone CT can evaluate the presence or absence of bone thinning, bone defects, and the height of the middle cranial fossa dura with almost 100% sensitivity [12]. Since the vestibular disorder risk factors can be known in advance, they are expected to be useful for the planning of surgery by the surgeon.

As a limitation of this study, the presence or absence of subjective vestibular symptoms on the day after surgery was evaluated, but the mechanism of the vestibular symptoms had not been clarified because the preoperative and postoperative objective tests of the vestibular function had not been performed. However, the results of bone conduction audiometry in the early postoperative period revealed no significant differences; the average bone conductive hearing level at 2 kHz was 3 dB higher in cases with vestibular symptoms than in cases without vestibular symptoms (Figure 3). Therefore, vestibular symptoms may be related to inner ear dysfunction.

Conclusion

In the primary tympanoplasty for cholesteatoma, 13.9% had vestibular symptoms the day after the operation. Attic and mastoid pearl masses, past histories of vestibular symptoms, and exposure of the dura mater were high-risk factors for the development of vestibular symptoms.

Disclosure Statement

No potential competing interest was reported by the authors.

Table 1. Demographic data and cholesteatoma staging

Subjects' background			**N**
	Sex	Male	80
		Female	86
	Age	range(years)[mean age ± SD]	50 ± 21
	Operative side	Right	88
		Left	78
	Past history of vestibular symptoms	Yes	40
		No	126
Classification			
	Pars flaccida	stage I	34
		stage II	104
	Pars tensa	stage I	4
		stage II	24
Operative strategy			
	One stage	stage Ⅰ	18
		stage Ⅱ	13
	Two stage	stage Ⅰ	20
		stage Ⅱ	115
	Canal wall up	stage Ⅰ	23
		stage Ⅱ	21
	Canal wall down	stage Ⅰ	15
		stage Ⅱ	107

Table 2　Relationship past history of vestibular symptoms and postoperative vestibular symptoms

past history of vestibular symptoms	vestibular symptoms				
	Yes N(%)	**No N(%)**	**odds ratio**	**95% CI**	**p value**
			3.92	1.39-11.12	<0.01
Yes	11(27.5）	29(72.5)			
No	11(8.7)	115(91.3）			

Table 3. Relationship stage of cholesteatoma and vestibular symptoms

		Vestibular symptoms				
Origin of cholesteatoma		**Yes N(%)**	**No N(%)**	**Odds ratio**	**95% CI**	**p value**
Pars flaccida				Inf	1.85-inf	<0.01
	stage I	0(0)	34(100)			
	stage II	20(19.2)	84(80.7)			
Pars tensa				Inf	0.03- Inf	1
	stage I	0(0)	4(100)			
	stage II	2(8.3)	22(91.7)			

Table 4. Relationship between the focal location and vestibular symptoms

Location of cholesteatoma		**Vestibular symptoms** **Yes N (%)**	**No N (%)**	**Odds ratio**	**95% CI**	**p value**
S1				1.25	0.28-4.32	0.75
	yes	4 (15.4)	22 (84.6)			
	no	18 (12.7)	124 (87.3)			
S2				0.34	0.06-1.26	0.13
	yes	3 (6.1)	46 (93.9)			
	no	19 (16.0)	100 (84.0)			
T				2.17	0.72-7.94	0.16
	yes	17 (16.0)	89 (84.0)			
	no	5 (8.1)	57 (91.9)			
A				Inf	0.98-inf	<0.05
	yes	22 (15.3)	122 (84.7)			
	no	0 (0)	24 (100)			
M				Inf	4.90-inf	<0.01
	yes	22 (22.7)	75 (84.7)			
	no	0 (0)	71 (100)			

Table 5. Relationship between the bone destructive findings and vestibular symptoms

		Vestibular symptoms				
Variance		**Yes N (%)**	**No N (%)**	**Odds ratio**	**95% CI**	**p value**
Exposure of the dura mater				5.90	2.10-17.37	<0.01
	yes	13 (31.7)	28 (68.3)			
	no	9 (7.2)	116 (92.8)			
Bone dehiscence of the Fallopian canal				4.37	1.56-13.60	<0.01
	yes	15 (24.2)	47 (75.8)			
	no	7 (6.7)	97 (93.3)			
Blue line				5.67	1.73-18.04	<0.01
	yes	8 (38.1)	13 (61.9)			
	no	14 (9.7)	131 (90.3)			

Table 6. Results of the multivariate analyses

	Odds ratio	**95% CI**	**p value**
Past history of vestibular symptoms	3.35	1.18-9.46	<0.05
Bone dehiscence of the Fallopian canal	2.91	0.92-8.14	0.07
Exposure of the dura mater	4.48	1.60-12.70	<0.01
Blue line	2.56	0.64-7.72	0.21

Table 7. Relationship between exposure of the dura mater and average height of the dura mater

Exposure of the dura mater	**n**	**Average height from L-SSC (mm)**	**SD**	**p value**
Yes	125	7.632	±1.88	<0.01
No	41	8.617	±1.59	

Table 8. The length from the superior semicircular canal to the bony edge

postoperative vestibular symptoms	n	the mean length from S-SCC to the bony edge(mm)	SD	p value
Yes	14	1.44	±0.65	0.53
No	55	1.56	±0.70	

Figure 1

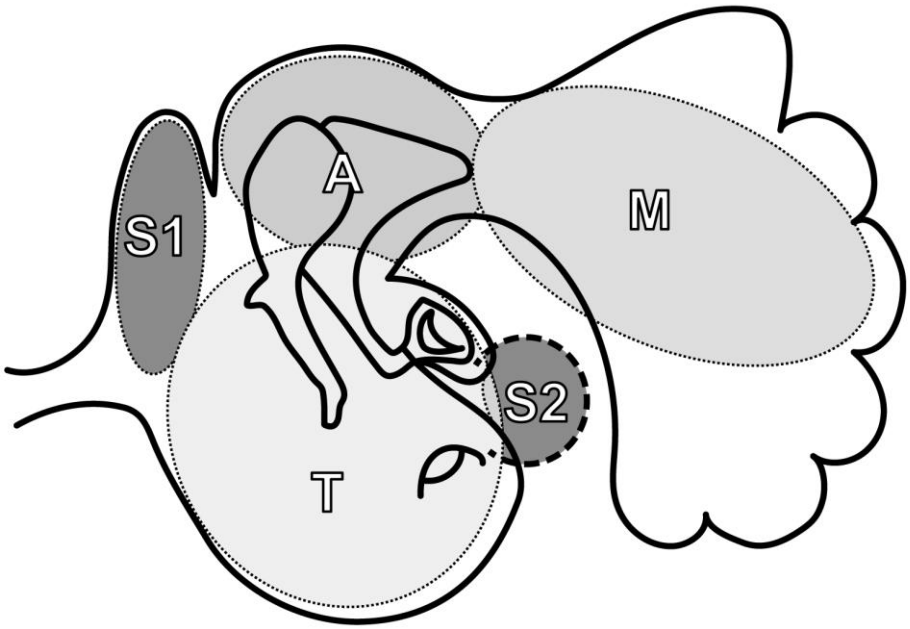

Figure 1: STAM system.

The STAM system was published by the European Academy of Otology and Neurotology and Japan Otological Society for the purpose of concisely assessing the extension and severity of cholesteatoma.

S1, supratubal recess; S2, sinus tympani; T, tympanic cavity; A, attic; M, mastoid.

Figure 2

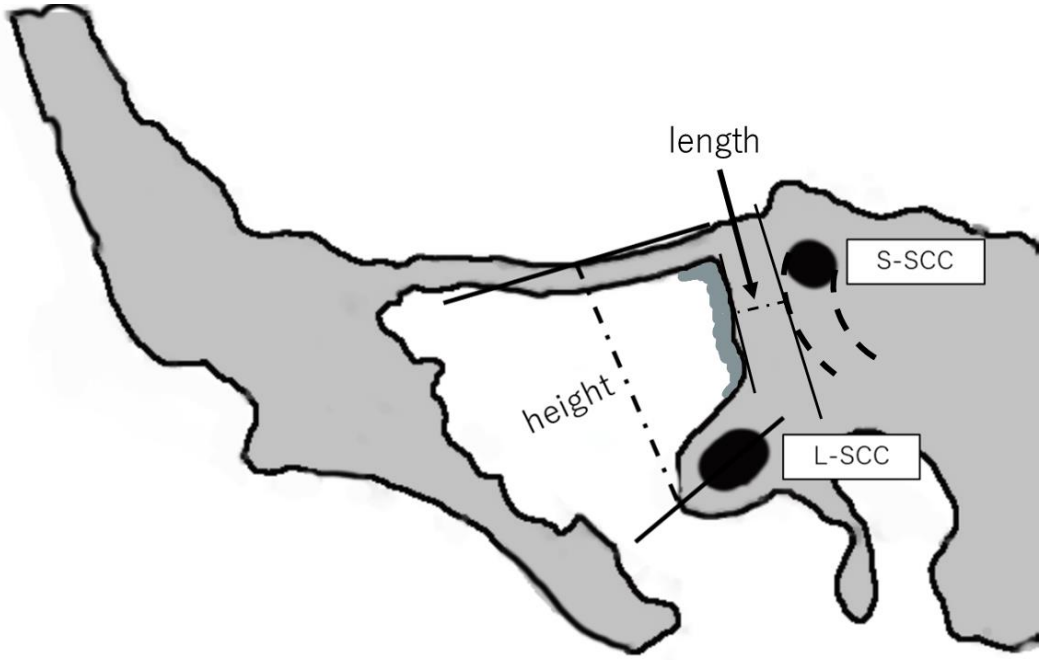

Figure 2: Measurement of the distance from the eminence of the lateral semicircular canal to the dura mater, and the distance from the superior semicircular canal to the bony edge.

The shortest distance from the extension of the axis of the lateral semicircular canal to the upper edge of the tegmen was measured. Similarly the shortest distance from the superior semicircular canal to the edge of the adjacent bony wall was also measured.

L-SCC, lateral semicircular canal; S-SCC, superior semicircular canal

Figure 3

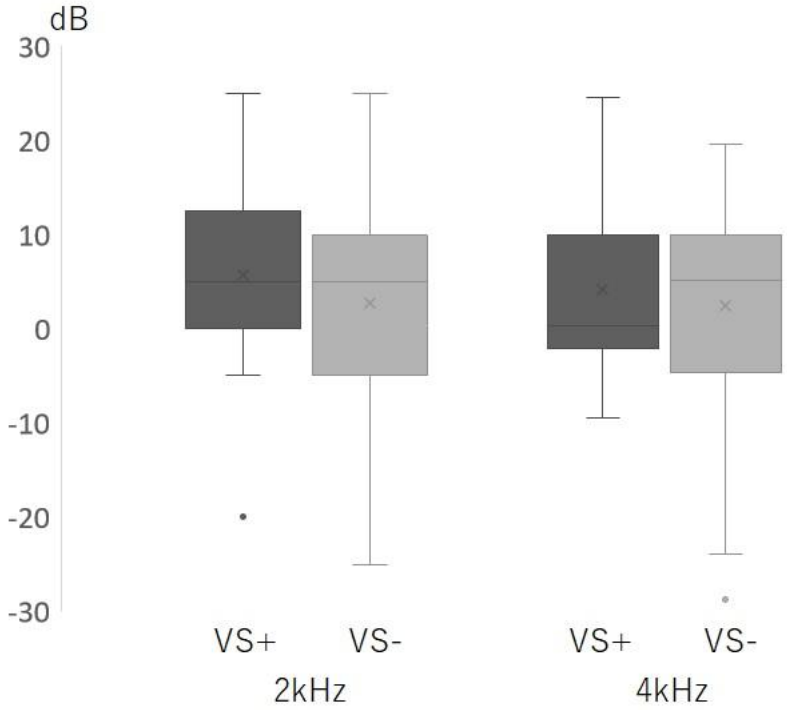

Figure 3: Difference in bone conduction hearing threshold before and after surgery.

The relationship between postoperative increase in bone conduction hearing threshold and dizziness was investigated. As a result of subtracting the preoperative data from the data several days after the operation, no significant difference was observed between the group with vestibular symptoms and the group without vestibular symptoms. In the comparison at 2 kHz, the threshold increase was observed more in the group with vestibular symptoms than in the group without vestibular symptoms about 3 dB after surgery.

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