

Prevalence and clinical significance of
spontaneous low-frequency air-bone gap
in Meniere's disease

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This certifies that the Master's Thesis
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ABSTRACT

Prevalence and clinical significance of spontaneous low-frequency
air-bone gap in Meniere's disease.

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Objectives: This study was performed to identify the prevalence and clinical significance of spontaneous low-frequency air-bone gap (LFABG) in Meniere's disease.

Study design: A retrospective study.

Methods: Three hundred and thirty-seven definite Meniere's disease patients were included. The prevalence of LFABG in this population was calculated and the following parameters were analyzed to identify the clinical significance of LFABG: 1) changes of hearing threshold after the resolution of LFABG; 2) correlation between LFABG and the result of electrocochleography; 3) changes in the number of vertigo spells after the resolution of LFABG; 4) correlation between LFABG and canal paresis values in caloric test; and 5) the difference in the prognosis between patients with and without LFABG.

Results: The prevalence of LFABG was 12.6%. Cochlear function was correlated with LFABG; the patients' hearing threshold was significantly decreased after the resolution of LFABG (from 48.9 ± 17.0 to 39.7 ± 19.6 dBnHL) and the SP/AP ratio showed a tendency to increase as LFABG increased ($R^2 = 0.09$, $P = 0.03$). The mean number of vertigo spells was significantly reduced after the resolution of LFABG (from 5.2 ± 8.5 to 0.5 ± 0.01 , $P = 0.02$). However, the prognosis was not different between patients with and without LFABG.

Conclusion: The prevalence of LFABG in Meniere's disease was 12.6%. Although the prognostic importance of LFABG was not significant, it is likely to reflect the aggravation of endolymphatic hydrops in the cochlear and vestibular compartments and may be useful for evaluating and treating patients with Meniere's disease.

Key words : Meniere's disease, air-bone gap, endolymphatic hydrops, vertigo, hearing.

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I. INTRODUCTION

Previous studies have reported a spontaneous low-frequency air-bone gap (LFABG) in approximately 30% of patients with Meniere's disease or Cogan syndrome ¹⁻³, the common pathological finding of which is the dilatation of the endolymphatic space (endolymphatic hydrops). It was postulated that such a LFABG may be caused by dampened stapedial mobility induced by endolymphatic hydrops, which can cause an increase in perilymphatic pressure ². However, there have been few reports on the incidence and prevalence of LFABG in Meniere's disease^{1,2}, and no report has described the clinical significance of LFABG in those patients. If the development or aggravation of endolymphatic hydrops in the cochlear compartment is a cause of spontaneous air-bone gaps in patients with Meniere's disease, then patient symptoms and cochlear functions, such as hearing thresholds and the ratio of summing potential and action potential (SP/AP ratio) in electrocochleography (ECoG),

are likely to be associated with LFABG. Furthermore, if endolymphatic hydrops develops in the vestibular compartment simultaneously with cochlear hydrops, vestibular symptoms, such as vertigo spells, may be correlated with LFABG development. In this study, we sought to investigate the prevalence and clinical significance of spontaneously developed LFABG in Meniere's disease patients.

II. PATIENTS AND METHODS

1. Selection of patients

Three hundred and thirty-seven consecutive patients diagnosed with definite Meniere's disease based on the guidelines of the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) [1995]⁴ were studied retrospectively. The subjects consisted of 113 men and 224 women, and their mean age was 50.4 ± 13.8 years. The mean disease duration of the patients was 48.5 ± 45.2 months and the mean follow-up period was 13.2 ± 11.3 months. The lesion sides were left in 182 cases, right in 144 cases, and bilateral in 11 cases. Pure tone audiogram (PTA), extratympanic ECoG, impedance audiometry, and caloric test analyses were performed to evaluate the hearing and vestibular function of these patients. PTAs were performed regularly at 6-month intervals but also if a patient complained of an aggravated hearing threshold. This study was approved by institutional review board of author's institute.

2.Evaluating spontaneous LFABG

The prevalence of LFABG was investigated in this population. LFABG was calculated by averaging 3 different frequencies, including 250, 500, and 1,000 Hz. LFABG was regarded as present if it was detected in more than 2 of the continuing frequencies and if the calculated value was equal to or greater than 10 dBHL. Patients who showed LFABG in pure tone audiograms at least once during the follow-up period were included for the calculation of prevalence. Middle ear pathology was ruled out in the patients with LFABGs by carefully examining their tympanic membranes and performing impedance audiometry with the stapedial reflex. Patients with middle ear pathologies were excluded from this study. If the LFABG had developed after endolymphatic sac surgery, it was also excluded from the prevalence of spontaneous LFABG because this condition has been shown to result from endolymphatic sac surgery⁵.

3.Analysis of the clinical significance of LFABG

First, the relationship between LFABG and cochlear functions was investigated. For analysis, the changes of hearing threshold between at the LFABG development and after the resolution of LFABG were compared, and then, the correlation between the amount of LFABG and SP/AP ratio were investigated by linear regression.

Second, the relationship between LFABG and vestibular function was analyzed. Vestibular function tests were not routinely followed-up in author's

institute. Therefore, we analyzed changes of number of vertigo spells between the period of LFABG and the period of no LFABG instead of analyzing changes of vestibular function test results. The numbers of vertigo spells occurring 1 month before and after the date of LFABG development, and occurring 1 month before and after the LFABG disappearance were compared. If a patient showed LFABG 2 or more times, the number of vertigo spells during each period was compared to each following period of LFABG resolution. In addition, the correlation between caloric weakness and the amount of LFABG was investigated by linear regression. Patients who underwent chemical labyrinthectomy were included in the analysis of LFABG prevalence but excluded from the analysis of cochlear and vestibular functions because the chemical ablation of cochlear and vestibular function could affect the laboratory results and number of vertigo spells.

Third, authors tried to investigate if LFABG affected long-term prognosis of Meniere's disease. For this, prognostic difference between the patients with LFABG and without LFABG was analyzed. Patients whose follow-up period was longer than 2 years ($n = 24$ for the patients with LFABG and $n = 120$ for the patients without LFABG) were assigned to class A, B, C, D, E, or F according to the 1995 guidelines of AAO-HNS⁴ for the analysis of prognosis. Patients who were intractable to medical treatment and underwent invasive procedures such as endolymphatic sac surgery, chemical labyrinthectomy, and vestibular neurectomy were assigned to class F.

4.Data analysis

Values are presented as the means \pm SD. The differences in the hearing thresholds and the number of vertigo spells between LFABG development and no LFABG periods were analyzed using student t-test. Linear regression was used to analyze the correlation between the LFABG and the results of laboratory tests (SP/AP ratio in ECoG and canal paresis values) in the patients with LFABG. For the analysis of prognostic differences between patients with and without LFABG, the chi-square test was used. Differences were considered to be significant at $P < 0.05$.

III. RESULTS

1.Prevalence of LFABG

Among 337 patients, LFABG was detected in 47, and the prevalence of LFABG was 13.9%. The mean LFABG and hearing threshold at the time of development of LFABG were 17.0 ± 7.8 dB and 46.5 ± 17.4 dBHL, respectively. An air-bone gap (ABG) of more than 10 dB was detected at all 3 low frequencies (250, 500, and 1,000Hz) in 17 patients and at 2 frequencies in 30 patients. At follow-up, LFABG was detected 2 times in 3 patients, and it persisted in only 1 patient. LFABG was observed on the contra-lateral sides in 8 of 47 patients (17.0%).

2.LFABG and cochlear function

Among the 47 patients who developed LFABG, the results of follow-up PTA were available in 23 patients for further analysis; PTA was not followed-up in 13 patients, and follow-up PTA was performed after chemical labyrinthectomy or endolymphatic sac surgery in 11 patients. The hearing threshold decreased significantly after the resolution of LFABG from 48.9 ± 17.0 to 39.7 ± 19.6 dBnHL ($P = 0.001$, Fig 1).

Figure 1

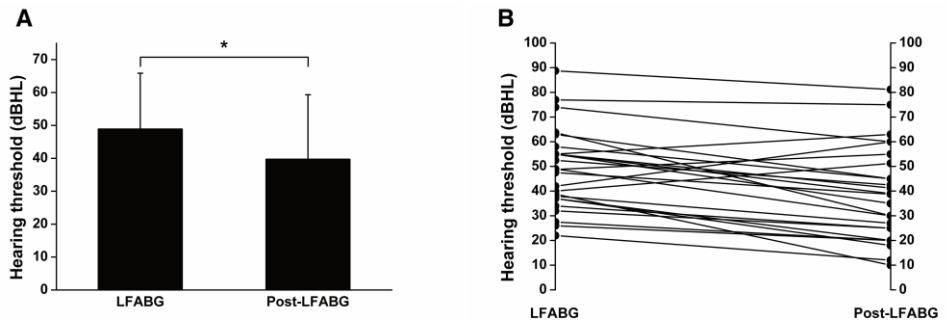


Figure 1. Changes in hearing threshold after the resolution of LFABG ($n = 25$, LFABG persisted in 1 case and was detected twice in 3 cases). The hearing threshold decreased significantly after the resolution of LFABG, from 48.9 ± 17.0 to 39.7 ± 19.6 dBnHL (A) ($P = 0.001$). Individual traces of hearing threshold changes after the resolution of LFABG (B). *, $P < 0.05$.

Then, the correlation between LFABG and SP/AP ratio was analyzed, because SP/AP ratio was known to represent cochlear hydrops, although there were debates about its sensitivity. The SP/AP ratio showed a tendency to

increase as LFABG increased, even though the distribution of SP/AP values according to LFABG was wide ($R^2 = 0.09$, $P = 0.03$, Fig 2).

Figure 2

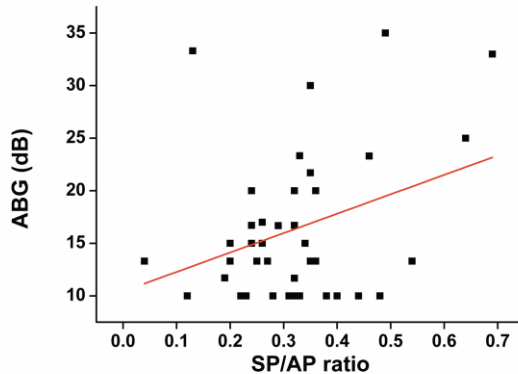


Figure 2. Correlation between the SP/AP in ECoG and LFABG ($n = 47$). The SP/AP ratio in ECoG showed a tendency to increase as LFABG increased ($R^2 = 0.09$, $P = 0.03$).

3. LFABG and vestibular function

In the 23 patients with available follow-up PTA data for further analysis, the mean number of vertigo spells was reduced significantly after the resolution of LFABG ($P = 0.02$). The mean number of vertigo spells near the time of LFABG development was 5.2 ± 8.5 , whereas the mean number of vertigo spells near the time of LFABG disappearance was 0.5 ± 0.01 (Fig 3).

Figure 3

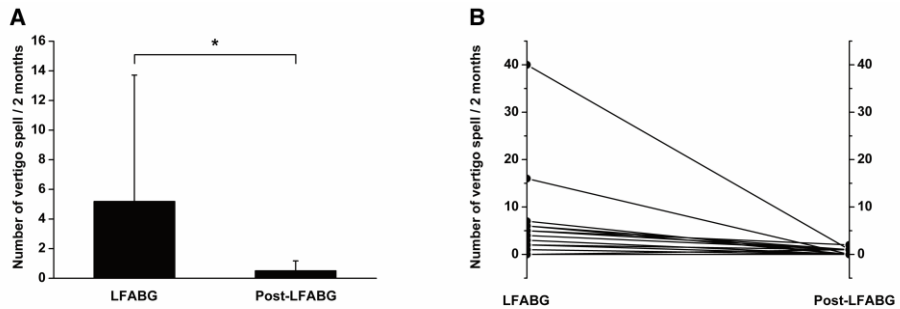


Figure 3. Difference in the mean number of vertigo spells during the period of LFABG development and after the resolution of LFABG (n=25, LFABG persisted in 1 case and was detected twice in 3 cases). The mean number of vertigo spells was significantly reduced after the resolution of LFABG ($P = 0.02$). The mean number of vertigo spells near the time of LFABG development was 5.2 ± 8.5 , whereas the mean number of vertigo spells near the time of LFABG disappearance was 0.5 ± 0.01 (A). Individual traces of changes in the number of vertigo spells (B). *, $P < 0.05$.

In one patient showing persistent LFABG until the last follow-up date, the number of vertigo spells increased (from 5-6 times/year to 3 times/week). However, canal paresis value did not correlate with the amount of LFABG ($R^2 = -0.01$, $P > 0.05$, Fig 4).

Figure 4

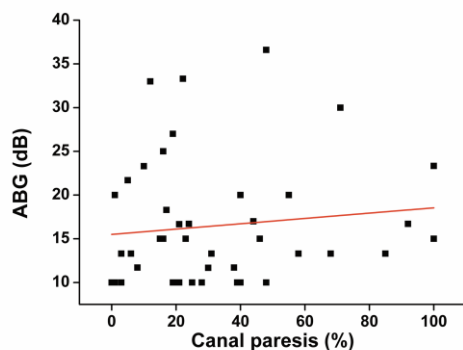


Figure 4. Correlation between the canal paresis values and LFABG (n = 47). canal paresis value did not correlate with the amount of LFABG ($R^2 = -0.01$, $P > 0.05$).

4.LFABG and prognosis

The prognostic difference for non-invasive treatment between patients with LFABG and without LFABG was not significant ($P > 0.05$). Vertigo spells were relatively well controlled with medical treatment (class A and B) in 54.1% of patients with LFABG and in 58.8% of patients without LFABG. The treatment failure rate (class F) was 33.3% and 16.7% in patients with LFABG and without LFABG, respectively, and this difference was not statistically significant ($P > 0.05$). Although the proportion of intractable cases (class F) between the 2 groups was not significantly different, the proportion of intractable cases tended to be larger among patients with LFABG. These results are summarized in Table 1.

Table 1. Difference in prognosis between patients with and without LFABG.

Class	Number of patients with LFABG (%)	Number of patients without LFABG (%)
A	5 (20.8)	29 (24.2)
B	8 (33.3)	41 (34.2)
C	1 (4.2)	20 (16.7)
D	1 (4.2)	6 (5.0)
E	1 (4.2)	4 (3.3)
F	8 (33.3)	20 (16.7)

Patients whose follow-up period was longer than 2 years (n = 24 for patients with LFABG and n = 120 for patients without LFABG) were assigned to class A, B, C, D, E, or F according to the 1995 guidelines of AAO-HNS. The prognostic difference between the 2 groups was not significant ($P > 0.05$). LFABG, Low-frequency air-bone gap.

IV. DISCUSSION

Generally, LFABG can be detected in patients with middle ear pathology, such as ossicular fixation, or with inner ear third windows, such as enlarged vestibular aqueducts or superior canal dehiscence. However, it has been suggested that restraining the sound conduction within inner ear fluid can result

in LFABG². It has also been reported that approximately 30% of patients demonstrate LFABG in Meniere's disease^{1,2}, and the compliance of the lesion side ear was decreased when patients complained of aural fullness⁶. The mechanism of LFABG was described to involve increased endolymphatic pressure that decreases the mobility of stapes, which eventually causes increased air-conduction thresholds^{2,6}. In our study, the prevalence of LFABG (~14%) was lower than that reported in previous studies (~30%). However, few studies have been conducted on the incidence and prevalence of spontaneous LFABG in Meniere's disease, and the patient groups in previous studies were smaller than in this study. In Muchnik's report², which detected LFABG in 32.5% of patients, patients were diagnosed with Meniere's disease if they complained of recurrent episodic vertigo, tinnitus, and fluctuating progressive sensorineural hearing loss and if they showed positive results in a glycerol dehydration test. LFABG was defined to be present if an air-bone gap was at least 20 dB at one frequency (if an ABG was present at 250 Hz, an air-bone gap also had to be present at another frequency) or if an ABG of at least 15 dB at one frequency and 10 dB at another frequency was discovered. In our opinion, the prevalence of Meniere's disease in this previous study was likely over-estimated. First, these authors included patients who had positive glycerol tests. Glycerol tests are not essential for the diagnosis of Meniere's disease, according to the 1995 diagnostic criteria of AAO-HNS⁴, which we used for the selection of patients in our study. Not all Meniere's disease patients show

positive results in the glycerol test, and endolymphatic hydrops could be more severe in patients with positive glycerol test results than in patients with negative glycerol results, which could have resulted in an increased prevalence of LFABG in this previous study. Second, the criteria for LFABG in Muchnik's study were slightly different from those used in our study, and this previous study included patients demonstrating LFABG of more than 20 dB at one frequency if it was not present only at 250 Hz. Wider criteria than those were used in our study could have increased the prevalence of LFABG in Meniere's disease. However, our study also had some limitations related to identifying the real prevalence of LFABG in Meniere's disease, which could have caused an under-estimation of the real prevalence. First, our study was retrospective, and follow-up PTA was performed in a limited number of cases. Second, our institution is a tertiary care referral center where patients whose vertigo spells that are well-controlled through non-invasive treatment may not be referred. Therefore, the real prevalence of LFABG could have been underestimated. For an estimation of the real prevalence of LFABG in Meniere's disease, a well-designed prospective study, which includes regular hearing and vestibular function evaluation according to patients' symptoms, should be conducted.

We tried to investigate the clinical significance of LFABG by analyzing the relationship between LFABG and cochlear/vestibular function. We did not compare the cochlear/vestibular functions between the patients with LFABG and without LFABG in this study, because cochlear and vestibular functions in

Meniere's disease differ between patients according to the disease duration and stage of disease. Considering a various disease duration and stages of patients in this study, a comparison of the difference in cochlear/vestibular functions between patients with and without LFABG is not likely to be meaningful. Therefore, we analyzed the relationship between LFABG and cochlear/vestibular functions by analyzing the changes of hearing threshold after resolution of LFABG, correlation of LFABG and SP/AP ratio, correlation of LFABG and canal paresis values, and changes of number of vertigo spells after the resolution of LFABG.

LFABG seemed to be correlated with cochlear function in this study, and the hearing threshold at the time of LFABG development was increased significantly compared to that at the time of LFABG disappearance. In other words, most LFABG was likely to develop during the period of hearing aggravation, which could occur alongside the aggravation of endolymphatic hydrops. In addition, the SP/AP ratio of ECoG showed a tendency to increase with the amount of LFABG, which also indicates the possibility of increased amount of cochlear hydrops. It would be helpful for identifying endolymphatic hydrops if ECoG was followed-up after the resolution of LFABG; nevertheless, changes in the SP/AP ratio after the disappearance of LFABG could not be confirmed because we did not routinely follow-up ECoG in Meniere's disease patients. However, the sensitivity of the ECoG test in Meniere's disease was reported to be fairly low (55-75 %) ⁷⁻¹⁰, and the changes in the SP/AP ratio or

the SP/AP ratio itself may not have accurately represented the current status of endolymphatic hydrops. This possibility may explain the wide distribution of the SP/AP ratio in the correlation analysis between canal paresis values and SP/AP ratio.

It was interesting that the number of vertigo spells was significantly higher during the period of LFABG development, which may indicate that endolymphatic hydrops in the vestibular compartment developed alongside the cochlear hydrops. Because LFABG mainly reflects cochlear function, it may not represent whole vestibular function in Meniere's disease. Canal paresis values did not correlate with LFABG, because vestibular function of patients could be decreased according to the disease duration and even in the patients with large LFABG with short disease duration could have showed relatively favorable vestibular function. Therefore, if the vestibular function test can be followed-up at the time of LFABG development and at the time of LFABG resolution, it would help to identify the coincidence and relationship between cochlear and vestibular hydrops. Actually, several reports have suggested the relationship between altered caloric and VEMP responses in the lesion side during Meniere attacks ¹¹⁻¹³. However, in our study, caloric test were not routinely followed-up during the period of LFABG development; thus, we could not identify changes in these results after LFABG disappearance.

Consequently, the hearing threshold may increase and vertigo spells may occur at a high incidence during the period of LFABG development. Although

an increase in the number of vertigo spell and hearing threshold was observed temporarily during this period, the final prognosis is not likely to be different between patients with and without LFABG. Therefore, attention would be better directed toward controlling vertigo spells and hearing fluctuations in the period of LFABG development during the follow-up of Meniere's disease patients.

V. CONCLUSION

The prevalence of LFABG in Meniere's disease was 12.6%, which was lower than that reported in previous studies. The number of vertigo spells and hearing thresholds were significantly higher during the period of LFABG development. Although the prognostic importance of LFABG was not significant, it is likely to reflect the aggravation of endolymphatic hydrops and may present useful information for evaluating and treating Meniere's disease patient

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ABSTRACT(IN KOREAN)

메니에르병에서 자발적인 저주파수 기도골도차의

유병률 및 임상적 중요성

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이 현 진

연구 목적

메니에르병에서 자발적인 저주파수 기도골도차(low-frequency air-bone gap)의 유병률 및 임상적 중요성 확인

연구 설계

후향적 연구

연구 방법

본 연구에는 명확한(definite) 메니에르병으로 진단된 337명의 환자가 포함되었다. 선정된 환자군에서 저주파수 기도골도차(low-frequency air-bone gap)의 유병률을 확인했으며, 임상적 중요성을 확인하기 위해 다음과 같은 변수와의 상관관계를 분석하였다

- 1) 저주파수 기도골도차의 회복 후 청력 역치 변화
- 2) 저주파수 기도골도차와 전기와우도의 상관관계
- 3) 저주파수 기도골도차의 회복 후 어지럼증 횟수 변화
- 4) 저주파수 기도골도차와 온도안진검사의 반규관 마비와의 상관관계
- 5) 저주파수 기도골도차가 있는 군과 없는 군의 예후 차이

결과

메니에르병에서 저주파수 기도골도차를 보이는 환자의 유병률은 12.6% 였다. 와우의 기능은 저주파수 기도골도차와 연관성을 보였으며, 저주파수 기도골도차가 회복된 환자군에서 청력역치가 의미 있게 감소하였다. (from 48.9 ± 17.0 to 39.7 ± 19.6 dBnHL) 또한, 저주파수 기도골도차가 증가함에 따라 SP/AP비가 증가하는 경향을 보였다. ($R^2 = 0.09$, $P = 0.03$) 저주파수 기도골도차에서 회복된 후에 어지럼증의 평균 횟수가 의미 있게 감소하였다. (from 5.2 ± 8.5 to 0.5 ± 0.01 , $P = 0.02$). 그러나 저주파수 기도골도차의 유무에 따른 예후의 차이는 관찰되지 않았다.

결론

메니에르병에서 저주파수 기도골도차와 예후와의 관련성은 확실하지 않았다. 그러나 저주파수 기도골도차가 전정-와우 기관에서 내림프수종의 악화를 반영하는 것으로 보이며, 청력역치가 회복됨에 따라 어지럼증의 횟수가 감소하는 것으로 보아 메니에르병 환자의 평가와 치료에 유용한 지표가 될 것으로 기대된다.

핵심되는 말 : 메니에르병, 기도골도차, 내림프수종, 현훈, 청력