

ORIGINAL RESEARCH

Immediate and short-term effects of Gufoni and Appiani liberatory maneuver for treatment of ageotropic horizontal canal benign paroxysmal positional vertigo: A prospective randomized trial

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Abstract

Objective: To examine the treatment effects of repositioning maneuvers with the head turned 45° downwards (Gufoni maneuver) and 45° upwards (Appiani maneuver) in 25 patients with ageotropic horizontal semicircular canal (HSCC) benign paroxysmal positional vertigo (BPPV).

Methods: Patients were randomly assigned to the Gufoni or Appiani maneuvers, and their immediate and short-term efficacy was investigated.

Results: The immediate treatment response was successful in four of 16 patients who were treated with the Appiani maneuver and were not successful in any of the nine patients treated with the Gufoni maneuver. The patients who showed spontaneous resolution during follow-up outnumbered the patients who showed resolution of ageotropic HSCC BPPV immediately after the repositioning maneuvers.

Conclusion: This study showed a very low immediate resolution rate of ageotropic HSCC BPPV after the Gufoni maneuver; this may be attributed to the less effectiveness of the Gufoni maneuver against debris that often exists in the canal side of the cupula. Another interesting finding was that the rate of spontaneous resolution during the follow-up period was higher than that of immediate resolution after the repositioning maneuvers, which may support the recently proposed hypothesis that ageotropic positional nystagmus can also be evoked by causes other than the otolithic attachment on the cupula, such as a slight change in the biochemical composition of the inner ear fluids.

Level of Evidence: 3.

KEYWORDS

benign paroxysmal positional vertigo, cupulolithiasis; ageotropic, horizontal semicircular canal, treatment outcome

Jiyeon Lee and Dong-Han Lee contributed equally and are co-first authors of this article.

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1 | INTRODUCTION

Benign paroxysmal positional vertigo (BPPV) arises from the horizontal semicircular canal (HSCC) in approximately 5.1% to 59.8% of all BPPV patients.¹⁻⁴ HSCC BPPV is characterized by direction-changing positional nystagmus during the supine roll test. Otolith debris attached to the cupula is known as a cause of ageotropic type HSCC BPPV (cupulolithiasis). Several physical maneuvers, including barbecue rotation, forced prolonged position, therapeutic head-shaking in the horizontal plane, cupulolith repositioning by mastoid oscillation, and Gufoni maneuver,⁵ have been introduced for the treatment of ageotropic HSCC BPPV. In 1998, Gufoni et al first described the Gufoni maneuver, which has many features in common with the Semont maneuver, to treat patients with either geotropic or ageotropic type HSCC BPPV.⁵ For geotropic HSCC BPPV, the patient is quickly laid down on the healthy side, and the head is quickly turned 45° toward the floor and kept in this position for 2 to 3 minutes. The patient is then returned to the starting position.⁵ For ageotropic HSCC BPPV, the patient is quickly laid down on the affected side, and the head is quickly turned 45° toward the floor and kept in this position for 2 to 3 minutes. The patient is then returned to the starting position.⁵ The only difference between the Gufoni maneuver for geotropic HSCC BPPV and for ageotropic HSCC BPPV is the side on which the patient is laid down from the seated position. However, the Gufoni maneuver for ageotropic HSCC BPPV has been performed differently depending on the clinicians. Although the patient's head was turned 45° downwards after being laid down on the affected side in some studies,⁵⁻⁷ the patient's head was turned 45° upwards after being laid down on the affected side in other studies.⁸⁻¹¹ The treatment result of the maneuver with head turned 45° downwards was comparable to that of the maneuver with head turned 45° upwards.^{7,8} The purpose of this prospective study was to examine the immediate and short-term treatment effects of the Gufoni maneuver with the head turned 45° downwards (original Gufoni maneuver) and with the head turned 45° upwards (the Appiani maneuver) in 25 consecutive patients with ageotropic HSCC BPPV.

2 | PATIENTS AND METHODS

2.1 | Subjects

We enrolled 25 consecutive patients diagnosed with ageotropic HSCC BPPV, who visited the outpatient clinic or emergency room of Konkuk University Medical Center, Seoul, Korea, between March 2018 and August 2018. The inclusion criteria for this study were as follows: (a) Complaining of vertigo associated with head motion, (b) Direction-changing horizontal nystagmus toward the uppermost ear (ageotropic nystagmus) in the supine head roll test. The exclusion criteria were as follows: (a) Otologic symptoms suggesting other labyrinthine diseases, (b) Recent history of labyrinthine disorders including sudden sensorineural hearing loss, vestibular neuritis, and Meniere's disease, or disorders of the central nervous system, (c) BPPV patients

with multiple canal involvement and those with ageotropic HSCC BPPV who showed a transition from other subtypes of BPPV.

All patients underwent routine neurologic examinations and neuro-otologic examinations for spontaneous and gaze-evoked nystagmus, horizontal and vertical smooth pursuit and saccades, limb ataxia, and balance function. No focal neurologic deficit was detected in the initial and two follow-up visits of the patients. A written informed consent was obtained from all participants. This study was approved by the Institutional Review Board (KUH-1110069).

2.2 | Diagnosis of ageotropic HSCC BPPV and lateralization

A supine roll test was conducted to diagnose ageotropic HSCC BPPV. In the supine position, the patient's head was turned to the right and left sides. Ageotropic nystagmus was observed without fixation using a video Frenzel goggles system (SLMED, Seoul, Korea). The patients also underwent bilateral Dix-Hallpike tests and a straight head-hanging test to exclude BPPV involving the posterior or anterior semicircular canal. According to Ewald's second law, the induced nystagmus was stronger when the head was turned to the healthy side.¹² When the nystagmus intensity was similar on both sides in the supine roll test, a bow and lean test or identification of the null plane were utilized to determine the affected side.¹³ The bowing nystagmus mostly beats toward the contralesional side, and the leaning nystagmus mostly beats toward the ipsilesional side. A null plane, at which the nystagmus ceases, is mostly identified on the ipsilesional side.

2.3 | Treatment maneuvers and evaluation of the treatment efficacy

We attempted to examine the immediate and short-term treatment effects of the Gufoni and Appiani maneuvers without comparing the treatment efficacies between them. A therapeutic maneuver was randomly selected using a computerized random number function in Microsoft Excel. The Gufoni maneuver was performed as follows⁵⁻⁷: (a) the patient was seated in the center of the examination table (Figure 1A-1); (b) the patient was briskly brought down on the affected side (Figure 1A-2); (c) the head was then quickly turned downwards at 45° and held for 2 to 3 minutes in that position (Figure 1A-3); (d) finally, the patient was returned to the starting position (Figure 1A-4). The Appiani maneuver was performed as follows¹⁴: (a) the patient was seated in the center of the examination table (Figure 1B-1); (b) the patient was quickly moved into a side-lying position on the affected side and kept in that position for 1 minute (Figure 1B-2); (c) the head was then quickly turned upwards at 45° and held for 2 minutes in that position (Figure 1B-3); (d) finally, the patient was returned to the starting position (Figure 1B-4). The patients were blinded to the treatment they received. The immediate treatment response was evaluated by the supine roll test 30 minutes after a single maneuver. Successful treatment was defined as the

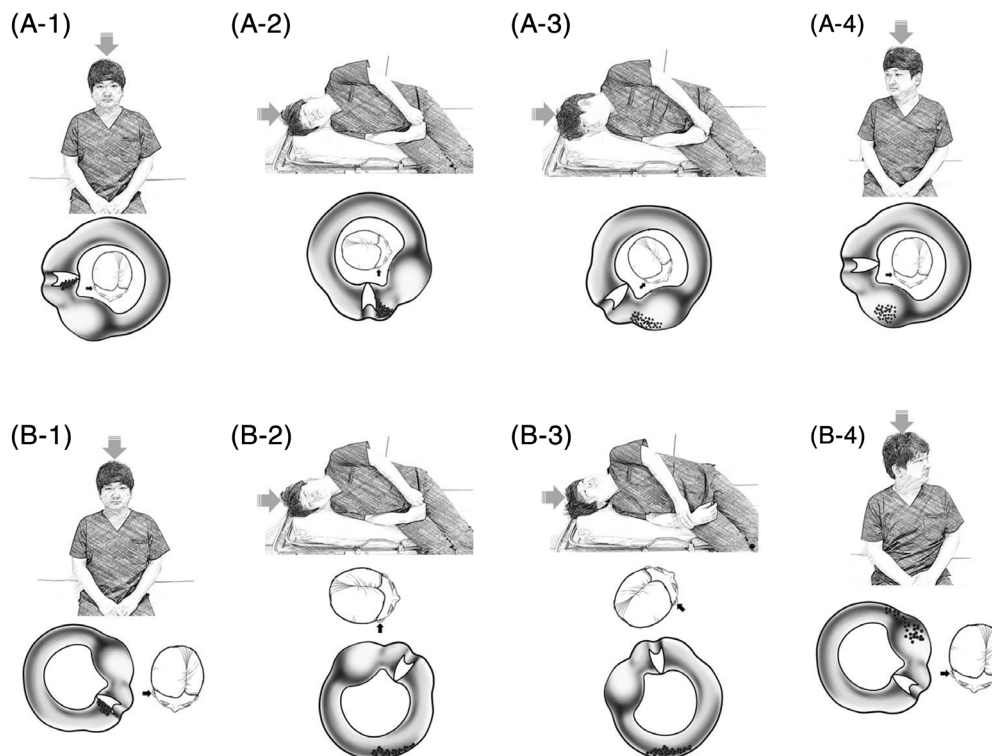


FIGURE 1 Repositioning maneuvers to treat a patient with right-sided ageotropic horizontal semicircular canal (HSCC) BPPV. A, The Gufoni maneuver. The patient is seated in the center of the examination table (A-1). The patient is quickly brought down on the affected side (A-2). The patient's head is quickly turned downwards by 45° and held for 2 to 3 minutes in this position (A-3). The patient is returned to the starting position (A-4). In the lower panels, the movement of the right (small black arrow) HSCC (viewed from the top, large gray arrow in the upper panels) is represented, and the supposed movement and detachment of the otolithic particles from the cupula is shown (adapted from Casani et al⁶). B, The Appiani maneuver. The patient is seated in the center of the examination table (B-1). The patient is quickly moved into a side-lying position on the affected side and kept in this position for 1 minute (B-2). The head is then quickly turned upwards by 45° and held for 2 minutes in this position (B-3). Finally, the patient is returned to the starting position (B-4). In the lower panels, the movement of the right (small black arrow) HSCC (viewed from the top, large gray arrow in the upper panels) is represented, and the supposed movement and detachment of the otolithic particles from the cupula is shown (adapted from Appiani et al¹⁴).

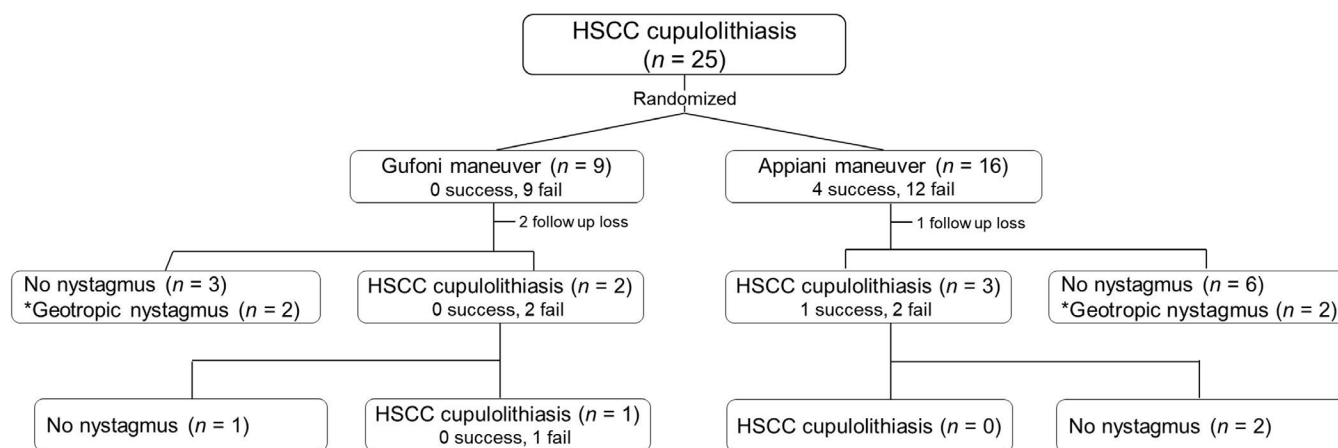


FIGURE 2 A summary of the treatment results. *The observed geotropic nystagmus showed a prolonged duration of more than 2 minutes. HSCC, horizontal semicircular canal

resolution of positional nystagmus or transformation to transient geotropic nystagmus. When the first treatment maneuver was unsuccessful, the patient again received the previously applied maneuver. If the

second treatment maneuver was also unsuccessful, it was considered a treatment failure. Patients with treatment failure were arranged for a follow-up visit 1 to 4 days later. The patients who showed treatment

TABLE 1 Demographic and clinical characteristics (n = 25)

	Gufoni maneuver (n = 9)	Appiani maneuver (n = 16)	P value
Age, mean ± SD	53.3 ± 11.9	50.3 ± 14.1	.607
Sex, male:female	5:4	3:13	.087
Affected side, right:left	4:5	9:7	.688
Duration of vertigo, days	2.56 ± 1.33	2.19 ± 0.98	.559

failure at the first follow-up, again received the same treatment maneuver, and were scheduled for the second follow-up. The mean period from the first treatment to the first follow-up and the first follow-up to the second follow-up was 3.2 and 3.5 days, respectively. We did not reassess the patients who showed a successful response (Figure 2). The patients did not receive any post-treatment restrictive instructions.

2.4 | Statistical analysis

Mann-Whitney *U* test was used to assess the differences of age and mean symptom duration between Gufoni and Appiani maneuver groups. Fisher's exact test was used to assess the differences of sex and affected side ratio between the two groups. All statistical analyses were performed using SPSS version 22.0 (IBM, Armonk, New York).

3 | RESULTS

3.1 | Demographic characteristics

Selected demographic characteristics of the patients are summarized in Table 1. Twenty-five patients with ageotropic HSCC BPPV were enrolled and randomly assigned to the Gufoni (n = 9) or the Appiani maneuver (n = 16). The mean age was 53.3 years in the Gufoni maneuver group and 50.3 years in the Appiani maneuver group, which was not significantly different ($P = .607$, Mann-Whitney *U* test). The male-female ratio was 5:4 in the Gufoni maneuver group and 3:13 in the Appiani maneuver group, which was not significantly different ($P = .087$, Fisher's exact test). The affected side was the right side in 4 (44%) of 9 patients in the Gufoni maneuver group, and 9 (56%) of 16 patients in the Appiani maneuver group, which was not significantly different ($P = .688$, Fisher's exact test). The mean symptom duration until the initial assessment was 2.56 days in the Gufoni maneuver group and 2.19 days in the Appiani maneuver group, which was not significantly different ($P = .559$, Mann-Whitney *U* test).

3.2 | Immediate and short-term treatment efficacy

In nine patients who were treated with the Gufoni maneuver, the immediate treatment response was not successful in any of the patients (Table 2; Figure 2). Two patients did not come to the hospital for the first follow-up, and seven patients underwent a positional

TABLE 2 Treatment results of Gufoni and Appiani maneuver

	Gufoni maneuver (n = 9)	Appiani maneuver (n = 16)
First day (immediate response)		
Success rate	0 (of 9, 0%)	4 (of 16, 25.0%)
Ageotropic nystagmus	9 (of 9, 100%)	12 (of 16, 75.0%)
First follow-up		
Follow-up loss	2	1
Spontaneous resolution	5 (of 7, 71.4%)	8 (of 11, 72.7%)
Success rate	0 (of 2, 0%)	1 (of 3, 33.3%)
Ageotropic nystagmus	2 (of 2, 100%)	2 (of 3, 66.7%)
Second follow-up		
Follow-up loss	0	0
Spontaneous resolution	1 (of 2, 50.0%)	2 (of 2, 100%)
Success rate	0 (of 1, 0%)	NA
Ageotropic nystagmus	1 (of 1, 100%)	NA

Abbreviation: NA, not applicable.

nystagmus test. Ageotropic nystagmus during the supine roll test was not observed in five of seven patients (Table 2), of whom three showed no nystagmus and two showed a weak geotropic nystagmus over a prolonged duration of 2 minutes (Figure 2; Video S1). Two patients, who exhibited ageotropic nystagmus, were treated with the Gufoni maneuver at the first follow-up, which was not successful in any of the two patients (Table 2; Figure 2). On the second follow-up, one patient showed no nystagmus and the other patient still showed ageotropic nystagmus. The Gufoni maneuver was conducted in the patient with ageotropic nystagmus, which was not successful (Table 2; Figure 2).

In 16 patients who were treated with the Appiani maneuver, the immediate treatment response was successful in four patients (Table 2; Figure 2). One patient did not come to the hospital for the first follow-up, and 11 patients underwent a positional nystagmus test. Ageotropic nystagmus was not observed during a supine roll test in 8 of 11 patients (Table 2), of whom six showed no nystagmus and two patients showed ipsicanal conversion from ageotropic to weak geotropic nystagmus over a prolonged duration of 2 minutes (Figure 2). Three patients, who exhibited ageotropic nystagmus, were

treated with the Appiani maneuver at the first follow-up, which was not successful in two patients (Table 2; Figure 2). On the second follow-up, both the patients showed no nystagmus (Table 2; Figure 2).

4 | DISCUSSION

The present study demonstrated that the immediate resolution rate of positional vertigo and nystagmus after the Gufoni or Appiani maneuver was only 16% (4 of 25 patients with ageotropic HSCC BPPV), which is lower than that reported in previous studies.^{5-10,14-16} Physical maneuvers for HSCC cupulolithiasis are aimed at detaching the otolithic debris, which could be attached either on the utricular or canal side of the cupula. When the otolithic debris is attached to the utricular side of the cupula, otolithic detachment results in immediate resolution of positional vertigo and nystagmus. Gufoni et al proposed a repositioning maneuver to detach the otolithic adhesion on the utricular side using gravity and inertia of the particles,^{5,7} which was also called a modified Semont maneuver later (Figure 1A).^{6,15} The quick movement from the seated position to lateral decubitus on the affected side, followed by a subsequent 45° downward head rotation, would displace otolith debris into the utricle (Figure 1A). Vannucchi et al described that the ampulla is in a vertical plane to favor movement of debris in the third step of Gufoni maneuver (45° downward head-turn and hold for 2-3 minutes).¹⁷ However, although it is currently believed that the axis of HSCC cupula is oriented in a medial to lateral direction at an angle of 30° from the sagittal plane,^{13,18} they seemingly assumed that the cupula axis was oriented in a lateral to medial direction at an angle of 90° from the sagittal plane, as shown in Figure 1A.⁵⁻⁷ From the present anatomical point of view, it is questionable whether the 2 to 3 minutes wait in the third step of Gufoni maneuver help the utricular side debris enter the utricle.

The present study showed that immediate resolution of ageotropic HSCC BPPV was not achieved in any patient after the Gufoni maneuver, although effectiveness of the Gufoni maneuver in ageotropic HSCC BPPV has been reported in several previous studies (success rate: ranging 20.2%-81.3%).¹⁹ However, caution should be taken when comparing the results among different studies. Because ageotropic HSCC BPPV may include various pathophysiologic types according to the location of otoconial debris (canalithiasis of short arm/anterior part of long arm or cupulolithiasis of utricular/canal side debris), the efficacy of the Gufoni maneuver also may vary according to the pathophysiologic types. In the present study, all 25 patients initially showed persistent ageotropic nystagmus on the supine roll test, which is suggesting HSCC cupulolithiasis (rather than canalithiasis) as a causable mechanism. The second step (lies down suddenly on affected side) of the Gufoni maneuver may detach the canal side debris from the cupula resulting in transformation of the ageotropic HSCC BPPV into geotropic form. However, if this process fails, the subsequent steps of the Gufoni maneuver seem to be of little help in resolving the canal side debris. Therefore, if our study coincidentally includes more patients with canal side cupulolithiasis due to the small

sample size, it is likely that the immediate treatment response of Gufoni maneuver would be lower than expected.

In 2005, Vannucchi et al reported that, in 43 patients with ageotropic HSCC BPPV, 5 (11.6%) patients showed symptom free after 1 session of Gufoni maneuver, whereas 28 (65.1%) patients showed nystagmus switching into geotropic form.¹⁷ However, the authors only included patients with transient (not persistent) ageotropic nystagmus, meaning that most of them were likely due to canalithiasis mechanism. Their high nystagmus switching rate (65.1%) may be attributed to this canalithiasis dominant patients characteristics. In the second step (lies down suddenly on affected side) of the Gufoni maneuver, the vector of gravitational force may induce the debris from the ampulla toward the posterior arm of the LSCC, resulting in nystagmus switching from ageotropic into geotropic form.¹⁷ As will be described next, what makes this process more efficient seems to be the third step of the Appiani maneuver (brisk head-turn 45° upward).

The heterogeneity of diagnostic and treatment protocols could lead to discrepancies in outcomes between different studies. In 2002, Casani et al reported that, in the initial 25 patients with ageotropic HSCC BPPV, 5 (20%) patients showed nystagmus switching into geotropic form while performing the diagnostic procedure, and the remaining 20 patients underwent a nystagmus switching procedure (rapid 180° head-turn toward healthy side) often up to four times.⁶ During this procedure, nine patients showed successful nystagmus switching into geotropic form, and two patients became symptom free. Finally, remaining nine patients underwent Gufoni maneuver, achieving resolution in four (44.4%) patients after one session of the Gufoni maneuver, and resolution in one patient after two sessions of the same maneuver, and another one patient showed nystagmus switching into geotropic form. Because they selected patients who did not respond at the preceding nystagmus switching attempts, patients with canal side cupulolithiasis or anterior arm canalithiasis were likely to be excluded for undergoing the Gufoni maneuver, and this may lead to seemingly higher response rate of Gufoni maneuver due to utricular side debris dominant patient characteristics. Similarly, repeated supine head roll maneuver prior to performing a Gufoni maneuver may induce nystagmus switching into geotropic form, affecting the pathophysiologic characteristics of patients participating in the following Gufoni maneuver.^{17,20}

On the other hand, Appiani et al proposed a repositioning maneuver to treat patients with an ageotropic variant of HSCC BPPV based on the hypothesis that the syndrome is caused by the presence of free-floating otolith particles inside the endolymph of the anterior arm of the HSCC (Figure 1B).¹⁴ The quick movement from the seated position to lateral decubitus on the affected side, followed by a subsequent 45° upward head rotation, would displace otolith debris into the posterior arm of the HSCC (Figure 1B). A successful maneuver results in the transformation of an ageotropic variant of HSCC BPPV into a geotropic variant. Since the introduction of these maneuvers, there has been confusion regarding the naming and methods for performing the maneuvers. For example, although Gufoni et al and Mandala et al treated ageotropic HSCC BPPV patients with the

Gufoni maneuver (45° downward head-turn),^{5,7} Casani et al and Oh et al used the same maneuver to treat ageotropic HSCC BPPV under the name of modified Semont maneuver.^{6,15} On the other hand, the Appiani maneuver (45° upward head-turn) has been conducted to treat ageotropic HSCC BPPV under the name of Gufoni maneuver in many studies.^{8-11,16} In addition to the confusion in naming the maneuvers, the duration of maintaining each position during the maneuver varied according to the studies, and there have been no studies specifying the minimum speed required to lie down or rotate the head at each step of the maneuver. Since each step of the Gufoni or Appiani maneuver requires sufficient inertial force to detach or move the otoconia, between-investigator heterogeneity of performing the therapeutical procedures may affect the outcome.

Another interesting finding was that the patients, who continued to show spontaneous resolution during the follow-up period, outnumbered the patients who showed resolution of BPPV immediately after the repositioning maneuvers (Table 2). Although it is difficult to determine whether repositioning maneuvers contributed to the spontaneous resolution of BPPV in the present study, it has been reported that the natural course of HSCC cupulolithiasis is truly short even without any treatment.^{21,22} Imai et al reported that the average period from the onset to natural remission of positional vertigo in HSCC cupulolithiasis was 13 days, and hypothesized that the head movements in daily life cause the otolithic debris to fall off from the cupula.²² Shim et al reported that the mean period between symptom onset and vertigo remission was 3.7 days, and the mean period from the initial diagnosis to the disappearance of positional nystagmus in HSCC cupulolithiasis was 4.4 days in HSCC cupulolithiasis.²¹ They observed much shorter natural symptom remission of ageotropic HSCC BPPV than that of geotropic form. Therefore, they speculated that the utricle-side cupulolithiasis, rather than either the canal-side cupulolithiasis or anterior arm canalithiasis, is the predominant pathology underlying HSCC cupulolithiasis because the pathway from the utricle-side of the cupula to the utricle is much shorter than that from the canal side of the cupula to the utricle. However, their findings were in contrast to the previous reports,^{6,23,24} therefore, this speculation remains debatable. Considering all the above mentioned, the discrepancy of the outcome between different studies may be partly attributed to the difference in onset duration between the studies. The onset duration in our study was relatively shorter (2.56 ± 1.33 and 2.19 ± 0.98 days in the Gufoni and Appiani maneuver groups, respectively) compared to that in other study (ie, average 18 days, range: 2-52 days in Casani et al's study⁶). The spontaneous dissolution of otoconia over time may cause a better movement of otoconia from the anterior arm to the posterior arm of HSCC, or cause an easier detachment from the cupula, which lead to a better immediate response to the therapeutic maneuver. However, there is no objective evidence to support this speculation.

It has been recently assumed that, in addition to otoconial attachment on the HSCC cupula or free floating otoconia in the anterior arm of the HSCC, ageotropic positional nystagmus can also be evoked by other causes such as a slight change in the biochemical composition of the inner ear fluids.^{1,25} If a heavier cupula or lighter endolymph

occurs due to a change in the density of the cupula-endolymph system, it is expected that it will not respond well to the repositioning maneuver. Although it is reasonable to assume that these change in the density of cupula-endolymph system would affect all three semi-circular canals, horizontal nystagmus has been predominantly reported. The main reason has been speculated that the vertical and torsional components of nystagmus might be canceled each other.²⁶ This pathophysiologic perspective may be another possible explanation for the reason underlying the low immediate success rate of repositioning maneuvers and a high spontaneous resolution rate during the follow-up period. However, further investigation on whether spontaneous resolution is influenced by the previous repositioning maneuver is needed for the precise outcome measurement of the repositioning maneuver treatment in ageotropic HSCC BPPV.

This study has several limitations. Due to the small sample size, our results may be limited to be generalized. Moreover, some patients did not attend follow-up visits, limiting the reporting of short-term efficacy of the maneuvers. We think they probably did not visit the hospital because their symptoms were relieved. In addition, the risk for investigator bias introduced by a single investigator is another limitation of this study. Further study with a larger sample size and more controlled protocol is required in the future.

5 | CONCLUSION

This study showed that the immediate resolution rate of ageotropic HSCC BPPV after the Gufoni maneuver was very low compared to that of the Appiani maneuver, which may be attributed to the less effectiveness of the Gufoni maneuver against debris that often exists in the canal side of the cupula. The rate of spontaneous resolution during the follow-up period was higher than that of immediate resolution after the repositioning maneuvers, which may support the recently proposed hypothesis that ageotropic positional nystagmus can also be evoked by other causes other than the otolithic attachment on the cupula, such as a slight change in the biochemical composition of the inner ear fluids.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

AUTHOR CONTRIBUTIONS

Chang-Hee Kim: Conceptualization and project administration. **Jiyeon Lee, Dong-Han Lee, Haemin Noh, Jung Eun Shin, and Chang-Hee Kim:** Data curation and writing—review & editing. **Jiyeon Lee, Dong-Han Lee, and Chang-Hee Kim:** Formal analysis, methodology, visualization, and writing—original draft.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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