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ORIGINAL RESEARCH

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Clinical impact of hyperbaric oxygen therapy combined with steroid treatment for sudden sensorineural hearing loss: A case–control study

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Abstract

Objectives: The aim of present study was to evaluate the clinical efficacy of hyperbaric oxygen therapy (HBOT) as a primary therapy combined with standard systemic corticosteroid treatment for sudden sensorineural hearing loss (SSNHL) compared to treatment without the use of HBOT (non-HBOT) through clinical data and advanced analytical approaches.

Study Design: Case–control study.

Methods: Conducted across three Japanese medical centers involving 298 SSNHL patients diagnosed between 2020 and 2023. Inclusion criteria encompassed first onset and treatment, WHO grade 3 or 4 initial hearing impairment, receipt of systemic corticosteroid therapy within 14 days of symptom onset, and initiation of HBOT within the same timeframe for the case group. The primary outcome measure was the difference in hearing improvement (mean hearing level in decibels, dB) between the two groups, assessed by pure-tone audiometry at baseline and 3 months post-treatment, using the inverse probability of treatment weighting (IPTW) method adjusted for covariate differences.

Results: The study included 67 patients in the HBOT group and 68 in the non-HBOT group. The HBOT group exhibited significantly greater hearing improvement (IPTW-adjusted difference: 7.6 dB, 95% CI 0.4–14.7; $p = 0.038$). Patients without vertigo in the HBOT group demonstrated substantial hearing improvement (11.5 dB, 95% CI

2.3–20.6; $p = 0.014$), whereas those with vertigo showed no significant improvement (−1.8 dB, 95% CI −11.8–8.3; $p = 0.729$). The HBOT group also had a significantly higher association with complete recovery (IPTW-adjusted odds ratio: 2.57, 95% CI 1.13–5.85; $p = 0.025$).

Conclusion: In SSHNL, HBOT combination therapy yielded slightly but significantly improved hearing outcomes compared to non-HBOT treatment.

Level of Evidence: 4.

KEYWORDS

case–control study, hyperbaric oxygen therapy, prednisolone, sudden sensorineural hearing loss

1 | INTRODUCTION

Sudden sensorineural hearing loss (SSNHL) is defined as a sensorineural hearing loss of ≥30 decibels (dB) affecting at least three consecutive frequencies and occurring within a 72-h window with unknown cause.[1] Treatment modalities for SSNHL have traditionally encompassed steroids, anti-inflammatory agents, vasodilators, diuretics, plasma expanders, anticoagulants, and antivirals.[2] However, the effectiveness of these treatments has not been conclusively demonstrated in large-scale randomized trials or meta-analyses.[2,3]

In the late 1970s, circulatory disturbances were proposed as a primary pathophysiological mechanism underlying SSNHL,[4] and hyperbaric oxygen therapy (HBOT) became a comprehensive treatment option for SSNHL. The efficacy of HBOT, particularly when initiated within 2 weeks of SSNHL onset, has been variably reported in the literature.[5–7] Although a meta-analysis indicated a significant improvement in hearing outcomes for individuals with SSNHL treated with HBOT, the clinical relevance of these findings has been questioned due to limited patient numbers, methodological limitations, and inconsistent reporting practices.[8] Consequently, HBOT is currently classified as a Grade B treatment recommendation in the United States guidelines for SSNHL.[1] Recent systematic reviews have also underscored the potential benefits of HBOT, particularly as part of combination therapy, suggesting a mean absolute hearing improvement of ∼10 dB with HBOT compared to treatments excluding HBOT.[9,10]

This additional evidence has heightened interest in HBOT, prompting the need to ascertain its clinical effectiveness in the treatment of SSNHL. Therefore, we conducted a case–control study using clinical data and a new statistical method to evaluate the efficacy of HBOT as a primary treatment for SSNHL compared with non-HBOT.

2 | MATERIALS AND METHODS

2.1 | Participants

Participants for the case group were recruited from Toyota Kosei Hospital, Aichi, Japan, between January 2020 and March 2023. The control group consisted of individuals selected during the same period from Nagoya City University Hospital and the Japanese Red Cross Aichi Medical Center Nagoya Daini Hospital, both located in Aichi, Japan.

This study focused on patients diagnosed and treated for SSNHL, as documented in their electronic medical records. All participants met the following inclusion criteria: (i) initial episode of SSNHL and commencement of first-line therapy; (ii) unilateral hearing loss of ≥30 dB affecting at least three consecutive frequencies within 72 h of onset; (iii) WHO grade 3 or 4 hearing impairment at initial assessment[11]; (iv) initiation of prednisolone treatment within 14 days of symptom onset, with an initial dose of ≥60 mg/day; (v) for non-resolved cases, auditory follow-up conducted 3 months post-initial visit; (vi) exclusion of cases that meet the diagnostic criteria for Meniere's disease[12] or ALHL,[13] patients with detected infectious or autoimmune diseases and other etiologies such as organic pathologies like acoustic neuroma. In the case group, HBOT was administered within 14 days of symptom onset. This is in accordance with the definition of HBOT as initial treatment in AAO-HNS.[1] The case group was thus defined as the HBOT group, and the control group as the non-HBOT group. Ethical approval for this study was obtained from the Institutional Review Boards of each participating institution, and the research adhered to the principles of the Declaration of Helsinki. (Approval number: 60-23-0099). This study follows STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) recommendations.[14]

As illustrated in Figure 1, a total of 140 patients were initially included in the HBOT group, and 158 in the non-HBOT group, all diagnosed with SSNHL. Exclusions from the HBOT group comprised 73 patients: 34 due to grade 1–2 hearing loss, 24 for inadequate follow-up, 4 for receiving prednisolone <60 mg, and 9 for not undergoing HBOT. In the non-HBOT group, 80 were excluded: 58 for grade 1–2 hearing loss, 4 for inadequate follow-up, and 18 for receiving prednisolone <60 mg. After applying these eligibility criteria, the final analysis included 67 patients in the HBOT group and 68 in the non-HBOT group.

2.2 | Treatment protocol and follow-up

Patients in both study groups received systemic prednisolone therapy, administered either orally or intravenously, with an initial dose of at

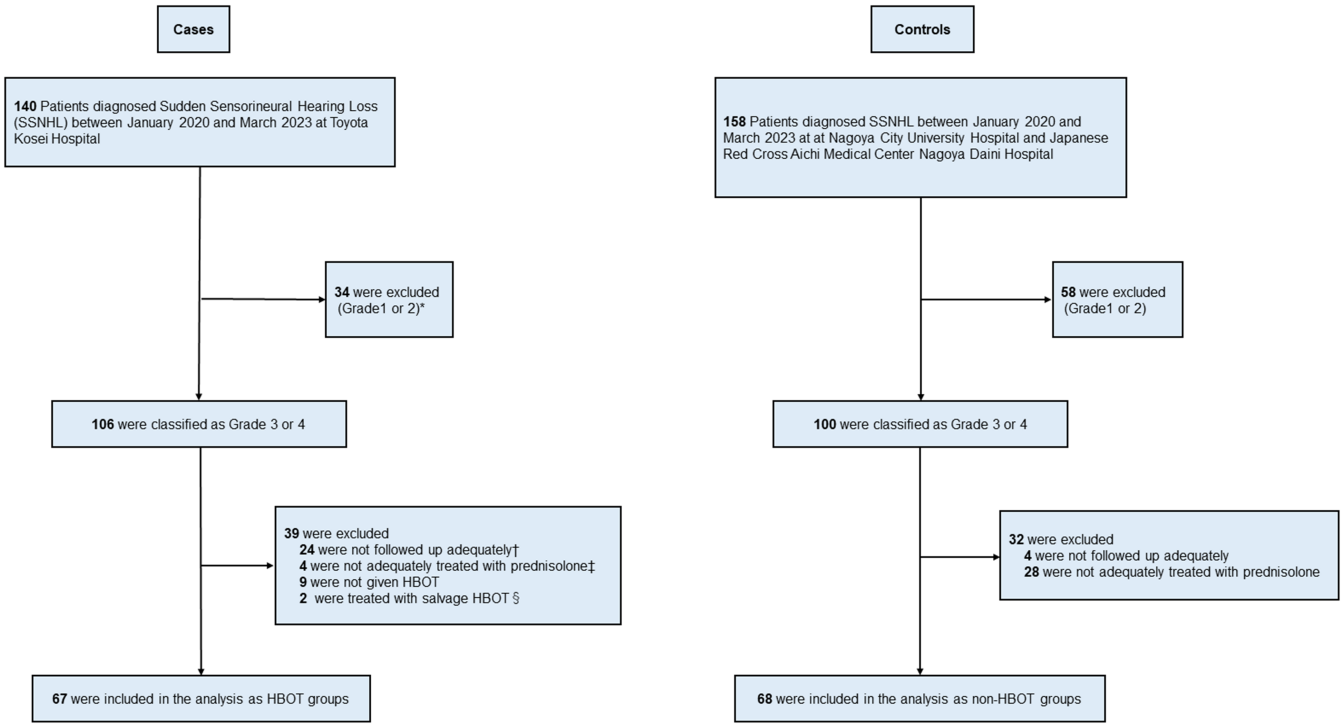

FIGURE 1 Flow chart of hyperbaric oxygen therapy (HBOT) group and non-HBOT group selection process.

least 60 mg/day, which was then gradually tapered. Additionally, the HBOT group underwent hyperbaric oxygen therapy (KHO-2000S, Kawasaki Engineering Co., Ltd.), delivered once daily from Monday to Friday, for a typical total of 10 sessions. The HBOT protocol involved an oxygen pressurization method using a Type 1 device, consisting of 10 min of pressurization, 60 min at 2 atmosphere absolute (ATA), and 10 min of decompression.

Concomitant treatments in both groups included intratympanic steroid injections (ITSI) and intravenous prostaglandin E1 (PGE1). ITSI, primarily combined with prednisolone and HBOT, was indicated for patients with grade 4 hearing loss, except when declined by the patient. This treatment involved four injections of dexamethasone (1.65 mg/0.5 mL). Intravenous PGE1, primarily in patients with diabetes or vertigo, was administered as alprostadil at a dosage of 10 μg/2 mL in 100 mL saline, daily for 7 days.

Hearing evaluation was conducted through pure-tone audiometry performed before initiating treatment and 3 months after the start of treatment. Pure-tone audiometry assessed threshold values at 125, 250, 500, 1000, 2000, 4000, and 8000 Hz. The pure-tone average (PTA) was calculated as the mean of the thresholds at four frequencies (500, 1000, 2000, and 4000 Hz). Thresholds that could not be measured due to the limitations of the audiometric equipment were recorded as "scaled-out" values. The hearing level after 3 months of treatment was considered the final hearing threshold. Hearing recovery was categorized into the following three groups: complete recovery (CR), defined as a final hearing threshold within 10 dB of the unaffected ear; hearing improvement ≥10 dB; and no improvement, characterized by hearing improvement less than 10 dB.[15] Hearing improvement was calculated as the difference between the initial hearing threshold and the final hearing threshold.

Patient data were obtained via chart reviews. Vertigo was defined as spontaneous vertigo in the presence of directionally fixed horizontal or horizontal-torsional nystagmus. The duration from the onset of hearing loss to the initiation of prednisolone treatment in both groups was recorded as the number of days to treatment initiation.

2.3 | Statistical methods

In this study, our primary objective was to assess the difference in hearing improvement between the HBOT group and the non-HBOT group. This improvement was quantified as the change in the mean hearing level, measured in dB. Secondary outcomes included the analysis of hearing improvement stratified by frequency ranges (125, 250, 500, 1000, 2000, 4000, 8000 Hz) and various subgroups. These subgroups encompassed factors such as sex, age, comorbidities (diabetes mellitus, hypertension), presence of vertigo, WHO's Grades of hearing impairment at the initial assessment, and combination therapy (ITSI or PGE1). Additionally, to evaluate whether HBOT is associated with higher complete hearing recovery (CR) or higher hearing improvement of at least 10 dB, we calculated the odds ratios (ORs) and 95% confidence intervals (95% CIs) estimated by unconditional logistic regression models.

The primary exposure of interest in this study was HBOT. To estimate treatment effects, we utilized propensity scores (PS) to adjust for differences between patients in the HBOT and non-HBOT groups.

This adjustment was achieved through inverse probability of treatment weighting (IPTW) methods.[16,17] The aim was to estimate the average treatment effect (ATE), which in this context refers to the differential impact on hearing improvement when shifting the entire population from an untreated to a treated status.

The IPTW method enabled the creation of a weighted cohort with similar measured characteristics, as determined by PS. This approach facilitated the inclusion of all patients without necessitating patient matching. To estimate PS, a multivariable logistic regression model was employed, incorporating various potential confounders, which included: sex (male, female), age (<60, ≥60), initial PTA at baseline (continuous variable), presence of vertigo (yes, no), comorbidities [diabetes mellitus (yes, no), hypertension (yes, no)], prednisolone dosage (continuous variable), combination therapy (ITSI or PGE1, yes, no), and days to start of treatment (continuous variable).

Patients in the HBOT group were assigned a weight of 1/PS, whereas those in the non-HBOT group received a weight of 1/(1 − PS). The balance of covariates was assessed using standardized differences, revealing most to be under a 10% difference. However, for several covariates where the imbalance exceeded 10% (as shown in Figure S1), a stratified analysis was conducted to mitigate bias related to each covariate.

To assess the association between hearing recovery (CR and ≥10 dB) and treatment group, we applied ORs and 95% CIs estimated by unconditional logistic regression models adjusted by IPTW methods. Additionally, as a sensitivity analysis, we compared the treatment effects of patients treated with PSL alone and HBOT combined with PSL alone.

In assessing the distribution of background characteristics, *p* values for continuous variables—including age, initiation of treatment, initial pure tone audiometry (PTA) results, PTA results for the unaffected side, prednisolone dosage, and the number of hyperbaric oxygen therapy (HBOT) sessions—were calculated using the Mann–Whitney *U* test. Meanwhile, *p* values for categorical variables—such as sex, presence of comorbidities, vertigo symptoms, initial PTA grade, and types of treatment interventions (intratympanic steroid injection (ITSI) and prostaglandin E1 (PGE1) administration)—were determined using the Chi-square test. All analyses were performed using Stata SE statistical software (version 16; Stata Corp LLC, College Station, Texas). Two-sided *p* values <0.05 were considered to indicate statistical significance.

3 | RESULTS

3.1 | Participant characteristics

Participant demographics and baseline characteristics are summarized in Table 1. Age and comorbidities including diabetes mellitus and hypertension, as well as PTA and unaffected-side PTA, were comparable between the HBOT and non-HBOT groups. Specifically, there were no significant differences in the initial PTA between the HBOT group (90.8 ± 14.5 dB) and the non-HBOT group (89.5 ± 16.2 dB; $p = 0.608$). Compared to the non-HBOT group, the HBOT group demonstrated a higher prevalence of males (55% in HBOT groups and 38% in non-HBOT) and a lower incidence of vertigo (22% in HBOT groups and 40% in non-HBOT). Treatment modalities varied, with ITSI being more common in the HBOT group (66% in HBOT vs. 21% in non-HBOT), whereas higher doses of prednisolone (67.1 mg in HBOT vs. 60.1 mg in non-HBOT) and PGE1 (62% in HBOT vs. 1% in non-HBOT) were noted in the non-HBOT group.

TABLE 1 Patient characteristics.

	HBOT group ($n = 67$)	Non-HBOT group ($n = 68$)	*p*-value*
Age, y	56.9 ± 15.6	59.2 ± 16.2	0.343
Sex——no. (%)			
Male	37 (55)	26 (38)	
Female	30 (45)	42 (62)	0.048
Start of treatment, days[a]	3.9 ± 3.2	2.9 ± 3.2	0.019
Comorbidities——no. (%)			
Diabetes mellitus	21 (31)	18 (26)	0.532
Hypertension	19 (28)	15 (22)	0.399
Vertigo——no. (%)[b]	15 (22)	27 (40)	0.030
Initial PTA, dB			
Average[c]	90.8 ± 14.5	89.5 ± 16.2	0.608
Grade——no. (%)[d]			
3 (61–80 dB)	17 (25)	21 (31)	
4 (81 dB-)	50 (75)	47 (69)	0.477
Unaffected side PTA, dB			
Average	24.0 ± 19.3	22.1 ± 16.5	0.824
Treatment			
Prednisolone dose	60.1 ± 1.2	67.1 ± 13.7	<0.001
Number of HBOT sessions	11.6 ± 8.2	N.A.	
Intratympanic steroid injection	44 (66)	14 (21)	<0.001
Prostaglandin E1	1 (1)	42 (62)	<0.001

Note: Values for continuous variables are presented as mean ± SD.
Abbreviation: HBOT, hyperbaric oxygen therapy.
**p* values for continuous variables were calculated using the Mann–Whitney *U* test, and *p* values for categorical variables were calculated using the Chi-square test.
[a]Start of treatment was defined as the date of initiation of oral or intravenous prednisolone treatment.
[b]Vertigo was defined as nystagmus findings on examination.
[c]The pure-tone average (PTA) was defined as the mean value of the measurements taken at the 500, 1000, 2000, and 4000-Hz frequencies.
[d]Grade was based on WHO's Grades of hearing impairment.

3.2 | Hearing improvement

Post-treatment PTA average was 49.7 ± 28.5 dB in the HBOT group and 56.7 ± 27.2 dB in the non-HBOT group. The average hearing improvement was 41.1 dB (95% CI, 35.5–46.6) for the HBOT group

TABLE 2 The intergroup differences in hearing improvement.

	Hearing improvement				Hearing improvement of HBOT compared to non-HBOT					
	HBOT ($n = 67$)		Non-HBOT ($n = 68$)		Crude[a]			IPT weighted[b]		
	Mean (dB)	(95% CI)	Mean (dB)	(95% CI)	Mean (dB)	(95% CI)	*p*-value	Mean (dB)	(95% CI)	*p*-value
Average[c]	41.1	(35.5–46.6)	32.8	(27.6–37.9)	8.3	(0.8–15.8)	0.030	7.6	(0.4–14.7)	0.038
125 Hz	25.3	(20.5–30.1)	18.1	(13.1–23.0)	7.2	(0.4–14.0)	0.039	8.9	(3.0–14.6)	0.003
250 Hz	37.8	(31.9–43.8)	28.6	(22.4–34.8)	9.2	(0.7–17.8)	0.034	9.2	(1.2–17.1)	0.024
500 Hz	48.5	(42.4–54.6)	37.1	(31.1–43.1)	11.4	(2.9–19.9)	0.009	11.3	(2.7–19.9)	0.010
1000 Hz	44.7	(39.1–50.3)	36.3	(30.2–42.4)	8.4	(0.1–16.6)	0.046	7.1	(−1.8–15.9)	0.120
2000 Hz	37.0	(30.7–43.3)	31.3	(25.5–37.1)	5.7	(−2.8–14.2)	0.187	5.4	(−2.8–13.6)	0.195
4000 Hz	34.0	(27.7–40.4)	26.3	(21.0–31.4)	7.8	(−0.4–15.9)	0.061	6.5	(−1.0–13.9)	0.089
8000 Hz	20.1	(13.8–26.5)	16.5	(11.8–21.3)	3.6	(−4.2–11.5)	0.365	1.3	(−5.2–7.7)	0.700

Abbreviations: 95% CI, 95% Confidence Interval; HBOT, Hyperbaric oxygen therapy.
[a]The analysis was performed with a *t*-test without adjustment for confounding factors.
[b]IPT weighted refers to the inverse probability of treatment weighting (IPTW) method; adjusted for age, sex, baseline initial PTA average, vertigo, comorbidities, prednisolone dose, combination therapy, and the number of days to start treatment.
[c]Average was defined as the pure-tone average of 500, 1000, 2000, and 4000 Hz.

and 32.8 dB (95% CI, 27.6–37.9) for the non-HBOT group (left part of Table 2). The HBOT group showed a statistically significant improvement compared to the non-HBOT group with a mean difference of 8.3 dB (95% CI, 0.8–15.8; $p = 0.030$). Furthermore, even after adjustment by IPTW methods, hearing improvement of the HBOT group was significantly greater than the non-HBOT group with mean difference of 7.6 dB (95% CI, 0.4–14.7; $p = 0.038$, right part of Table 2 and Figure 2). When stratified by frequencies, the HBOT group had significantly greater hearing improvement compared to the non-HBOT group at 125, 250 and 500 Hz [125 Hz: 8.9 dB (95% CI, 3.0–14.6; $p = 0.003$), 250 Hz: 9.2 dB (95% CI, 1.2–17.1; $p = 0.024$), 500 Hz: 11.3 dB (95% CI, 2.7–19.9; $p = 0.010$), Figure 2]. Although the HBOT group tended to show better improvement in hearing from 1000 to 8000 Hz compared to the non-HBOT group, the difference did not reach statistical significance by the IPTW method.

3.3 | Stratification by confounders

When stratification was performed by clinical confounders, IPT-weighted hearing improvement tended to be consistently higher in the HBOT group compared to the non-HBOT group except with vertigo and hypertension (Figure 2B). This trend was even observed in the prednisolone-alone treatment group.

Regarding vertigo, patients without vertigo showed a significant hearing improvement of 11.5 dB (95% CI, 2.3–20.6; $p = 0.014$) in HBOT compared with the non-HBOT group. In contrast, patients with vertigo showed no difference in hearing improvement between the two groups (−1.8 dB; 95% CI, −11.8–8.3; $p = 0.729$). There was no difference between the two groups of patients with hypertension, either (−6.6 dB; 95% CI, −19.3–6.1; $p = 0.311$).

3.4 | Association between HBOT and CR/ hearing improvement of 10 dB or more

The detail of hearing improvement of each group is shown in Figure 3. The number of patients with CR was 29 (43.3%) in the HBOT group and 18 (26.5%) in the non-HBOT group (Figure 2C, and red bars in Figure 3). Compared with the non-HBOT group, the HBOT group was significantly associated with higher CR with an IPTW-adjusted OR of 2.57 (95% CI, 1.13–5.85; $p = 0.025$). Hearing improvement of 10 dB or more was observed in 61 (91.0%) patients in the HBOT group and 58 (85.3%) in the non-HBOT group (Figure 2C, and blue bars in Figure 3). The HBOT group showed a higher OR of hearing improvement of 10 dB or more compared to the non-HBOT group, however, statistical differences were not observed (IPTW-adjusted OR 2.12; 95% CI, 0.65–6.92, $p = 0.336$).

3.5 | Sensitivity analysis

As a sensitivity analysis, we compared the treatment effects between patients treated with HBOT plus PSL alone ($n = 22$) and non-HBOT receiving only PSL ($n = 20$). In the HBOT groups with PSL alone, the mean difference in hearing improvement compared to the group receiving PSL alone was 7.6 dB (95% CI, −3.6–18.9; $p = 0.184$, upper part of Table S2), following adjustment for the IPTW method. Consistent with the overall analysis, patients in the HBOT plus PSL group experienced hearing improvements at low frequencies (125, 250, and 500 Hz) and among those without vertigo, when compared to the non-HBOT receiving only PSL. These findings were observed regardless of statistical significance.

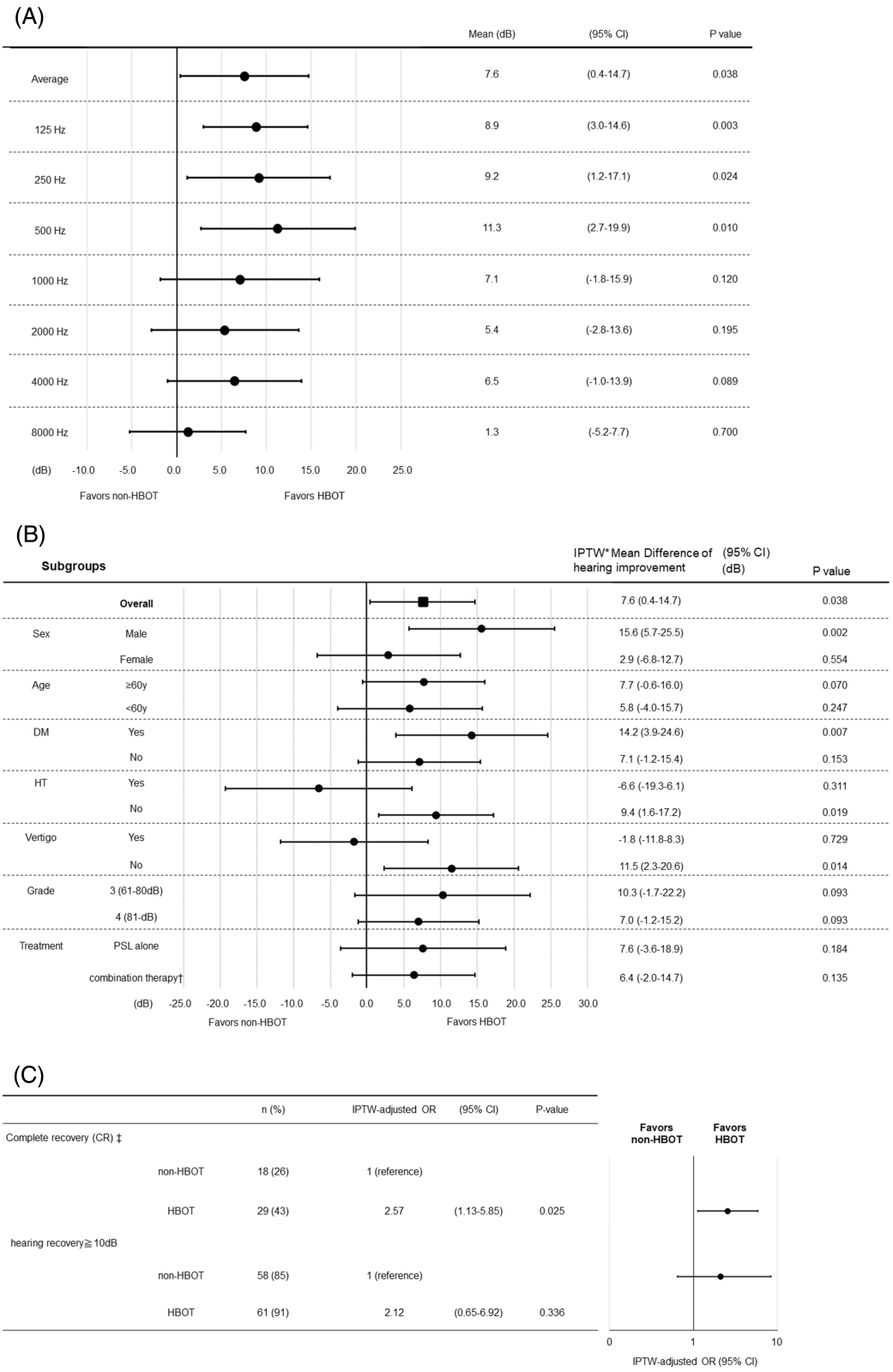

FIGURE 2 (A) The intergroup difference in hearing improvement of HBOT compared to non-HBOT, IPT weighted. (B) Subgroup analysis of hearing improvement of HBOT compared to non-HBOT. (C) The odds ratio of hearing recovery.

4 | DISCUSSION

This study demonstrated a 7.6 dB higher improvement in PTA in the HBOT group compared to the non-HBOT group, with statistical significance adjusted by the IPTW method. Notably, this improvement was more pronounced at lower frequencies and among patients without vertigo. To our knowledge, this is the first study assessing the impact of HBOT on SSNHL using the IPTW method.

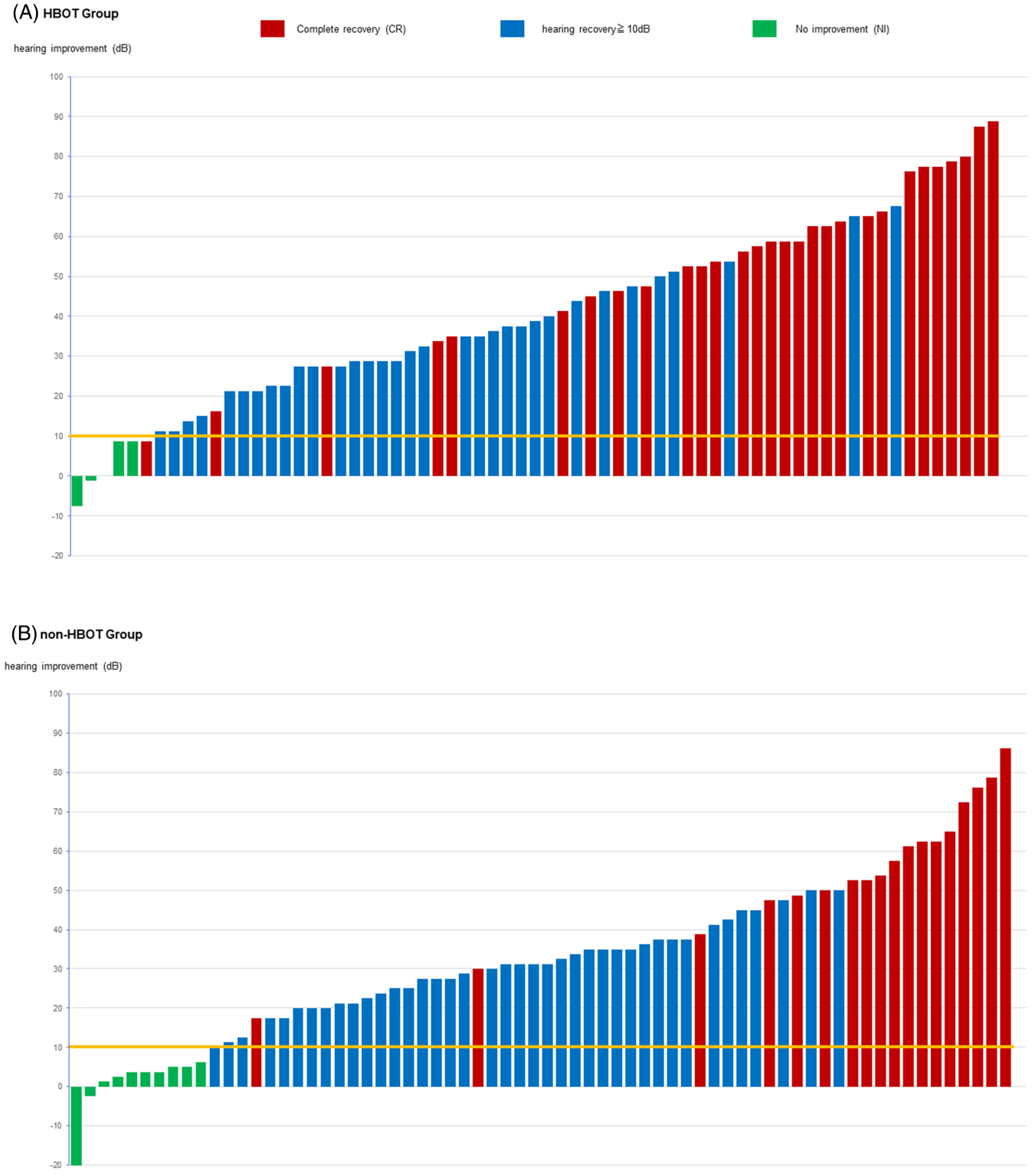

FIGURE 3 Waterfall plots show hearing improvement in the HBOT and non-HBOT groups.

Previous research into HBOT for SSNHL included 12 randomized controlled trials (RCTs),[5,6,15,18–26] and three meta-analyses.[8–10] A significant trial by Krajcovicova et al[5] reported an 11.5 dB improvement in hearing when HBOT supplemented pharmacotherapy as a first-line treatment for SSNHL. A meta-analysis by Joshua et al.,[10] encompassing three RCTs, found a significant hearing improvement of 10.3 dB (95% CI: 6.5–14.1 dB) in the HBOT group. Furthermore, another meta-analysis that evaluated 19 observational studies found that the HBOT group exhibited an average hearing improvement of 8.74 dB more than the non-HBOT group, along with an OR for CR of

1.61.[9] Moreover, despite its role as a salvage treatment, the Ajduk et al.[27] retrospective study on hyperbaric oxygen salvage therapy in SSNHL found an average hearing improvement of 7.4 dB at all frequencies (250–8000 Hz). The results of our study, demonstrating an average difference in hearing improvement of 7.6 dB and a higher CR rate with an OR of 2.57, are consistent with those previous findings, reinforcing the validity of our outcomes, although the clinical significance of the HBOT on SSNHL remains unclear. Further investigation is needed to determine the clinical relevance of HBOT combination therapy for SSNHL.

Our results that the effect of HBOT was limited to low-frequency ranges and patients without vertigo suggest a potential relationship between the efficacy of HBOT and specific types of ischemia within the auditory system in SSNHL. Although the etiology of SSNHL remains unclear to date, impaired circulation in the inner ear is a recognized contributing factor.[28–30] HBOT, by enhancing the oxygen partial pressure delivered to the inner ear, is theorized to mitigate ischemic damage and foster vascular recovery post-SSNHL.[31] Additionally, there has been conjecture regarding the potential for HBOT combination therapy to ameliorate hearing loss at lower frequencies.[6,32] Tange et al.[33] have noted that ischemia in the proper cochlear artery, which predominantly affects the apical turns of the cochlea, is likely to result in SSNHL at lower frequencies. In contrast, ischemia in the vestibulocochlear artery, impacting the saccule, posterior ampulla, and basal turn of the cochlea, tends to cause partial high-frequency hearing loss accompanied by vertigo.

Our hypothesis cautiously suggests that HBOT may have a potential for differential efficacy in treating ischemia affecting the proper cochlear artery compared to ischemia affecting the vestibulocochlear artery. This tentative suggestion is based on reports that the vestibulocochlear artery, which enters the basal cochlea which is responsible for processing high-frequency sounds, is particularly susceptible to ischemic damage.[34] Therefore, one may say that in patients experiencing high-frequency hearing loss or vertigo induced by basal vestibular dysfunction, the efficacy of HBOT appears to be limited. On the other hand, clinical experience seems to suggest that damage in the lower frequency region related to the proper cochlear artery tends to be treatable.[35] Given this background, it is hypothesized that in cases of SSNHL without vertigo, which are thought to primarily involve selective damage to the proper cochlear artery, the role of HBOT in enhancing blood oxygenation might provide specific therapeutic benefits. This hypothesis is grounded in the understanding that HBOT can increase dissolved oxygen in the blood,[31] potentially mitigating the effects of ischemia in the inner ear circulation. However, it is important to underscore that this hypothesis remains speculative and must be interpreted with caution. The complexity of SSNHL and the varied mechanisms underlying its pathogenesis necessitates a careful and measured approach, with further research required to substantiate any claims regarding the specific efficacy of HBOT in these contexts.

Regarding the number and duration of HBOT treatments, a common recommendation of the previous evidence indicates a minimum of 90 min of 2.0 ATA HBOT, administered either through 10 sessions of 90 min or 15 sessions of 60 min, for the treatment of patients with SSNHL.[10] Our treatment regimen, consisting of ten 60-min sessions of HBOT at 2.0 ATA, appears to be less intensive than protocols reported in previous studies. Further investigation is warranted to establish the optimal HBOT protocol.

This study boasts several methodological strengths, including the selection of control participants from the same regions and time frame as the cases, thereby bolstering internal validity, and the adherence of clinicians to institutional standards minimizing information bias. Furthermore, the extraction of cases and controls from the general treatment population underpins the study's external validity.

The limitation of the present study warrants mention. Firstly, disparities in patient backgrounds and treatment approaches were observed. A significantly higher proportion of patients in the non-HBOT group experienced vertigo, a recognized worse prognostic factor in a previous study,[36] implying that the hearing improvement observed in the non-HBOT group might have been affected. Additionally, it cannot be discounted that a significantly higher number of patients in the HBOT group received ITSI as combination therapy, potentially influencing the observed improvement in hearing within the HBOT group. Although we employed IPTW to adjust for these confounding factors, the balance achieved through IPTW was only modest. Moreover, IPTW can only account for known variables, leaving room for potential bias from unmeasured factors. Previous studies have suggested that ITSI may contribute to hearing improvement,[27,37–40] emphasizing the need for cautious interpretation of our findings in the context of potential uncontrolled confounding. However, the sensitivity analysis comparing PSL alone to HBOT combined with PSL showed a similar trend to the overall analysis, which may indicate the robustness of the present result. Secondly, the limited sample size of our study constrains the precision of our findings. However, the statistical significance of our results, despite the small sample size, and their consistency across various subgroups, may suggest the robustness of our conclusions. Thirdly, a disproportionately large number of patients in the HBOT group were lost to follow-up, with 24 patients (~16%) in the HBOT group not completing the follow-up. We speculate that this may be attributed to patients preferring hearing follow-up at a nearby clinic after completing initial treatment. However, the potential impact of selection bias may be mitigated, given that patient attrition occurs independently of treatment efficacy. Fourthly, this study did not assess word/speech understanding scores. Although previous meta-analysis[10] and a RCT report[5] in the literature have evaluated hearing recovery solely based on PTA results, we also consider it necessary to include them in future studies for a comprehensive evaluation of hearing outcomes. Lastly, not all patients underwent magnetic resonance imaging (MRI), thereby not completely excluding the possibility of acoustic neuromas. However, because the presence of acoustic neuromas is likely to be non-differential between the case and control groups, any resulting misclassification would typically bias the results toward null findings.

5 | CONCLUSION

Patients treated with HBOT combination therapy showed slightly but significantly better hearing improvement compared to those treated without HBOT for SSHNL. HBOT may have a beneficial impact on SSHNL outcomes when used in conjunction with other treatments.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest and source of funding.

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SUPPORTING INFORMATION

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

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