

## Original Article

# Treatment based on audiometric configuration and prognostic factors for sudden sensorineural hearing loss by regression analysis

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**Abstract:** Objective: To investigate the viability of classifying sudden sensorineural hearing loss (SSNHL) by audiometric configuration. Methods: Patients (530 ears) with SSNHL were classified as hearing loss (HL) types, A-D: A, SSNHL at low frequencies; B, SSNHL at middle-high frequencies; C, SSNHL at all frequencies ( $PTA \leq 80$  dB HL); and D, profound SSNHL at all frequencies ( $PTA \geq 81$  dB HL). Patients were treated with regimens dependent on HL type. Analyses included association of treatment outcomes with HL type, symptoms, age, concomitant disease, and timing of treatment. Results: Five hundred and one patients (530 ears) were recruited, including 248 men and 253 women. The short-term effective rates after treatment were 72.52% for type A, 40.00% for type B, 46.07% for type C, and 58.71% for type D; these differences were significant. The univariate logistic regression analysis showed 4 factors related to the therapeutic effect of SSNHL treatment: age, type of audiometric curve, affected side, and time from onset to intervention. The multivariate logistic analysis indicated 4 independent risk factors associated with therapeutic effect: age, type of audiometric curve, affected side, and time from onset to intervention. Conclusions: The outcome of treatment for SSNHL may be closely related to the HL type based on audiometric results. The efficacy of treatment is improved if applied within 7 days of onset. The selection of treatment for SSNHL can benefit from reference to the type of audiometric curve.

**Keywords:** Sudden sensorineural hearing loss, glucocorticoids, audiometric test, treatment, prognosis, logistic regression analysis

## Introduction

Sudden sensorineural hearing loss (SSNHL) is a loss of  $> 30$  dB, affecting at least 3 consecutive frequencies, and occurring within 72 hours [1]. In the United States, SSNHL affects 5 to 20 individuals per 100,000, with about 4000 new cases per year [1]. A report from Germany indicated a wide distribution of ages in patients with SSNHL (average 50-60 y), and no gender preference [2]. In most patients, hearing loss in SSNHL is unilateral; bilateral involvement is  $< 5\%$  [3].

SSNHL indicates an abnormality of the cochlea, auditory nerve, or higher aspects of central auditory perception or processing. At presentation, up to 90% of patients report no discernible cause for the hearing loss (HL), which is

then presumptively attributed to vascular, viral, or multiple etiologies [4]. About 32-65% of cases recover spontaneously [5-7].

Because the etiology of SSNHL has not been decided definitively, the choice of treatment remains controversial. For example, there are many reports of the use of systemic and topical steroids, antiviral agents, rheologic agents, diuretics, hyperbaric oxygen, and others. It has been difficult to compare the efficacy of these treatments. Factors that affect prognosis for recovery include patient age, presence of vertigo at onset, degree of HL, audiometric configuration, and time between onset of HL and treatment [7, 8].

Various audiometric curves may confirm SSNHL, and each may reflect differences in

## Treatment and prognosis in SSNHL

**Table 1.** Distribution of gender and ear side of patients by HL type, n (%)

	Male	Female	Left ear	Right ear	Bilateral ear
A	30 (32.97%)	61 (67.03%)	45 (49.45%)	46 (50.55%)	0 (0.00%)
B	33 (55.93%)	26 (44.07%)	32 (54.24%)	26 (44.07%)	2 (1.69%)
C	93 (52.24%)	81 (47.76%)	88 (50.57%)	82 (47.13%)	8 (2.30%)
D	92 (51.98%)	85 (48.02%)	78 (44.07%)	75 (42.32%)	48 (13.56%)
Total	248 (49.50%)	253 (50.50%)	(48.50%)	229 (45.71%)	58 (5.79%)

pathogenesis. Thus, the audiometric configuration may be an important tool for determining treatment. To investigate associations between the clinical characteristics, efficacy, and prognostic factors of SSNHL and different audiometric configurations, we retrospectively analyzed the data of 501 SSNHL patients. Herein, we also discuss the usefulness of classifying SSNHL based on the audiometric curve.

### Methods

#### *Patient population*

This is a retrospective analysis of 501 patients with SSNHL (530 ears) treated from February 2011 to May 2014. The patients comprised 248 males (49.50%) and 253 females (50.55%); 472 patients were affected unilaterally, and 29 patients were affected bilaterally.

#### *Audiometry and HL types*

Conventional audiometry was applied to all patients. Acute HL was classified as 4 types (A-D) based on the audiometric curve. Their definition follows. Type A includes low frequencies, with PTA  $\geq$  15 dB HL at 250, 500, and 1000 Hz. Type B is HL at middle-to-high frequencies, with PTA  $\geq$  15 dB HL at 2000, 4000 and 8000 Hz. Type C is HL at all frequencies, with PTA  $\leq$  80 dB HL; and Type D is profound HL at all frequencies, PTA  $\geq$  81 dB HL.

#### *Treatment*

All patients were treated with 15 mg of ginkgo leaf extract dipyrindamole by intravenous injection 2x/d; oral 1 mg/kg prednisone 1x/d in the morning for 3 d; and 10  $\mu$ g of alprostadil 1x/d. In addition, patients of HL types C and D were administered 10 U of batroxobin by intravenous injection on the first day and 5 U every second day afterwards. When hematic fibrinogen decreased to  $\leq$  0.5 g/L, batroxobin was withdrawn. If hearing did not improve obviously

after 7 days of treatment, the medicines listed above were administrated for a further 7 days, and also 40 mg of intratympanic methylprednisolone every second day, 5x.

#### *Judgment of treatment outcome*

Treatment outcomes were judged as follows: complete recovery, defined as final hearing improved to normal or pre-treatment level; partial recovery,  $>$  30 dB HL gain; slight recovery, 15-30 dB HL gain; or no response,  $<$  15 dB HL gain. The overall recovery rate was defined as the percentage of the total number of patients who achieved complete, partial, or slight recovery.

#### *Statistical analysis*

All data are presented as mean  $\pm$  standard deviation. After examining variance equivalence and normal distribution, univariate and multivariate logistic analyses were each applied to determine the prognostic factors of SSNHL.

Logistic regression analyses were performed using outcome as the dependent variable, with scores of 0 or 1 for no recovery and overall recovery, respectively. The independent variables were: gender, age, audiogram curve type, onset of treatment, affected ear, concomitant symptoms, and concomitant diseases. Gender was input as 0 (female) or 1 (male). Age was input directly, in number of years. Audiogram curve type was input as 0, 1, 2, or 3 for types A, B, C, or D, respectively. Onset of treatment was listed directly, as number of days. The affected ear was input as 0, 1, or 2 for right, left, or bilateral ear. Concomitant symptoms were input as 0-3 for none, vertigo, tinnitus, and vertigo + tinnitus. Concomitant diseases were input as 0-3 for none, hypertension, diabetes, and hypertension + diabetes.

All statistical processing was conducted with SPSS version 16.0 for Windows (IBM, Armonk,

**Table 2.** Characteristics and recovery rate of patients by age and disease features, n (%)

		No recovery	Overall recovery	Total
Age, y	≤ 18	7 (30.43%)	15 (65.33%)	23
	19-60	191 (45.80%)	226 (54.20%)	417
	≥ 61	56 (62.22%)	34 (37.78%)	90
Audiogram curves	A	25 (27.47%)	66 (72.53%)	91
	B	36 (60.00%)	24 (40.00%)	60
	C	96 (53.93%)	82 (46.07%)	178
	D	83 (41.29%)	118 (58.71%)	201
Onset of treatment, d	≤ 7	122 (37.31%)	205 (62.69%)	327
	8-14	69 (33.01%)	34 (33.00%)	103
	≥ 15	74 (74.00%)	26 (26.00%)	100
Symptoms	Tinnitus	151 (45.76%)	179 (54.24%)	330
	Vertigo	13 (65.00%)	7 (35.00%)	20
	Tinnitus + vertigo	73 (57.00%)	55 (43.00%)	128
	Neither	24 (46.15%)	28 (53.85%)	52
Concomitant disease	Hypertension	22 (61.10%)	14 (38.90%)	36
	Diabetes	29 (45.31%)	35 (54.69%)	64
	Neither	199 (46.28%)	231 (53.72%)	430
Affected ear	Unilateral	214 (45.34%)	258 (54.66%)	472
	Bilateral	38 (65.52%)	20 (34.48%)	58

**Table 3.** Clinical factors related to hearing recovery in SSNHL in univariate analysis

	Coefficient	SE	P	OR (95% CI)
Gender	-0.142	0.175	0.417	0.868 (0.616-1.222)
Age	-0.027	0.006	0.000	0.973 (0.962-0.984)
Audiogram curve type	-1.497	0.334	0.000	0.224 (0.116-0.431)
Affected ear	-1.324	0.324	0.000	0.266 (0.141-0.502)
Onset of treatment	-0.060	0.012	0.000	0.942 (0.921-0.964)
Accompanied symptom	-0.387	0.331	0.370	0.679 (0.355-1.299)
Accompanied diseases	-0.956	6.005	0.073	0.384 (0.179-0.826)

SE = standard error, OR = odds ratio, CI = confidence interval.

NY). A *P*-value < 0.05 was considered statistically significant, and statistical significance was determined by the Wald chi-squared test.

## Results

### Demographics

Among the 501 patients with SSNHL, 243 (48.50%), 229 (45.71%), and 29 (5.79%) were affected in the left ear only, the right ear only, and the bilateral ears, respectively (**Table 1**). The mean age of the patients was 45.39 ± 15.78 y (range, 13 to 86 y). Patients were stratified by hearing loss type based on the audiogram (types A-D) as described in the Methods.

There were 91 ears of type A (17.17%), 60 of type B (11.32%), 178 of type C (33.58%), and 201 of type D (37.92%). The mean hospitalization was 10.48 ± 3.97 days. Only 2 patients reported ear pain after treatment with intratympanic methylprednisolone. No severe adverse event occurred, including no perforation of the tympanic membrane.

### Univariate logistic regression analysis of possible prognostic factors

Based on hearing recovery, patients were divided into 2 groups: hearing recovery and no recovery (**Table 2**). Seven univariates were analyzed: gender, age, audiogram curve type, affected ear, onset of treatment, accompanied symptom, and concomitant diseases. The results showed that age, audiometric curve type, onset of treatment, and affected ear were 4 independent risk factors that were associated with the therapeutic effect of treatment for SSNHL (each, *P* = 0.000; **Table 3**).

The overall recovery rates among patients at different ages were significantly different, with the best efficacy shown in patients younger than 18 years, and the worst efficacy in patients older than 61 years (*P* = 0.000; **Table 3**). This suggests that younger patients may have a better prognosis than older patients.

The treatment outcome was significantly different among the 4 hearing loss types (*P* = 0.000; **Table 3**). The percentage of patients who experienced at least some response to treatment, that is, the effective rate, was highest in those with type A (72.53%), while the effective rate of type B (40.00%) was the worst (**Table 2**).

**Table 4.** Clinical factors related to hearing recovery in SSNHL in multivariate analysis

	Coefficient	SE	P	OR (95% CI)
Age	-0.024	0.006	< 0.0001	0.977 (0.965-0.989)
Audiogram curve type	-1.002	0.363	0.035	0.367 (0.180-0.748)
Affected ear	-1.145	0.347	0.002	0.318 (0.161-0.628)
Onset of treatment	-0.056	0.011	< 0.0001	0.946 (0.925-0.967)

Patients with only one ear affected (54.66%) had a much better outcome than did those with bilateral ears (34.48%; **Table 2**). The *P* values were 0.000 in the univariate logistic analysis (**Table 3**) and 0.002 in the multivariate logistic analysis (**Table 4**).

Among these patients, the onset of treatment ranged from 4 h to 1 y (average, 10.6 d; **Table 2**). The efficacy of treatment in patients who were treated within 7 days and those treated after 7 days was significantly different (*P* = 0.000; **Table 3**). The overall recovery rate of patients who were treated within 7 days was 62.7%, and the overall recovery rate of patients who were treated within 8-14 days was 33.0%; 26.0% were treated < 14 days after onset (**Table 2**). The patients who were treated within 7 days had much better outcomes than did the patients treated after 7 days. Timely treatment was a positive factor in prognosis.

Among the 530 ears with SSNHL, there were, respectively, 330 (62.3%), 20 (3.8%), 128 (24.2%), and 52 (9.8%) that presented with tinnitus, vertigo, tinnitus plus vertigo, and neither tinnitus nor vertigo (**Table 2**). The overall recovery rates were not statistically different among the groups with tinnitus, vertigo, tinnitus plus vertigo, or, with neither tinnitus nor vertigo (*P* = 0.370; **Table 3**).

*Multivariate logistic regression analysis of possible prognostic factors*

Parameters with a *P* value < 0.05 in the univariate analysis were used in the multivariate analysis. Age, affected ear, audiometric curve type, and onset of treatment were candidates for multivariate analysis. It was found that age (*P* < 0.0001), audiometric curve type (*P* = 0.035), onset of treatment (*P* < 0.0001), and the affected ear (*P* = 0.002) were related to the therapeutic effect of treatment for SSNHL (**Table 4**).

**Discussion**

This study showed that the efficacy of treatment for patients with different types of audiometric curves were significantly different. We found the highest rate of efficacy

(72.52%) in patients of type A, the lowest rate (40%) in the patients of type B, and 46.07% and 58.71% rates in the patients of type C and type D, respectively. The difference in effective rates among types is consistent with another report [9]. These results indicate that the prognosis for SSNHL of low frequencies is the best, and that a loss of middle-to-high frequencies is the worst. The better prognosis for type A may be due to a possible SSNHL etiology related to endolymphatic hydrops, which is sensitive to medicine. The poor prognosis of type B may be due to hair cell damage as the cause of SSNHL [1].

The traveling-wave theory states that the high frequency zone is at the bottom of the cochlea where the metabolic rate is higher than in other areas [1]. This region could be damaged more easily if the blood supply is insufficient, and subsequent recovery of hearing is poor [1]. The HL of low frequency type (type A) and flat type (type C) is a positive factor in recovery, and HL of high frequency type is a negative factor. Some other studies also support this conclusion [9, 10]. Furthermore, the probable cause of HL in all frequencies (types C and D) is micro-circulatory insufficiency in the inner ear [11]. These findings indicate that audiometric configuration is related to prognosis, due to differences in pathogenesis. We propose that it is necessary to treat SSNHL based on audiometric configuration.

In the present study, the majority of patients presented with tinnitus (62.3%), while the remainder had vertigo (3.8%), or both tinnitus and vertigo (24.2%). This is similar to other reports [11]. Thus, tinnitus was far more common than vertigo as a presenting symptom in this SSNHL population.

Overall, the effective rate of treatment for patients with tinnitus (54.2%), was better than for patients with vertigo (35%), while no statisti-

cally significant difference was shown by the univariate logistic regression analysis. This indicates that neither tinnitus nor vertigo is associated with the prognosis of SSNHL. However, some reports proposed that vertigo was a negative prognostic factor in SSNHL. Raluca Enache and Codrut Sarafoleanu et al. [10] found that among 8 patients with vertigo, none of them experienced a good recovery. It was reported that the presence of vertigo indicates a poor prognosis; only 14% of these patients achieved complete recovery of hearing [12].

Systemic steroids have become standard treatment for SSNHL. The American Academy of Otolaryngology-Head and Neck Surgery for SSNHL recommends glucocorticoids as the first choice treatment for SSNHL [1]. A report from Germany recommends rheologic agents as the first choice and glucocorticoids as the second choice [2]. The main role of glucocorticoids in SSNHL is anti-inflammatory, eliminating edema of the cochlea and immunosuppression. We used oral steroids 1 mg/kg (maximum 60 mg) for 3 days. A meta-analysis indicated that prostaglandin E1 was an effective and promising treatment strategy [13]. We also used alprostadil which contained prostaglandin E1. Batroxobin can reduce the fibrinogen content of the blood, decreasing viscosity and lowering vascular resistance, thereby improving microcirculatory perfusion. With regards to this, we applied batroxobin to treat SSNHL in types C and D.

In recent years several studies have supported the use of a systemic or intratympanic glucocorticoid, or combination of them, as a treatment of choice in SSNHL [14-19]. There is much evidence to suggest that intratympanic glucocorticoid treatment improves treatment success by increasing intracochlear corticosteroid and reducing the incidence of toxic side effects. In our study, only 2 patients complained of ear pain after treatment with intratympanic methylprednisolone. No severe adverse event occurred, including no perforation of the tympanic membrane. However, the optimal drug, dosage, treatment schedule, duration of treatment, and standard protocol requires randomized and double-blind studies.

In our study, both the univariate and multivariate logistic analyses showed that patients who

were treated within 7 days had a significantly better rate of response rated than did those treated between 7-14 days or > 7 days after onset ( $P = 0.000$  and  $P < 0.0001$ , respectively). This indicates that successful treatment may depend on early treatment. Ljiljana Cvorovic and Dragoslava Deric et al. [20] also reported that the best improvement was obtained by patients treated within 7 days of onset. Some studies indicated that an interval between onset and treatment < 7 days is a positive prognostic factor in SSNHL [10]. Therefore, patients should be diagnosed and treated as early as possible. On the other hand, it is still worth treating patients with a longer course, as improvement has been reported possible in patients with histories of more than 6 months [21].

The present study found that hypertension is not a prognostic factor in SSNHL, although the overall recovery rate of treatment for patients with hypertension (38.90%), was worse than that of patients without hypertension (53.72%). Diabetes was not related to the prognosis of SSNHL in this study. A number of studies in the literature have found that risk factors for the development of SSNHL include diabetes mellitus, cigarette smoking, hypertension, and hyperlipidemia [22-24]. Other studies suggest that these factors do not have any significant influence on the threshold recovery in SSNHL [25]. Claudia Aimoni and Chiara Bianchini et al's. [22] findings suggested that diabetes mellitus was associated with the risk of SSNHL, but they did not analyze the prognosis of SSNHL. Dimitrios Assimakopoulos and Vasilis Danilides et al. [26] also reported that diabetes did not affect the prognosis of SSNHL. Michiaki Fukui and Yoshihiro Kitagawa et al. [27] claimed that the prognosis of patients without diabetes was significantly better than that of patients with diabetes.

In most patients, SSNHL is unilateral; bilateral involvement is < 5% [3]. In the present study, bilateral involvement was 5.79%, which is consistent with other reports in the literature. Jeong-Hoon Oh and Keehyun Park et al. [3] reported in a series of SSNHL cases that only 4.9% were bilateral. The overall recovery rate in the bilateral cases was only 37.5%, which was significantly lower than in the unilateral SSNHL patients. In the present study, both the univariate and multivariate logistic analyses indicated

that the recovery rate of patients affected unilaterally was significantly better than that of those with bilateral ear. This suggests that bilateral ear SSNHL is a negative prognostic factor.

### Conclusion

In summary, this study reports the short-term results of treatment of SSNHL. Great differences were found in the response to treatment for each type of SSNHL, with the best treatment efficacy for losses at low frequencies (type A) and the worst at middle-high frequencies (type B). This may be related to differences in the etiology of each type. Therefore, it is useful to classify SSNHL by the audiometric curve when considering treatment strategies. SSNHL patients with losses at low frequencies, younger than 18 years, unilateral ear, and treated within 7 days of onset had better outcomes than did those with losses in the middle-to-high frequencies, bilateral ear, accompanied by hypertension, and treated after one week. The final hearing assessments were performed upon patient discharge. A long-term follow-up is in progress.

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### Disclosure of conflict of interest

None.

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