

# The Long-term Prognosis of Residual Tinnitus with Idiopathic Sudden Sensorineural Hearing Loss

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## Abstract

**Objectives:**To analyze the factors affecting the long-term prognosis of tinnitus accompanied with unilateral idiopathic sudden sensorineural hearing loss (SSNHL). **Design:**A cohort study. **Setting:**Academic hospital. **Participants:**A total of 161 patients with sudden hearing loss accompanied by tinnitus were enrolled. All the patients had two separate telephone follow-ups and were asked about changes in tinnitus. **Main outcome measures:**The severity of tinnitus at admission and the outcome at discharge were assessed in terms of the patients' sex, age, level of hearing loss, type of audiogram, and so on. **Results and Conclusions:**Initial tinnitus level was remarkably associated with tinnitus efficacy at discharge and was an independent risk factor for the long-term prognosis of residual tinnitus after SSNHL (odds ratio 0.722, 95% confidence interval 0.550-0.949,  $p = 0.019$ ), and the median recovery time was  $23.00 \pm 3.80$  months.

## KEY POINTS

1. The severity of tinnitus associated with SSNHL is generally not very strong and is mostly classified as levels 3 and 4.
2. Initial tinnitus level was remarkably associated with tinnitus efficacy at discharge.
3. The short-term prognosis of tinnitus may be related to psychological changes caused by hearing recovery.
4. The long-term prognosis of residual tinnitus after SSNHL is related only to the initial tinnitus level.
5. Over time, residual tinnitus will gradually recover, with a median healing time of approximately 2 years.

**Key Words :** Residual tinnitus, SSNHL, Initial tinnitus level, Long-term prognosis, Affected factors

## INTRODUCTION

Tinnitus is the most common ear disease and represents a global issue(1, 2), with a prevalence of 5.1-42.7% around the world and increases with age. (3) Guidelines of different countries stratify chronic tinnitus differently, with 3 months in Japan(4) and 6 months in China, USA and Europe(1, 5, 6). According to guidelines, acute tinnitus resolves spontaneously(1, 7), but patients with chronic tinnitus are less likely to achieve self-improvement(1); however, that may not be correct. Previous studies on chronic tinnitus have shown that 20-50% of patients may heal within 5 years(8, 9).

Tinnitus is only a clinical symptom with complex etiology. Although hearing loss is indeed an initiating factor for tinnitus, the association is not simple and direct (10). Among the various classifications and severities of hearing loss, sudden hearing loss has the most definite association with tinnitus as more than 80% of SSNHL cases have been found to be accompanied by tinnitus (11). Tinnitus in SSNHL patients often lasts for more than 6 months. Although several studies have focused on the prognosis of tinnitus accompanied by SSNHL, the follow-up times were mostly within 1 year(12-16). Therefore, we investigated the long-term outcomes of tinnitus in 161 patients with SSNHL after standard treatments. We also analyzed possible factors affecting tinnitus recovery to provide clarification and counseling for patients with residual tinnitus after SSNHL to build reasonable confidence and set appropriate expectations.

## MATERIALS AND METHODS

### Study Design and Participants

From January 2014 to December 2015, 161 patients with unilateral SSNHL accompanied by newly developed tinnitus who were hospitalized in the Department of Otorhinolaryngology, Peking University People's Hospital, were enrolled. All of the patients' hearing was assessed by the same doctor. After admission, treatments were applied in accordance with the Chinese Guideline for Sudden Deafness(17). Systemic corticosteroids and hemodilution agents were administered as therapeutic measures. All patients received 40 mg of intravenous methylprednisolone for 5 consecutive days and hemodilution agents for 10 days, including 87.5 mg of intravenous EGb-761(Dr. Willmar Schwabe GmbH & Co., Germany) every day and 5 BU of intravenous batroxobin (Beijing Tobishi Pharmaceutical Co.), the first dose was doubled, and every other day based on fibrinogen levels.

### Inclusion and Exclusion Criteria

Inclusion criteria: 1) first-onset SSNHL; 2) unilateral hearing loss; 3) a time between onset and treatment [?] 60 days; 3) ipsilateral newly developed tinnitus associated with SSNHL; 4) normal hearing or age-related hearing loss in the contralateral ear. No restrictions on gender and age were set.

Exclusion criteria: 1) recurrent sudden deafness, pregnancy, or middle ear infections; 2) a definitive cause of deafness identified during treatment; 2) a history of tinnitus; 3) bilateral tinnitus; 4) no treatment according to the Chinese Guidelines for Sudden Deafness during the inpatient process for any reason (17).

### Evaluation of Tinnitus and Hearing Loss

Evaluation of tinnitus severity: Tinnitus in the patients was classified into seven grades according to the Feldmann standard (6): 1) 0: No tinnitus, 2) 1: Occasional tinnitus that does not affect the patient's daily life, 3) 2: Persistent tinnitus that is more prominent in quiet surroundings, 4) 3: Persistent tinnitus even in a noisy environment, 5) 4: Persistent tinnitus combined with attention and sleep disorders, 6) 5: Persistent severe tinnitus affecting the patient's ability to work, and 7) 6: Severe tinnitus provoking suicidal tendencies.

Efficacy evaluation of tinnitus: The evaluation was based on the Chinese classification of tinnitus severity(6),: 1) Cured: Tinnitus had disappeared or improved to grade 1, 2) Markedly effective: Tinnitus was alleviated by 1-3 grades but had not yet reached grade 1, 3) Effective: Tinnitus was alleviated to some extent but remained in the same grade, 4) Ineffective: Tinnitus was unchanged or even worsened. In this study, level 1 intermittent tinnitus was also counted as cured in this article.

Grades of hearing loss severity: The hearing thresholds at 0.50, 1.00, 2.00, and 4.00 kHz were measured. When the hearing thresholds at some frequencies could not be detected, the frequency threshold was considered the maximum audiometric intensity. The degrees of hearing loss were categorized as mild (26–40 dB HL), moderate (41–60 dB HL), severe (61–80 dB HL), and profound hearing loss (> 80 dB HL) (17).

Classification of hearing loss: Four audiogram shapes were defined in relation to the pattern of hearing loss (17): ascending, flat, profound, and descending. "Ascending" referred to cases in which the average threshold of 0.25 to 0.5 kHz was 20 dB higher than normal. When the difference in the hearing threshold did not exceed 20 dB at any frequency, the audiogram shape was classified as "flat." For patients with a flat audiogram and

a hearing threshold greater than 81 dB, the audiogram shape was classified as “profound.” The audiogram shape was described as “descending” when the average threshold of 4 to 8 kHz was 20 dB higher than normal.

Hearing recovery evaluation: Based the results of pure-tone audiometry (17) patients were divided into four groups: 1) Cured: A final hearing level less than 25 dB regardless of the size of the gain, 2) Markedly effective: Greater than 30 dB of gain for the average hearing threshold, 3) Effective: Gains greater than 15 dB and less than 30 dB, and 4) Ineffective: less than 15 dB of gain.

## Evaluation of Associated Factors

The participants were interviewed mainly regarding their health conditions. Clinical and demographic data were collected from medical records.

Demographic data included age and sex. The presence of the following chronic diseases or disorders was ascertained during the interviews: hypertension, diabetes, hyperlipidemia and a history of cholesteatoma, otitis media with effusion, or chronic otitis media. In addition, dizziness episodes were also recorded.

## Follow-up

All the patients participated in two separate telephone follow-ups conducted by two different independent doctors from January 2016 to April 2016 and from April 2018 to October 2018. The patients were asked about changes in tinnitus and when the changes occurred (Figure 1).

## Main Outcome Measures

Several possible factors were considered, including gender, age, the duration between disease onset and treatment, laterality, the tone of tinnitus, the initial level of tinnitus, the severity of hearing loss at admission, hearing recovery, follow-up tinnitus, follow-up time points, and other factors.

## Statistical Analysis

The clinical and epidemiological characteristics of the patients were summarized by descriptive statistics. Data sets were described with the median and/or range. Numerical data were compared using  $T$ -test, and categorical data were compared using the  $\chi^2$  test. The healing rate of tinnitus was calculated using the Kaplan–Meier method, and the log rank test evaluated differences between tinnitus healing rate distributions. Multivariable analyses were performed to analyze factors related to the outcome of tinnitus at discharge, and Cox proportional hazard models were applied to examine the healing rate with adjustments for other variables using a limited backward selection procedure. Risk ratios are presented with 95% confidence intervals. Statistical significance was defined as a two-tailed  $P < 0.05$  for all analyses. Statistical analyses were performed using SPSS software version 23.0 and GraphPad Prism 7.0.

## RESULTS

### Study Populations

In this study, none of the 161 enrolled patients had level 0 or 6 tinnitus. Ninety-six cases were level 3 (59.6%), and 41 cases (25.5%) were level 4. Only three cases (1.9%) were level 1, 16 cases (9.9%) were level 2, and five cases (3.1%) were level 5. To avoid large difference between the groups, we divided all the patients into three groups according to their initial level of tinnitus: 19 were in the mild (levels 1 and 2) group, 96 were in the moderate (level 3) group, and the remaining 46 were in the severe (levels 4 and 5) group. The basic information of the 161 patients at admission is presented in Table 1.

### General tinnitus efficacy at discharge and analysis of correlated factors

According to the efficacy evaluation of tinnitus, we divided the 161 patients into four groups at discharge: 24 cases were cured (14.9%), 11 cases were markedly effective (6.8%), 75 cases were effective (46.6%), and the remaining 51 cases were invalid (31.7%). The total effective rate was 68.3%. A  $T$ -test and the chi-square test were used for statistical analysis of related factors (Table 2). The analysis showed that the initial level of tinnitus at admission, hearing recovery, and laterality were related with the outcome of tinnitus at discharge

( $P < 0.1$ ). Then, binary logistic regression analysis was applied to explore the independent related factors of tinnitus efficacy at discharge. Here, we incorporated statistically remarkable factors including the initial level of tinnitus at admission, hearing recovery, laterality, and SSNHL grades, which were not statistically moderate but were clinically remarkable, into a multivariate analysis. The analysis showed that the initial level of tinnitus was an independent relevant factor for the efficacy of tinnitus at discharge ( $P = 0.000$ ).

### **Influencing factors of the long-term prognosis for residual tinnitus after SSNHL**

Based on the results of two follow-ups, we divided the final tinnitus prognoses of all the subjects into cured (including grades 0 and 1) and uncured. First, the univariate Cox regression analysis was used to screen the possible influencing factors (Table 3). The analysis showed that the laterality of SSNHL and the initial tinnitus degree may be related to the long-term prognosis of tinnitus ( $P < 0.05$ ). Then, the duration before treatment ( $0.05 < P < 0.10$ ), the laterality of SSNHL, and initial level of tinnitus, as well as hearing recovery at discharge, which was not statistically remarkable but was clinically remarkable, were all included in the multivariate Cox regression analysis. The results showed that the initial level of tinnitus was an independent factor for the long-term prognosis of residual tinnitus after SSNHL.

Finally, the healing rates of patients with different initial tinnitus levels were calculated using the Kaplan–Meier method (Figure 2). Moreover, the median healing time of patients with different initial tinnitus levels can be used to predict the healing time of tinnitus for patients with different initial levels (Table 4). The analysis showed that tinnitus at all levels tended to heal with time. A higher initial degree of tinnitus corresponded to a prolonged healing time. The median times for tinnitus healing for patients with initial tinnitus levels of 1 to 5 were as follows:  $1.00 \pm 0.00$  months,  $21.00 \pm 4.50$  months,  $33.00 \pm 3.76$  months, and  $37.00 \pm 11.50$  months, respectively. The median recovery time for all cases was  $23.00 \pm 3.80$  months (Table 4).

## **DISCUSSION**

### **Summary of main results**

In this study, we found that most initial tinnitus along with the onset of SSNHL of the cases were classified as level 3 and 4. Initial tinnitus level was remarkably associated with tinnitus efficacy at discharge and an independent risk factor for the long-term prognosis of residual tinnitus after SSNHL. The median recovery time was  $23.00 \pm 3.80$  months.

### **Hearing recovery is related to the short-term prognosis of tinnitus after SSNHL**

A total of 68.3% of the patients showed improvement in tinnitus to varying degrees at discharge, and hearing recovery was found to be a non-independent factor related to the short term prognosis of tinnitus. Regarding the pathology of tinnitus described earlier, hearing loss is the trigger of tinnitus. At the time of discharge, 92 patients (57.1%) showed improvement in hearing, but the degree of hearing recovery is not completely consistent with the prognosis of tinnitus. Even if hearing improves to some extent, the effect on the intensity of tinnitus is minimal. Therefore, we cannot simply use hearing recovery to explain the relief of tinnitus. The occurrence of tinnitus consisted of two components: perception and reaction(1). Reaction represents a complex connection between the auditory system and the emotional system. Several investigations have verified the spontaneous remission of psychiatric symptomatology over a waiting period (18, 19). The social desirability hypothesis states that no true change occurs in the number or intensity of symptoms, but instead, an increase in the threshold for reporting their presence occurs. The item content-priming cue-recall hypothesis states that over time and after repeated exposure to these items, subjects will report less negative states due to habituation or extinction(20). A meta-analysis of 11 studies with 314 individuals distressed by tinnitus who were randomly allocated to a waiting period of 6–12 weeks revealed mean decreases in symptoms of 3% to 8%(21). The short-term prognosis of tinnitus may be related to a decrease in the reaction (12-14). As hearing loss improves, their psychological reaction to tinnitus decreases.

### **Long-term prognosis of residual tinnitus after SSNHL**

Over time, the degrees of tinnitus in patients with different initial tinnitus levels were all alleviated to a certain extent. The degree of tinnitus relief and healing time are only related to the initial degree of tinnitus and the median recovery time for all the patients was 23 months.

Previous studies on residual tinnitus after SSNHL have shown a tendency for gradual improvement (13, 16). In 2013, Michiba T found that tinnitus appeared to improve 6 months after treatment but did not remarkably change between 6 and 24 months (13). In this article the median healing time showed that 2 to 3 years may be required for tinnitus to recover. Such improvements may be associated with the plasticity of the central auditory pathway. The tinnitus habituation theory (5) proposes that the brain selects which stimuli to ignore, and only the information that is considered valuable or dangerous will be perceived by the brain. According to the theory, most people consider the tinnitus of low informational value and does not require a reaction. However, tinnitus-related distress occurs when this processes is malfunctioning, which is more likely at times of increased stress, subsequently straining the cognitive resources causing chronic tinnitus and creating a vicious cycle with the emotional system (5). Recent studies have confirmed that once hearing loss starts, the most active compensation occurs in the thalamus, but not all of these signals can be transmitted to the auditory cortex. Meaningless and nonhazardous sounds are adapted to and ignored by the frontal-striatal circuits in the midbrain when patients do not pay attention to tinnitus over time. The frontal-striatal circuit region mainly consists of the ventromedial prefrontal cortex, the nucleus accumbens, and other important areas. These circuits can be collectively called the tinnitus clearance system as a gatekeeper of tinnitus. This explanation accounts for the clinical observation that most tinnitus cases resolve naturally (5, 22, 23). However, if a problem arises with this ‘gatekeeper’, the ability to clear tinnitus signals will be impaired. As a result, tinnitus may persist for a prolonged period. Factors affecting the function of this gatekeeper may include but are not limited to sleep, migraine, estrogen decline(22), trauma, depression, and sleep-disordered breathing(23, 24). However, some patients cannot self-heal and continue to experience slight intermittent tinnitus. Such patients should be given adequate education and counseling to relay that tinnitus is a “scar” on the auditory system, which may rationalize tinnitus, thus eliminating patients’ irrational thoughts and fear of tinnitus.

## Limitations

First, an anxiety and depression scale was not used to score the subject’s mental state, which may have impacted the analysis of the influencing factors. Second, most of the patients enrolled in this study had severe hearing loss, and the hearing recovery rate was low, which may result in a bias in the analysis of the relationship between hearing recovery and tinnitus prognosis. Thirdly, this study is a retrospective analysis and mainly relied on the subjective recall of patients, which could cause a recall bias in the statistical analysis. Furthermore, the follow-up interval in this study was relatively long at nearly 2 years, which can only reflect the status of tinnitus during the follow-up and illustrate the trend of tinnitus outcomes but cannot accurately locate the time point when tinnitus began to improve.

## CONCLUSION

The short-term prognosis of tinnitus may be related to psychological changes caused by hearing recovery. And the long-term prognosis of residual tinnitus after SSNHL is related only to the initial tinnitus level, with a median healing time of approximately 2 years.

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## Figure legend

**Figure.1 Follow-up flowchart**

**Figure.2 Recovery rate curves of patients with different initial tinnitus levels (K-M curve)**

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