Nomogram for predicting the prognosis of sudden sensorineural hearing loss patients based on clinical characteristics: a retrospective cohort study

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Background: Based on the clinical characteristics of patients, a nomogram predicting the prognosis of patients suffering from sudden sensorineural hearing loss (SSNHL) was constructed, which could aid in personalized treatment.

Methods: Data on the clinical characteristics of patients with SSNHL were collected and statistically analyzed. A nomogram for predicting the hearing prognosis of SSNHL patients were then constructed.

Results: A total of 356 patients were included in this study, including 227 and 129 in the recovery group (63.76%) and non-recovery group (36.24%), respectively. Univariable logistic regression demonstrated that age, gender, body mass index (BMI), marital, Audiogram curve, vertigo, hearing loss degree, and time to initial treatment were associated with hearing outcomes. Multivariate logistic models showed that age [odds ratio (OR): 0.479, 95% confidence interval (CI): 0.301–0.748, P<0.001], descending (OR: 0.116, 95% CI: 0.047–0.275, P<0.001) and flat audiogram curves (OR: 0.397, 95% CI: 0.159–0.979, P=0.045), profound hearing loss (OR: 0.047, 95% CI: 0.013–0.152, P<0.001), and treatment initiation after 1 week (8–14 days: OR: 0.047, 95% CI: 0.013–0.152, P<0.001; >14 days: OR: 0.131, 95% CI: 0.039–0.413) were risk factors for the hearing recovery. Logistic regression analyses were conducted to construct the prognostic nomogram. As estimated by the area under the receiver operating characteristic curve (ROC), the model had an accuracy of 0.867 (95% CI: 0.709–0.747). The validation analysis confirmed the high accuracy of the nomogram, and the decision curve showed that the model has potential clinical application value.

Conclusions: This study demonstrated that age, descending and flat audiogram curves, profound hearing loss, and initiating treatment after 1 week of SSNHL onset were independent risk factors associated with a worse hearing recovery prognosis. Using these factors, a nomogram with a high prediction accuracy was developed to predict the hearing recovery rate of SSNHL patients.

Keywords: Sudden sensorineural hearing loss (SSNHL); hearing; prognosis; prediction; nomogram

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Introduction

Sudden sensorineural hearing loss (SSNHL), a common emergency in otolaryngology, is defined as a sensorineural hearing loss with an unknown cause, and a hearing loss of ≥30 dB in at least 3 consecutive frequencies within 72 h (1). The incidence rate of SSNHL has been reported to be [5–160]/10,000 (2); however, as SSNHL has a certain natural recovery rate, the actual incidence is speculated to be higher than that reported. Early diagnosis, comprehensive evaluation, and active interventions are of great significance in improving the hearing, prognosis, and quality of life of patients.

Identifying factors and models that can accurately predict the prognosis of SSNHL is of great significance in disease prevention, treatment, and reducing the economic burden. Previous studies only focused on the prognostic factors of SSNHL (3-7), but a few studies have been conducted on prognostic models. Recently, some studies used machine learning to build a prognosis model for SSNHL (8,9). However, it should be noted that although this prediction model was accurate, it requires numerous variables to input to improve its applicability in clinical settings.

A nomogram is a statistical tool that can accurately predict the outcome of individual patients using multiple variables. Nomograms can be created using regression analysis (10), and well-designed nomograms can make more accurate predictions than experienced clinicians (11,12). Currently, a convenient and useful prediction tool for patients with SSNHL does not exist. Thus, this study sought to develop a nomogram to accurately predict the prognosis of SSNHL patients based on their clinical characteristics, which will help clinicians in determining patient prognosis and follow-up intensity. We present the following article in accordance with the TRIPOD reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-5647/rc).

Highlight box

Key findings
- Developed a useful nomogram predict hearing prognosis of a SSNHL patient.

What is known and what is new?
- A study reported nomograms.
- The nomogram developed in this study includes easily accessible clinical information, and provides a more accurate prediction.

What is the implication, and what should change now?
- Further large-scale researches are needed to validate present results.

Methods

Patient selection and data availability

The data of patients with SSNHL who were admitted to the otorhinolaryngology ward of a tertiary university hospital from November 2017 to December 2020 were retrospectively analyzed. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics board of Shenzhen Hospital, Southern Medical University (No. NYSZYYEC20210042). Due to the retrospective nature of the study, the requirement to obtain signed informed consent from the patients was waived. To be eligible for inclusion in this study, the patients had to meet the following inclusion criteria: (I) have experienced sudden unilateral sensorineural hearing loss within 72 hours with ≥30 dB hearing loss, involving 3 or more consecutive frequencies; (II) have unilateral hearing loss; and (III) have an unknown cause even after detailed clinical evaluation. Patients were excluded from the study if they met any of the following exclusion criteria: (I) had incomplete clinical data; (II) had a history of hereditary deafness; (III) had a history of head trauma and ear surgery; (IV) had an autoimmune disease; (V) had a history of excessive noise exposure; (VI) had a history of ototoxic drug use; and/or (VII) had retro cochlear lesions, such as vestibular schwannoma and stroke.

Clinical and audiometric data

The clinical features included age, gender, body mass index (BMI), marital status, complications (e.g., hypertension, diabetes, and hyperlipidemia), time to initial treatment, initial hearing loss, audiometric curve, hearing outcomes, imaging examination, and hematological examinations.

The pure tone averages (PTAs) were computed across fixed frequency bands (0.5, 1, 2, and 4 kHz) or affected frequencies. If no response was elicited, the maximum sound intensity generated by the audiometer was increased by 5 dB (13). The degree of initial hearing loss was divided into the following 4 levels according to the standard of the World Health Organization (1997): (I) mild: 26–40 dB; (II) moderate: 41–60 dB; (III) severe: 61–80 dB; and (IV) profound ≥81 dB.

Audiogram configuration

The classification method was modified according to the standard of Demeester *et al.* (14), and the audiogram configuration was categorized into the following 4 types: (I) Ascending: the difference between the poor low-frequency threshold and the good high-frequency threshold was >15 dB; (II) Descending: the difference between the average value of the 500-Hz and 1,000-Hz thresholds and the average value of the 4,000-Hz and 8,000-Hz thresholds was >15 dB; (III) Flat: the difference between the average threshold values of 250–500, 1,000–2,000, and 4,000–8,000 Hz was <15 dB, including total deafness type; and (IV) Irregular: any audiogram that did not qualify for categorization into any of the aforementioned 3 types. The patients were divided into 4 groups based on the time between hearing loss onset and treatment initiation (i.e., ≤3, 4–7, 8–14, and >14 days).

Treatment and Outcome assessment

All the patients received a unified standard of treatment, including systemic or local hormones, mecobalamin, and Ginkgo biloba extract (EGb761). A few patients were also treated with batroxobin. After 2 weeks of treatment, the patients in whom the treatments had poor effects were further treated with hyperbaric oxygen.

All hearing assessments were at the admission, 1th and 2nd week after systemic treatment. The hearing level of each patient was calculated by averaging the PTA of impaired frequencies after onset and the extent of hearing recovery is calculated using PTA after onset minus PTA after treatment. Only the mean hearing thresholds at affected frequencies was used to determine the dichotomized hearing outcome, which was derived from Siegel's criteria but modified (15).

Patients were classified into two groups according to their recovery in hearing observed in 2 weeks of follow-up: (I) recovery (including partial and complete recovery), which was defined as an improvement in PTA ≥15 dB; or (II) no recovery, which was defined as an improvement in PTA <15 dB.

Statistical analyses

The dichotomous variables are expressed as the percentage, and comparisons between the groups were determined using the chi-square test. Variables with a P value <0.15 in the univariate analyses were included as predictors in the logistic regression model. The stepwise regression method was used to select the relevant variables and construct the nomogram. The strength of the association between SSNHL recovery and the predictors was estimated using the odds ratio (OR) and 95% confidence interval (CI). The total score of the nomogram was classified using quartile ranges to assess the association between the total score and SSNHL recovery. Prediction accuracy is measured by the area under the receiver operating characteristic curve (AUC), which ranges from 0.5 to 1, with higher scores indicating better accuracy. Based on the calibration curves, the observed and predicted probabilities were compared. The clinic utility of the nomogram was evaluated using decision curve analysis (DCA) by calculating net benefits at different threshold probabilities. A P value <0.05 was considered statistically significant, and all tests were two-sided. The statistical analyses were performed using R version 3.6.3 and Python version 3.7.

Results

Clinical baseline characteristics and hearing recovery

A total of 356 patients were included in this study, including 227 (63.76%) in the recovery group and 129 (36.24%) in the non-recovery group. The ages of the patients ranged from 13 to 90 years (with 11 patients aged <20 years). The left ear was involved in 189 cases (53.09%) and the right ear in 167 cases (46.91%). The accompanying symptoms included 290 cases (81.46%) of tinnitus and 56 cases (15.73%) of vertigo.

The results of the comparisons of the general data between the 2 groups are set out in *Table 1*. To reduce the model error caused by the interaction between the variables, a correlation analysis was conducted to eliminate strongly correlated variables. However, on using the Kendall correlation test, no variables with a correlation coefficient >0.5 were observed.

The univariate analysis of the variables showed that the following variables were associated with poor hearing recovery: age; being female; being unmarried; a BMI of 24–27 kg/m^2; descending, flat, and irregular audiogram curves; vertigo; severe or profound initial hearing loss; and initiating treatment >8 days after onset of the hearing loss. Using the "Stepwise regression" logistic regression model, after excluding variables with P values >0.05, the following 4 predictors were found to be associated with the hearing

Table 1 Clinical characteristics and hearing recovery of the study participants

Parameter	Patients, n (%)	Without recovery, n (%)	With recovery, n (%)	P value
Age (years)				<0.001
≤20	11 (3.09)	2 (1.55)	9 (3.96)	
21–40	196 (55.06)	42 (32.56)	154 (67.84)	
41–60	119 (33.43)	67 (51.94)	52 (22.91)	
>60	30 (8.43)	18 (13.95)	12 (5.29)	
Sex				0.029
Male	147 (41.29)	63 (48.84)	84 (37.00)	
Female	209 (58.71)	66 (51.16)	143 (63.00)	
Marital				< 0.001
Married	265 (74.44)	110 (85.27)	155 (68.28)	
Unmarried	84 (23.60)	16 (12.40)	68 (29.96)	
Other	7 (1.97)	3 (2.33)	4 (1.76)	
BMI (kg/m^2)				0.063
≤23	218 (61.24)	69 (53.49)	149 (65.64)	
24–27	119 (33.43)	53 (41.09)	66 (29.07)	
≥28	19 (5.34)	7 (5.43)	12 (5.29)	
Vertigo				< 0.001
No	300 (84.27)	96 (74.42)	204 (89.87)	
Yes	56 (15.73)	33 (25.58)	23 (10.13)	
Tinnitus				0.758
No	66 (18.54)	25 (19.38)	41 (18.06)	
Yes	290 (81.46)	104 (80.62)	186 (81.94)	
Ear fullness				
No	190 (53.37)	74 (57.36)	116 (51.10)	
Yes	166 (46.63)	55 (42.64)	111 (48.90)	
Affected side				0.583
Left	189 (53.09)	66 (51.16)	123 (54.19)	
Right	167 (46.91)	63 (48.84)	104 (45.81)	
Hypertension				0.100
No	333 (93.54)	117 (90.70)	216 (95.15)	
Yes	23 (6.46)	12 (9.30)	11 (4.85)	
Diabetes				0.024
No	346 (97.19)	122 (94.57)	224 (98.68)	
Yes	10 (2.81)	7 (5.43)	3 (1.32)	

Table 1 (*continued*)

Table 1 (*continued*)

Parameter	Patients, n (%)	Without recovery, n (%)	With recovery, n (%)	P value
Hyperlipidemia				0.222
No	347 (97.47)	124 (96.12)	223 (98.24)	
Yes	9 (2.53)	5 (3.88)	4 (1.76)	
Tobacco				0.358
No	346 (97.19)	124 (96.12)	222 (97.80)	
Yes	10 (2.81)	5 (3.88)	5 (2.20)	
Audiogram curve				<0.001
Ascending	145 (40.730)	16 (12.403)	129 (56.828)	
Descending	53 (14.888)	31 (24.031)	22 (9.692)	
Flat	119 (33.427)	72 (55.814)	47 (20.705)	
Irregular	39 (10.955)	10 (7.752)	29 (12.775)	
Degree of hearing loss				<0.001
Mild	95 (26.69)	13 (10.08)	82 (36.12)	
Moderate	140 (39.33)	36 (27.91)	104 (45.81)	
Severe	61 (17.13)	28 (21.71)	33 (14.54)	
Profound	60 (16.85)	52 (40.31)	8 (3.52)	
Time to initial treatment (days)				<0.001
≤3	167 (46.91)	53 (41.09)	114 (50.22)	
4–7	123 (34.55)	37 (28.68)	86 (37.89)	
8–14	43 (12.08)	24 (18.60)	19 (8.37)	
>14	23 (6.46)	15 (11.63)	8 (3.52)	

BMI, body mass index.

recovery of SSNHL patients: age, hearing loss degree, audiogram curve, and time to initial treatment (*Table 2*).

Development and validation of a nomogram for predicting the hearing prognosis of SSNHL patients

The above-mentioned 4 predictors were subsequently used to construct a nomogram that could predict the hearing prognosis of patients (*Figure 1*). To estimate the recovery rate of SSNHL patients, the observed value of each predictor was assigned certain points by drawing a vertical line toward the top points scale. Individual patients' hearing prognostic assessment is calculated by summing the points for each prognostic factor.

Next, the total points of the nomogram were divided into 4 groups by quartiles. The patients of SSNHL recovery rates increased with the total points, and patients in quartile 4 (total points: 261.12–309.35) showed a higher hearing recovery rate than those in the lower quartiles (OR: 66.267, 95% CI: 25.46–210.599) (*Figure 2*).

Finally, the accuracy of the nomogram through internal validation. Receiver operating characteristic (ROC) curve analysis, with an AUC of 0.867 (95% CI: 0.827–0.906), indicating a good diagnostic performance (*Figure 3A*). Additionally, the internal bootstrap validation calibration curve demonstrated that the nomogram-predicted probabilities matched the clinical outcomes well (*Figure 3B*), and the decision curve showed that the model had potential

Table 2 Clinical risk factors for the prognosis of patients with SSNHL

Variables	Univariable logistic regression		Multivariable logistic regression	
	OR (95% CI)	P value	OR (95% CI)	P value
Age (per 20 years)	0.341 (0.240, 0.483)	<0.001	0.479 (0.301, 0.748)	<0.001
Sex				
Male	Reference			
Female	1.625 (1.049, 2.518)	0.03		
Marital				
Married	Reference			
No married	3.016 (1.660, 5.479)	<0.001		
Other	0.946 (0.208, 4.312)	0.943		
BMI (kg/m^2)				
≤23	Reference			
24–27	0.577 (0.364, 0.914)	0.019		
≥28	0.794 (0.299, 2.104)	0.643		
Vertigo				
No	Reference			
Yes	0.328 (0.183, 0.589)	<0.001		
Tinnitus				
No	Reference			
Yes	1.091 (0.628, 1.894)	0.758		
Ear fullness				
No	Reference			
Yes	1.287 (0.833, 1.990)	0.255		
Side				
Left	Reference			
Right	0.886 (0.575, 1.366)	0.583		
Hypertension				
No	Reference			
Yes	0.497 (0.213, 1.160)	0.106		
Dm				
No	Reference			
Yes	0.233 (0.059, 0.919)	0.037		
Hyperlipidemia				
No	Reference			
Yes	0.445 (0.117, 1.687)	0.234		

Table 2 (*continued*)

Table 2 (*continued*)

Variables	Univariable logistic regression		Multivariable logistic regression	
	OR (95% CI)	P value	OR (95% CI)	P value
Tobacco				
No	Reference			
Yes	0.559 (0.159, 1.967)	0.365		
Audiogram curve				
Ascending	Reference		Reference	
Descending	0.088 (0.041, 0.187)	<0.001	0.116 (0.047, 0.275)	<0.001
Flat	0.081 (0.043, 0.153)	<0.001	0.397 (0.159, 0.979)	0.045
Irregular	0.360 (0.148, 0.873)	0.024	0.478 (0.183, 1.293)	0.136
Degree of hearing loss				
Mild	Reference		Reference	
Moderate	0.458 (0.228, 0.920)	0.028	0.825 (0.36, 1.842)	0.642
Severe	0.187 (0.086, 0.404)	<0.001	0.484 (0.185, 1.241)	0.133
Profound	0.024 (0.009, 0.063)	<0.001	0.047 (0.013, 0.152)	<0.001
Time to initial treatment (days)				
≤3	Reference		Reference	
4–7	1.081 (0.652, 1.790)	0.763	0.561 (0.284, 1.088)	0.09
8–14	0.368 (0.186, 0.730)	0.004	0.311 (0.127 ,0.746)	0.009
>14	0.248 (0.099, 0.621)	0.003	0.131 (0.039, 0.413)	0.001

SSNHL, sudden sensorineural hearing loss; OR, odds ratio; CI, confidence interval; BMI, body mass index.

clinical application (*Figure 3C*).

Discussion

Based on the clinical characteristics of patients with SSNHL, this study found that age, descending and flat audiogram curves, profound hearing loss, and initiating treatment after 8 days of SSNHL onset were independent predictors of a poor prognosis in SSNHL patients. Perez Ferreira Neto *et al.* report that an interval of >2 weeks from SSNHL onset to treatment was an independent risk factor for the prognosis of SSNHL (6). The difference between the findings of Perez Ferreira Neto *et al.* and the present study could be attributed to the small sample size, the concentrated age of the patients, and the different data stratification approach adopted in the study of Perez Ferreira Neto *et al.*

SSNHL inevitably affects individuals of all ages, and the pathogenesis differs for different age groups (16). In 1977, a negative correlation was reported between age and prognosis in elderly patients (17), which is consistent with the prediction model results of the present study. With aging, the degeneration of the auditory system becomes severe, and the susceptibility of individuals to various injuries increases and the repairability and compensation ability of individuals decreases. Thus, aging is an adverse factor for the prognosis of SSNHL patients. However, age segmentation studies have shown that individuals aged >40 years who experience sudden deafness have a better prognosis than those aged <40 years (16), and age is a protective factor for sudden deafness in children and adolescents (18). However, this phenomenon was not observed in the current study. This difference in prognoses could be attributed to the inclusion criteria, insufficient segmentation, and inconsistent prognostic evaluation criteria between the various studies.

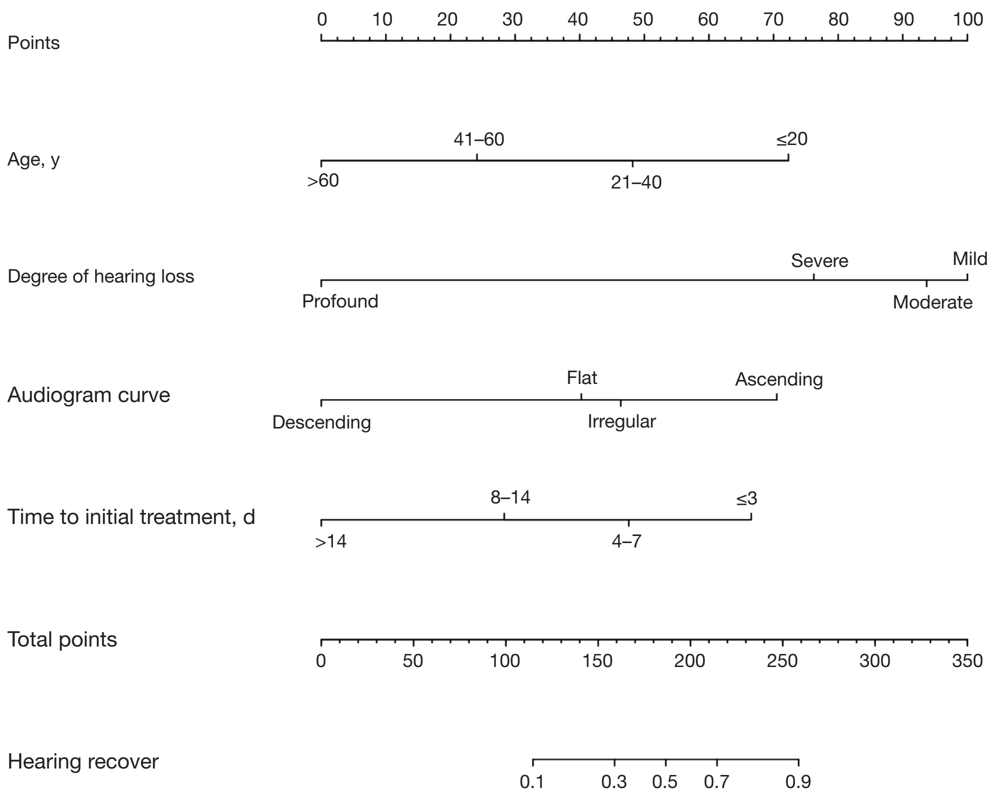

Figure 1 Nomogram for predicting the hearing recovery rate of SSNHL. The value of each variable was scored on a scale of 0 to 100, followed by the addition of the score for each variable. SSNHL, sudden sensorineural hearing loss.

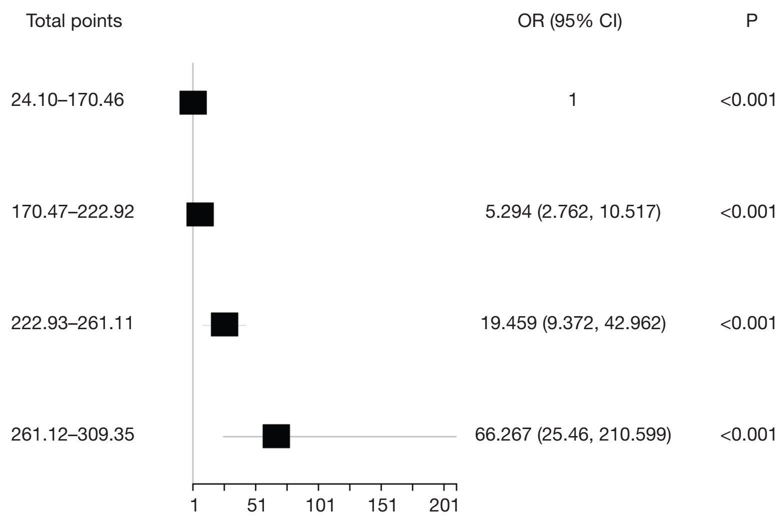

Figure 2 Association between the total points of the nomogram and the hearing recovery rate. OR, odds ratio; CI, confidence interval.

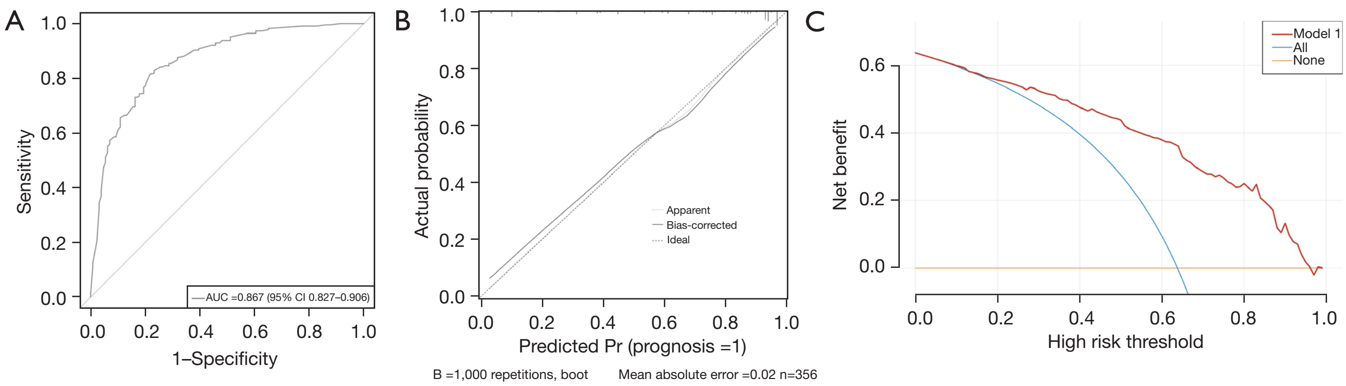

Figure 3 Evaluation of the nomogram model. (A) Receiver operating characteristic curve. (B) Nomogram calibration plot using bootstrap re-sampling (1,000 times), the solid line represents the performance of nomogram. (C) Decision curve analysis for the prediction model. Red line: Prediction model. Blue line: Assume all patients have hearing recovery. Orange line: Assume no patients have hearing recovery. AUC, area under the receiver operating characteristic curve; CI, confidence interval.

Further, the present study showed that the prognosis of different types of SSNHL varies, and that patients with the descending type of SSNHL had the worst prognosis and those with the ascending type of SSNHL had the best prognosis. This is consistent with the findings of previous studies (19,20). Different audiogram curves of SSNHL can have different pathogeneses. The susceptibility of hair cells at the bottom of the cochlea is different to that at the top, such that the hair cells at the bottom of the cochlea are sensitive to ototoxic drugs and hypoxia (21,22). Thus, high frequencies can easily cause damage, and the effects of treatments are poor. A possible mechanism by which ascending hearing loss occurs is membranous labyrinthine hydrops (23). Noguchi *et al.* (24) conjectured that low-frequency hearing loss is similar to the electrophysiological performance of Meniere's disease, and that hormones significantly reduce tissue edema and thus ensure satisfactory treatment efficacy.

The flat audiogram curve was also found to be a factor affecting hearing prognosis. Reports on the prognosis of patients with the flat type audiogram curve was vary (25-27), which could be attributed to the differing typing modes and treatment schemes used. Notably, the flat type also includes the total deafness type, whereby total deafness decreases hearing in all frequencies with a severe degree of decline.

Additionally, the presence of profound hearing loss and the treatment initiation time delay are clinically recognized prognostic factors of SSNHL, which have been confirmed in a number of studies (6,27,28). Compared with previous studies, we developed an easy-to-use nomogram based on clinical characteristics that could aid in decision making and patient prognosis. A recent study constructed a nomogram to predict the prognosis of SSNHL patients (29); however, it did not include the variable of the initial degree of hearing loss. The blood related parameters included in the aforementioned nomogram make it clinically complex. Additionally, a laboratory examination of patients with SSNHL is not recommended under the new guidelines (1). Conversely, the nomogram developed in this study includes easily accessible clinical information, and thus it is clinically simple to use and provides a more accurate prediction (AUC: 0.867, 95% CI: 0.827–0.906) than previously reported nomograms (concordance index: 0.798, 95% CI: 0.750–0.845). Moreover, the clinical decision curve analysis showed that the nomogram model had clinical applications; thus, this prognosis evaluation model could gain wide acceptance.

It is important to acknowledge the limitations of this model. Firstly, the nomogram was developed using retrospective data from single-center in-patient departments, thus, it lacks outpatient data and our ability to draw any causal inferences is limited. Secondly, we did not have independent external hospital data set, the nomogram did not have external validation sample for the prognosis prediction model. Further, our results and conclusions require validation using strictly designed prospective cohort studies. Thirdly, further efforts should be made to identify novel predictors for SSNHL; for example, genomics data could be used to improve prediction performance. Fourth, due to the uncertainty of the etiology of SSNHL, at present, there are no completely unified treatment standards. Notably, the effects of hyperbaric oxygen treatment are uncertain. In this study, hyperbaric oxygen treatment was considered a salvage treatment. Thus, the nomogram can only be used to assess the prognosis of SSNHL in general population.

Conclusions

Age, audiogram curves, hearing loss degree and time of onset were found to be independent predictors of hearing recovery prognosis of SSNHL patients. We developed a useful nomogram that could be included in the standardized evaluation of individual hearing prognosis of a SSNHL patient. However, further large-scale researches are needed to validate present results.

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Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-5647/rc

Data Sharing Statement: Available at https://atm.amegroups.com/article/view/10.21037/atm-22-5647/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-5647/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work, including ensuring that any questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics board of Shenzhen Hospital, Southern Medical University (No. NYSZYYEC20210042). Due to the retrospective nature of the study, the requirement to obtain signed informed consent from the patients was waived.

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